Análisis sistemático de las diferentes estrategias de tratamiento en la práctica clínica habitual e impacto de la instauración de protocolos de actuación para el tratamiento de la Fibrilación Auricular

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El Dr. **Lluís Mont Girbau**, Consultor Senior y Jefe de Sección de la Unidad de Arritmias del Servicio de Cardiología del Hospital Clínic de Barcelona,

CERTIFICA: Que **Naiara Calvo Galiano**, Licenciada en Medicina y Cirugía, ha realizado bajo su dirección la tesis titulada "**Análisis sistemático de las diferentes estrategias de tratamiento en la práctica clínica habitual e impacto de la instauración de protocolos de actuación para el tratamiento de la Fibrilación Auricular**" para optar al grado de Doctora en Medicina de la Universidad de Barcelona y que esta tesis cumple todos los requisitos necesarios para ser defendida en el Tribunal de Evaluación correspondiente.

Barcelona, Febrero del 2013

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Eskerrik asko!!!

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ABREVIATURAS

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AC: ablación percutánea

AI: aurícula izquierda

ACV: accidente cerebrovascular

CVE: cardioversión eléctrica

ETE: ecocardiografía transesofágica

FA: fibrilación auricular

FAA: fármacos antiarrítmicos

FEVI: fracción de eyección del ventrículo izquierdo

HTA: hipertensión arterial

HNF: heparina no fraccionada

IC: insuficiencia cardíaca

IECA: inhibidores del enzima de conversión de la angiotensina

RM: resonancia magnética

RS: ritmo sinusal

TAC: tomografía axial computarizada

VVPP: venas pulmonares

INTRODUCCIÓN

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1. Epidemiología de la Fibrilación Auricular

La fibrilación auricular (FA) es la arritmia sostenida más frecuente en la práctica clínica y es responsable de una elevada morbilidad y mortalidad y de un incremento del coste sanitario. Sus principales consecuencias directas son un aumento del riesgo de accidentes cerebrovasculares (ACV), insuficiencia cardíaca (IC), un incremento de la necesidad de hospitalización y de la prolongación de la estancia hospitalaria, así como una disminución de la calidad de vida y un deterioro de la función cognitiva (1,2).

La incidencia de FA se incrementa con la edad por lo que, dado el envejecimiento progresivo de la población, tanto su prevalencia como los ingresos hospitalarios debidos a esta arritmia han aumentado de forma significativa en los últimos años. Así, en el año 2000 el número de ingresos hospitalarios casi se triplicó con respecto a las 2 décadas previas (3) y se estima que un 10% de la población desarrollará FA a partir de los 75 años. Dado el previsible aumento de la prevalencia en los próximos años, esta entidad ha sido a menudo definida como la "nueva epidemia" del futuro.

2. Fisiopatología y etiología de la FA

La FA se puede presentar de forma paroxística, persistente o permanente. La forma paroxística se define como la FA que termina espontáneamente o tiene una duración inferior a 7 días. La FA persistente es aquella que dura más de 7 días o precisa de la cardioversión, ya sea farmacológica o eléctrica, para su terminación. Por último, la FA

permanente se define como aquella en la que la restauración a ritmo sinusal (RS) no es posible o se ha desestimado.

La FA normalmente implica la existencia de un foco con actividad focal rápida o un foco de reentrada a nivel de la unión del músculo cardíaco auricular y de las venas pulmonares (VVPP) (4). Se considera que en muchos casos la historia natural de la FA, en concreto de su evolución de las formas paroxísticas a las persistentes, es debida al remodelado auricular ocasionado por la propia arritmia o a la progresión de la enfermedad subyacente (5,6).

Hasta en un 90% de los casos, la FA paroxística se desencadena en focos localizados a nivel de las VVPP y responde bien a su aislamiento eléctrico. Sin embargo, a medida que la FA progresa, el sustrato auricular se vuelve más complejo, con un mayor grado de remodelado auricular, fibrosis y desestructuración de la estructura miocárdica auricular que se extiende más allá de las VVPP. Por este motivo, en estos casos el simple aislamiento eléctrico de las VVPP ofrece resultados más pobres y a menudo son necesarios procedimientos de ablación más extensos y complejos.

2.1. Factores de riesgo clásicos

Existen unos factores de riesgo de FA clásicos, bien definidos, cuyo control se asocia con una reducción del riesgo de FA. Sin embargo, a pesar de la puesta en marcha de estrategias dirigidas al control de estos factores de riesgo, la incidencia de FA continúa incrementándose en los países desarrollados, lo que pone de manifiesto la existencia de otros factores de riesgo menos reconocidos.

Hipertensión arterial

La hipertensión arterial (HTA) es el principal factor de riesgo para el desarrollo de FA (7). La HTA provoca una serie de cambios estructurales y funcionales en los cardiomiocitos, fibroblastos y células musculares lisas que con el paso del tiempo aumentan el grado de fibrosis e hipertrofia de las cámaras cardíacas y de la capa media arterial. Este último fenómeno condiciona una situación de isquemia relativa que a su vez favorece la aparición de arritmias. Así mismo, la hipertrofia ventricular izquierda aumenta el estrés parietal y produce activación del sistema nervioso simpático, lo que conlleva un incremento del automatismo y anisotropía, responsables también del desarrollo y mantenimiento de FA. El estudio de Framingham (8) demostró la importancia de la HTA sistólica en el desarrollo de FA. Más recientemente, Mitchell y col. (9) evaluaron la importancia de las cifras de presión arterial diastólica en el desarrollo de FA, sugiriendo que la presión de pulso, definida como la diferencia entre la presión arterial sistólica y la presión arterial diastólica, podría contribuir al desarrollo de FA de forma más significativa que la HTA sistólica aislada.

Insuficiencia cardíaca y cardiopatía estructural

La insuficiencia cardíaca, incluso en pacientes con fracción de eyección del ventrículo izquierdo (FEVI) conservada, contribuye al desarrollo de FA como consecuencia de la sobrecarga de presión y volumen auricular, así como de la disfunción ventricular diastólica. Todo ello conduce a la aparición de fibrosis, dilatación auricular y remodelado eléctrico auricular, substratos idóneos para la aparición, desarrollo y perpetuación de FA (10).

Edad

Como hemos comentado previamente, la prevalencia de FA se incrementa con la edad (11). En el estudio de Framingham, la prevalencia de FA era del 2% en personas de 60-69 años, del 5% en personas de edad comprendida entre 70-79 años y del 9% en el grupo de edad de 80 a 89 años (8).

Sexo masculino

El riesgo de FA es mayor en varones respecto a mujeres (8), aunque la razón de esta predisposición por el sexo masculino se desconoce.

Diabetes Mellitus e Hipertiroidismo

Factores metabólicos como la diabetes mellitus o el hipertiroidismo se han asociado con un incremento del riesgo de FA.

2.2. FA idiopática

Existe un tipo de FA, denominada FA idiopática o aislada, que es aquella que se presenta en menores de 60 años, en ausencia de HTA, cardiopatía estructural o cualquier otra causa definida de FA. La FA idiopática representa entre el 2 y el 30% de las consultas a los servicios de urgencias (12). Este tipo de entidad se presenta a menudo en pacientes con alguno de los denominados "nuevos factores de riesgo", como son la obesidad, la estatura alta, el síndrome de apnea obstructiva del sueño, el tabaquismo, la enfermedad pulmonar obstructiva crónica o la práctica de deporte de resistencia de intensidad elevada. En los últimos años, estos factores han demostrado un papel etiopatogénico en la aparición de FA, poniendo así en duda el término de "FA idiopática".

3. Procedimientos terapéuticos

El tratamiento de la FA tiene como objetivo evitar las complicaciones asociadas a la FA y lograr el control de los síntomas.

La prevención de las complicaciones asociadas a la FA se basa en evitar los fenómenos tromboembólicos, en controlar la frecuencia cardíaca y en la detección y tratamiento de las enfermedades asociadas. La reducción de los síntomas se consigue mediante el control de la frecuencia cardíaca, aunque en ocasiones se precisa además del control del ritmo cardíaco.

El estudio PIAF fue el primero en demostrar que el beneficio del control de la frecuencia cardíaca era comparable con una estrategia de control de ritmo mediante fármacos o cardioversión eléctrica (CVE) (13). Los estudios RACE y AFFIRM confirmaron estos hallazgos sugiriendo que ambas estrategias eran equivalentes en términos de mortalidad y morbilidad. Sin embargo, estos estudios no analizaron el efecto de los fármacos antiarrítmicos (FAA) y los análisis *posthoc* y *adhoc* de estos estudios demostraron que el RS se asociaba con un incremento del 47% en la supervivencia en comparación con la FA (HR 0,53) y que el uso de los FAA aumentaba la mortalidad en un 49% (HR 1,49). Por lo tanto, el beneficio del mantenimiento del RS parece estar lastrado por los efectos secundarios de los fármacos antiarrítmicos (14-18).
En los últimos años, la ablación percutánea de la FA (AC) se ha establecido como un tratamiento seguro y eficaz para restaurar el RS y obviar la necesidad de terapia con FAA en pacientes con FA, además de demostrar su superioridad comparada con los FAA en términos de disminución de los episodios de arritmia. Sin embargo, hasta la fecha se desconoce si el mantenimiento del RS mediante la AC es capaz de incrementar la supervivencia.

Por último, se han descrito una serie de factores predictores de mala respuesta a la AC de FA. En este grupo de pacientes, la ablación quirúrgica de la FA mediante técnicas mínimamente invasivas se ha propuesto como una alternativa eficaz.

3.1. Tratamiento farmacológico

De acuerdo con las últimas guías de práctica clínica para el manejo de pacientes con FA sintomática recurrente, los FAA constituyen la primera línea de tratamiento, siendo la AC una opción de segunda línea (salvo en casos muy seleccionados) (Figura 1) (19).

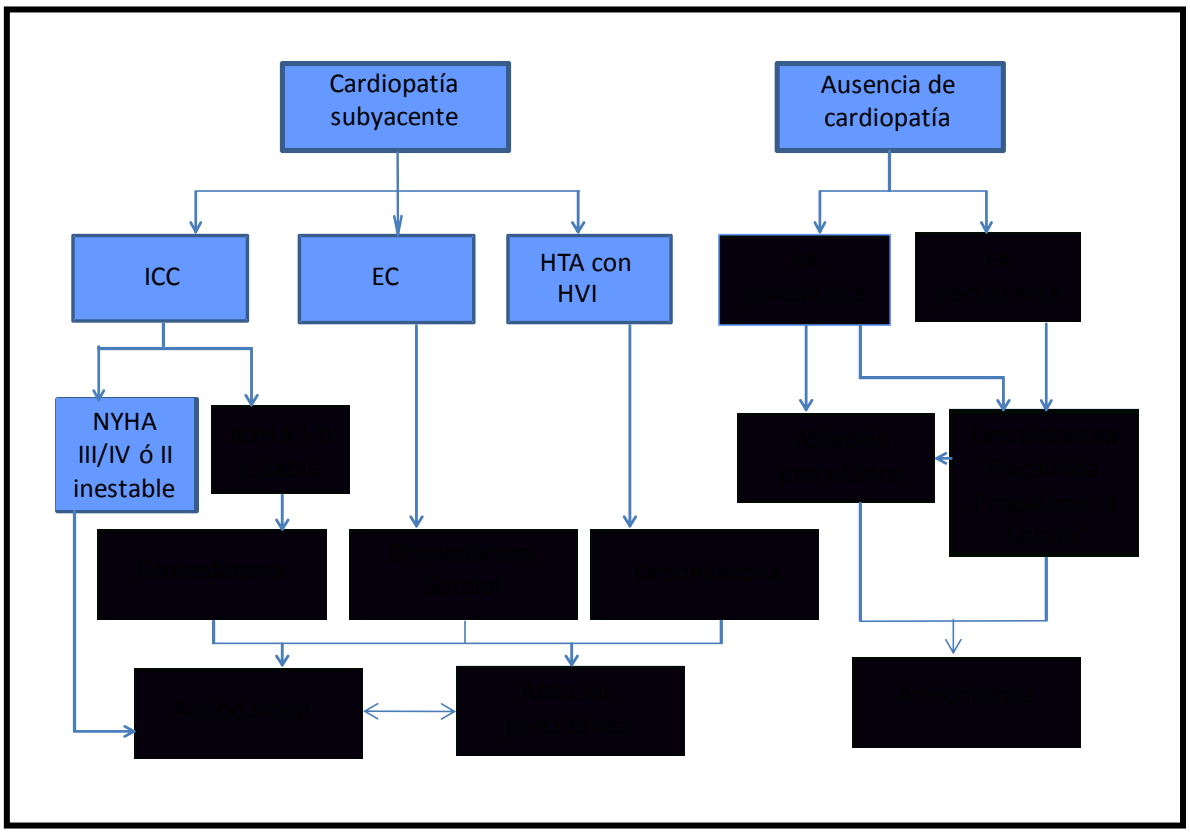

Figura 1. Estrategias para el tratamiento de la FA. FA: fibrilación auricular; HTA: hipertensión; HVI: hipertrofia ventricular izquierda; ICC: insuficiencia cardiaca congestiva; NYHA: clase funcional según la New York Heart Association.

3.1.1. Control del ritmo cardíaco

La recurrencia de la FA oscila entre el 71 al 84%, disminuyendo hasta el 44-67% bajo tratamiento antiarrítmico.

Los principales agentes antiarrítmicos para el control del ritmo son amiodarona, sotalol, ibutilide, flecainida, propafenona y, más recientemente, la dronedarona.

La elección del fármaco antiarrítmico depende en gran medida de la presencia o no de cardiopatía estructural o de insuficiencia cardíaca (figura 2).

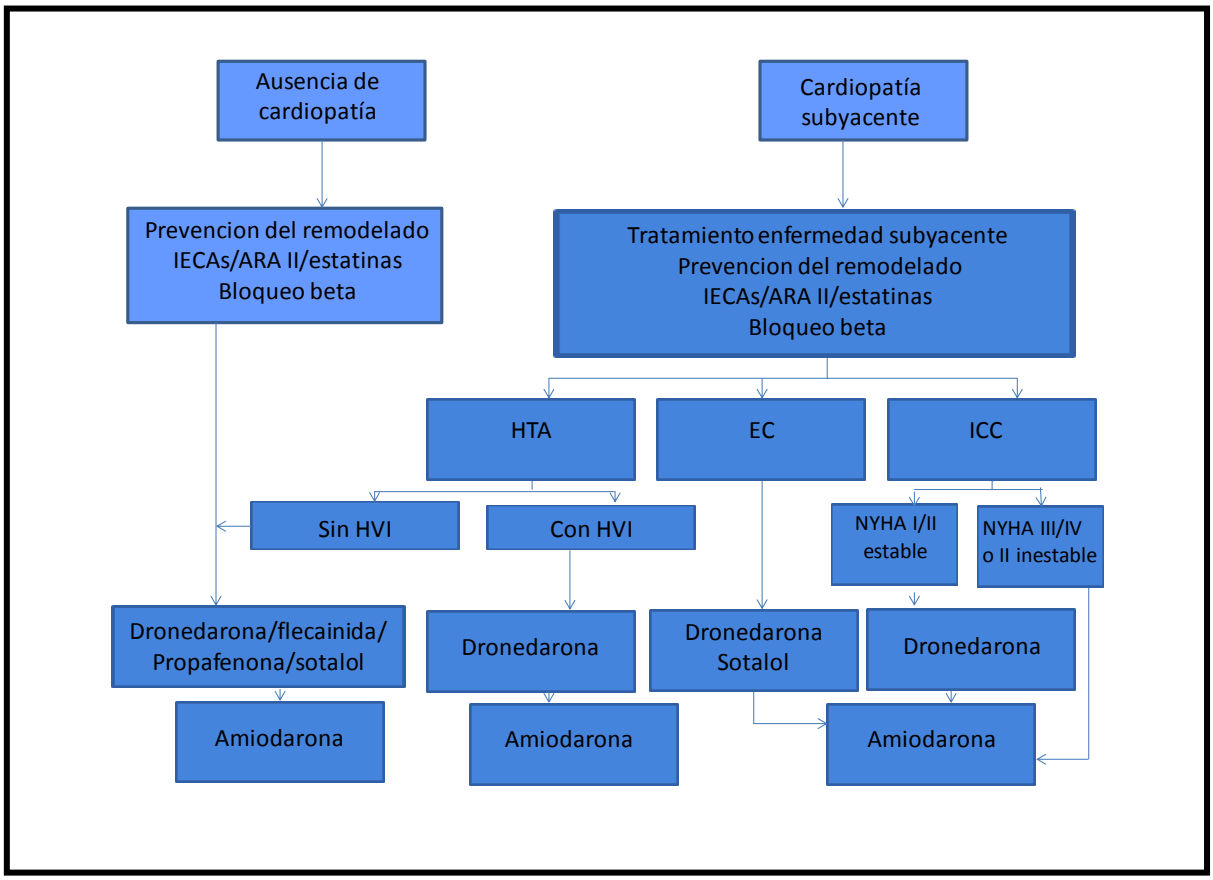

Figura 2. Elección del tratamiento antiarrítmico en función de la presencia o no de cardiopatía subyacente. ARA-II: antagonista del receptor de la angiotensina II; EC: enfermedad coronaria; HT: hipertensión; HVI: hipertrofia ventricular izquierda; ICC: insuficiencia cardiaca congestiva; IECA: inhibidor de la enzima de conversión de la angiotensina; inestable: descompensación cardiaca dentro de las 4 semanas previas; NYHA: clase funcional de la New York Heart Association.

La amiodarona, fármaco antiarrítmico de clase III, ha demostrado su eficacia y seguridad en numerosos estudios. Una revisión de 44 trabajos que incluyeron un total de 11322 pacientes con FA, demostró que, tras un seguimiento de 6 meses, el porcentaje de recurrencia de FA era significativamente menor bajo tratamiento con amiodarona en comparación con fármacos antiarrítmicos de clase I y sotalol (20). A pesar de que la amiodarona es considerada el fármaco más eficaz en la actualidad, su empleo se ve a menudo limitado por los efectos adversos extracardíacos, que condicionan un riesgo de abandono de la medicación casi 2 veces superior al de otros fármacos (21).

Los fármacos de la clase Ic, flecainida y propafenona, son eficaces y seguros para el mantenimiento del RS en pacientes sin cardiopatía estructural.

El sotalol es el fármaco de primera elección en pacientes con enfermedad coronaria, pero debe ser evitado en pacientes con hipertrofia ventricular izquierda significativa, insuficiencia cardíaca, y síndrome de QT largo congénito o adquirido por su elevado riesgo de proarritmia en esas condiciones.

La dronedarona es un fármaco de reciente comercialización que goza de propiedades electrofisiológicas similares a la amiodarona pero con menos efectos adversos extracardíacos, especialmente los derivados del metabolismo tiroideo. Sin embargo, a pesar de que los primeros estudios obtuvieron resultados muy prometedores, en la actualidad su uso está contraindicado en pacientes con insuficiencia cardíaca descompensada y disfunción ventricular severa, ya que en grupo de pacientes se ha demostrado un aumento de la mortalidad (22).

Nuevos fármacos antiarrítmicos como vernakalant, ranolazina y tedisamil están actualmente en investigación con el objetivo de mejorar la eficacia y seguridad farmacológica en el enfoque del control del ritmo cardíaco (23).

3.1.2. Tratamiento de la enfermedad subyacente

Más de la mitad de los casos de FA pueden explicarse, al menos parcialmente, por la presencia de factores de riesgo como HTA o la diabetes mellitus, por lo que el diagnóstico y tratamiento de las enfermedades subyacentes puede contribuir a la prevención de dicha arritmia.

3.1.3. Terapias selectivas de la aurícula izquierda

Una de las principales limitaciones del tratamiento para el control del ritmo es el riesgo de proarritmia ventricular. Con el fin de reducir este riesgo, actualmente están en investigación diversos fármacos cuyo mecanismo de acción se centra específicamente a nivel del miocardio auricular. Así, los fármacos dirigidos selectivamente a los canales iónicos principalmente expresados en las aurículas, como el IKur y IKACh o el bloqueo de los canales de Na^+ mediante fármacos de reciente desarrollo como son el vernakalant o la ranolazina (24), constituyen nuevas estrategias de tratamiento diana para el control del ritmo cardíaco.

3.1.4. Terapias dirigidas a la actividad focal

Estudios recientes se centran en el mecanismo de la despolarización tardía como desencadenante de los latidos ectópicos que dan origen a la FA. En este sentido, se están desarrollando nuevos abordajes dirigidos a la estabilización de los canales de RyR2 y a prevenir la fuga diastólica de calcio a través de la actividad de la Ca^2-calmodulina quinasa-II (25).

3.1.5. Prevención del remodelado auricular

Existe un segundo grupo de fármacos para el tratamiento de la FA, que son los conocidos como tratamientos "causales" de la FA (*upstream therapy*), y que tienen como objetivo prevenir o retrasar el remodelado miocárdico asociado a hipertensión, insuficiencia cardiaca o inflamación (p. ej., tras cirugía cardiaca), para así evitar el desarrollo de FA (prevención primaria),o bien, una vez establecida, disminuir su tasa de recurrencia o progresión hacia formas permanentes (prevención secundaria) (26).

Entre estos fármacos se incluyen los agentes inhibidores de la enzima angiotensina (IECA), los bloqueantes del receptor de angiotensina y las estatinas. El análisis del papel beneficioso de estos fármacos en la reducción de la incidencia de la FA en cardiopatía estructural y de la FA recurrente en pacientes después de la CVE ofrece resultados contradictorios (27). Sin embargo, basándonos en la evidencia actual, no parecen reducirse las complicaciones de la FA. Esteroides, ácidos grasos ω-3, espironolactona y pirfenidona son también fármacos destinados a evitar el desarrollo o bien la recurrencia de la FA, aunque carecen de un papel demostrado en la prevención de la remodelación del sustrato auricular y la fibrosis (28).

3.1.6. Control de la frecuencia cardíaca

Una frecuencia cardíaca excesivamente elevada puede empeorar los síntomas del paciente, además de contribuir al desarrollo de taquicardiomiopatía.

El estudio RACE II comparó los efectos sobre la morbilidad y mortalidad cardiovascular entre una estrategia de control de frecuencia cardíaca estricto (frecuencia cardíaca en reposo < 80lpm y <110lpm durante el ejercicio moderado) frente a un control menos riguroso (frecuencia cardíaca en reposo <110lpm). Tras 3 años de seguimiento, el control menos riguroso no fue inferior al control estricto ni en la

prevención de eventos cardiovasculares mayores ni en la tasa de mortalidad (29). A la vista de estos resultados, las guías clínicas recomiendan un control de la frecuencia cardíaca no riguroso en pacientes con función ventricular preservada.

3.2. Cardioversión eléctrica

La cardioversión eléctrica (CVE) es una estrategia destinada al control de la frecuencia cardíaca y está indicada en la fase aguda en pacientes con inestabilidad hemodinámica (indicación I, nivel de evidencia C) o en aquéllos con intolerancia a fármacos (indicación IIb, nivel de evidencia C), así como en el tratamiento electivo para el manejo de control del ritmo a largo plazo en pacientes con FA (indicación IIa, nivel de evidencia B). Se recomienda el pretratamiento con amiodarona, flecainida, propafenona, ibutilida o sotalol para aumentar el éxito de la cardioversión eléctrica y prevenir la recurrencia de FA.

3.3. Ablación percutánea de la FA

La AC de la FA se ha establecido como una estrategia segura y eficaz para el tratamiento de la FA. A lo largo de los años, se han ido estableciendo diferentes modalidades de tratamiento. Así, Haissaguerre y col. (30) y Chen y col. (31) demostraron que la FA tiene su origen en latidos prematuros procedentes de las VVPP y que la AC de la FA a este nivel era eficaz para la prevención de los episodios. De este modo, el primer abordaje en el tratamiento de la FA consistió en localizar y ablacionar el foco desencadenante de la FA en la VP correspondiente. Sin embargo, no solamente el detectar el foco de origen de la FA a menudo resulta difícil cuando la extrasístole auricular es infrecuente, sino que también la FA puede ser desencadenada por

extrasístoles de diferente origen, tanto en la AI como en la AD. Ello llevó a desarrollar nuevos enfoques que consistían en aislar eléctricamente las VVPP de la aurícula izquierda (AI) (32) mediante el aislamiento segmentario de las VVPP (33), la ablación circunferencial extensa (34), la ablación lineal de la AI (35), la ablación de electrogramas auriculares complejos fragmentados (CAFEs) (36) o la ablación de los plexos ganglionares (37).

No hemos de olvidar que la ablación de FA es un procedimiento complejo, que debiera ser realizado por médicos expertos, tras una cuidadosa evaluación de los riesgos y beneficios de cada paciente, y que resulta de vital importancia identificar aquellos pacientes en los que la tasa de éxito del procedimiento es inferior a la media.

3.3.1. Electrofisiología de las venas pulmonares

En la década de 1960 se describieron las propiedades de conducción eléctrica de las VVPP y sus uniones con la AI (38). Más tarde, se descubrió que el automatismo anormal o la actividad desencadenada a nivel de las VVPP pueden resultar en el desarrollo de FA o contribuir a su mantenimiento. Otros estudios pusieron de manifiesto que las VVPP, la pared posterior de la AI (39-41) y la unión a nivel de las VVPP y la AI son también lugares que promueven los circuitos de reentrada responsables del desarrollo de FA (42).

3.3.2. Indicaciones de la ablación por catéter de la FA:

Varios estudios han demostrado que el principal beneficio de la AC de la FA es la mejora en la calidad de vida promovida por la abolición de los síntomas relacionados con la arritmia. Por tanto, y de acuerdo a los documentos de consenso de *HRS/EHRA/ECAS* (43), la principal indicación para la AC de la FA es la presencia de

FA sintomática y refractaria a por lo menos a un fármaco antiarrítmico de la clase I ó III. Sin embargo, existen condiciones especiales en las que la AC puede considerarse como estrategia de primera elección (indicación de clase II). Entre ellas se encuentran los casos de FA paroxística en individuos jóvenes o de los pacientes que rechacen el tratamiento antiarrítmico.

3.3.3. Metodología del procedimiento de AC

A. Evolución de la técnica

La AC ha experimentado una importante evolución a lo largo de los años. El abordaje inicial basado en la búsqueda de los factores desencadenantes responsables del inicio de la FA en las VVPP (30) se vio lastrado por la dificultad en la identificación de estos focos así como por la dificultad en reproducir los hallazgos. Con el objetivo de superar estas limitaciones, Haissaguerre y col. (44) desarrollaron un enfoque de ablación dirigido al aislamiento eléctrico del miocardio de las VVPP. Esta técnica -el aislamiento segmentario de la VP- consistía en la identificación y ablación de los sitios más precoces de activación del miocardio de las VVPP, a nivel del ostium de las VVPP. Posteriormente, Pappone y col. (45,46) introdujeron una técnica basada en el aislamiento circunferencial de las VVPP mediante radiofrecuencia guiada por un sistema de navegación electroanatómico. Sin embargo, la experiencia reveló que a menudo los sitios de inicio o mantenimiento de la FA se ubicaban en el antro de las VVPP, lo que, junto con el reconocimiento de la estenosis de VVPP como una complicación de la aplicación de radiofrecuencia (RF) en el interior de la vena pulmonar, provocó un cambio en la estrategia de ablación dirigida al aislamiento de las VVPP a nivel antral. La ablación a este nivel se realizaba bien de forma segmentaria y guiada por un catéter de mapeo circular (44,47) posicionado cerca del ostium (ablación

segmentaria de las VVPP) (45); o bien mediante lesiones de ablación circunferenciales continuas más amplias alrededor de las VVPP ipsilaterales (ablación circunferencial amplia o WACA) (45,46,48). Los estudios que han comparado la eficacia de ambos procedimientos ofrecen resultados contradictorios (49,50) aunque en un estudio randomizado se ha demostrado que el aislamiento circunferencial amplio con verificación de bloqueo de la conducción es un tratamiento más eficaz que el aislamiento segmentario (51). Además, en un estudio aleatorizado reciente, se ha demostrado que con el empleo de un catéter circular para guiar y confirmar el bloqueo de las VVPP se obtienen mejores resultados que con la confirmación del aislamiento de las VVPP basándose únicamente en la reducción de los potenciales registrados por el catéter de mapeo (52).

El objetivo primario del procedimiento de ablación es la reducción de la amplitud de los potenciales dentro de las VVPP (46,53), la eliminación (o disociación) de los potenciales de VVPP registrados por los catéteres circulares dentro de las VVPP ipsilaterales (49,50,54-56), y el bloqueo de salida de las VVPP (57).

B. Tecnología y herramientas para el procedimiento de ablación

B.1. Herramientas pre-procedimiento

El conocimiento previo de la anatomía de la AI puede facilitar el procedimiento de AC gracias a la descripción anatómica de las VVPP y de la AI, ya que permite planificar el tipo de procedimiento a realizar, así como integrar las imágenes obtenidas para guiar la ablación.

- *Ecocardiografía transtorácica*

El estudio ecocardiográfico forma parte de las investigaciones básicas del estudio del paciente con FA y es fundamental para describir la morfología y función del corazón y,

más específicamente, para definir el tamaño de la AI. En este sentido, una de sus principales aplicaciones consiste en caracterizar el tamaño de la AI, definido bien por el diámetro anteroposterior o bien por el volumen auricular, siendo ambos parámetros predictores de éxito de la AC (58-60).

- *Ecocardiografía transesofágica (ETE)*

La ETE es la técnica más sensible y específica para detectar potenciales fuentes y mecanismos cardioembólicos Las guías clínicas y los documentos de consenso recomiendan la realización de ETE previo al procedimiento de ablación en pacientes con FA persistente, AI dilatada y una puntuación en la escala de riesgo CHADS2>2. Sin embargo, existen pocos datos en la literatura acerca de su utilidad en pacientes con perfil de riesgo bajo y su uso varía enormemente de unos centros a otros.

- *Resonancia magnética (RM) y tomografia axial computarizada (TAC) de la AI y de las VVPP*

Ambas técnicas permiten la descripción detallada de la AI, conocer el número, anatomía y distribución de las VVPP, y descartar la presencia de trombos intracavitarios. Asimismo, estudios recientes de Marroux y col. han demostrado que es posible predecir el resultado de la AC mediante radiofrecuencia gracias a la determinación del grado de fibrosis en la AI a través de estudios de RM (61,62). Sin embargo, son necesarios estudios más amplios que reproduzcan los hallazgos de la detección de fibrosis mediante RM y validen la utilidad de la RM para la detección del nivel de fibrosis como predictor de respuesta de la ablación.

B.2. Herramientas intra-procedimiento

- *Fuentes de energía*

Para el procedimiento de ablación de la FA se emplean principalmente 2 fuentes de energía con el fin de obtener lesiones transmurales que consigan el aislamiento eléctrico de las VVPP. La radiofrecuencia, que es la energía más ampliamente empleada, consiste en la aplicación de una corriente eléctrica alterna mediante un catéter transvenoso. Por otro lado, la crioablación consigue el aislamiento de las VVPP mediante las lesiones de congelación obtenidas con un balón que las ocluye totalmente a nivel de sus *ostia.*

- *Nuevas tecnologías*

En los últimos años han surgido diferentes herramientas para facilitar el aislamiento eléctrico de las VVPP: el empleo de sistemas de navegación electroanatómicos, el desarrollo de catéteres con sensores que detectan el grado de contacto entre el catéter y el tejido, la ablación mediante ultrasonidos o láser, y la ablación mediante sistema de navegación robótica, como el sistema de navegación magnético (Stereotaxis^{TM}) (63-65) y el sistema de navegación electromecánico (Sensei^{TM}; Hansen Medical) (66,67). Sin embargo, no existen en la actualidad estudios randomizados que demuestren si estas nuevas tecnologías consiguen una mejora en la eficacia, seguridad o reducción del coste del procedimiento.

- *Técnicas de imagen intraprocedimiento*

La RM, TAC, la angiografía de las VVPP o la ecocardiografía intracardiaca o transesofágica permiten definir en tiempo real la anatomía de la AI y las VVPP y guiar el procedimiento de ablación, además de detectar las complicaciones intraprocedimiento.

3.3.5. Resultados

A la hora de definir la eficacia de la AC de la FA es importante tener en cuenta que existen diferentes aspectos que pueden influir en los resultados publicados en la literatura. Así, los resultados están condicionados por el tipo de FA, la edad del paciente, la presencia de cardiopatía subyacente, de obesidad, de apnea del sueño o del tamaño de la AI, entre otros factores. Otras consideraciones importantes son la duración del período de enfriamiento (*blanking period*), la frecuencia y la intensidad de la monitorización de la arritmia, o el uso de fármacos antiarrítmicos.

Calkins y col. (68) examinaron en una meta-análisis la seguridad y la eficacia de AC de la FA y el tratamiento farmacológico. La tasa de éxito tras un primer procedimiento sin tratamiento antiarrítmico fue del 57% (IC 95%: 50%-64%), tras múltiples procedimientos y sin tratamiento antiarrítmico fue del 71% (IC del 95%: 65%-77%), y la tasa de éxito tras múltiples procedimientos y con tratamiento antiarrítmico fue del 77% (IC 95%: 73%-81%). En comparación, la tasa de éxito del tratamiento farmacológico fue de tan solo de 52% (IC del 95%: 47%-57%).

Recientemente, se han publicado los resultados de una encuesta mundial sobre la seguridad y eficacia de los procedimientos de ablación de FA llevados a cabo entre los años 2003 a 2006 (69). Durante un seguimiento de 10±8 meses, 85 centros participantes comunicaron un total de 192 procedimientos por centro con una tasa de éxito del 70% libre de tratamiento antiarrítmico y una tasa adicional de éxito del 10% en presencia de fármacos antiarrítmicos previamente ineficaces.

El éxito de la ablación de la FA paroxística fue un 35% y un 66% mayor que el éxito de la ablación de FA persistente y de FA persistente de larga evolución, respectivamente. Por otra parte, hemos de tener presente que la mayoría de los procedimientos de ablación de FA publicados en estos estudios fueron realizados en pacientes varones de

raza caucásica, menores de 70 años de edad (70). Por el contrario, son pocos los datos en la literatura acerca de poblaciones especiales, como son los pacientes ancianos, los pacientes deportistas con FA idiopática o los pacientes con IC.

3.3.6. Complicaciones

La AC de la FA es uno de los procedimientos más complejos de la electrofisiología intervencionista, con un porcentaje de complicaciones que se sitúa en torno al 6%. La complicación más frecuente potencialmente letal, a menudo relacionado con la punción transeptal, es el taponamiento cardíaco, con una incidencia de entre el 1,2-6% dependiendo de las series. Otras complicaciones mayores incluyen el embolismo coronario o cerebral, la estenosis de venas pulmonares, las lesiones esofágicas, las complicaciones derivadas del acceso vascular (hematoma, pseudoaneurisma,…), la lesión del nervio frénico, y otras complicaciones muy poco frecuentes, como la ruptura del aparato valvular mitral o las lesiones derivadas de la exposición radiológica. Entre las complicaciones menores destacan la pericarditis y aquéllas relacionadas con el acceso vascular (71).

La curva de aprendizaje de los operadores y la evolución de la metodología y la tecnología ha permitido reducir de forma significativa el porcentaje de complicaciones con los años.

3.4. Ablación quirúrgica de la FA

3.4.1. Desarrollo del procedimiento de Cox-Maze

El procedimiento de Maze fue desarrollado para el tratamiento quirúrgico de la FA en 1987 por el Dr. James Cox (72-74), con el fin de interrumpir todos los circuitos

macroreentrantes responsables del desarrollo de flutter o FA, y así recuperar el RS, la sincronía auriculoventricular y, presumiblemente, reducir la incidencia de ACV (75). El seguimiento a largo plazo de 198 pacientes sometidos al procedimiento de ablación quirúrgica Cox-Maze III demostró que, entre los pacientes sometidos a cirugía aislada para el tratamiento de la FA, 96% recuperaron el RS con o sin fármacos antiarrítmicos y 80% estaban en RS y libres de tratamiento antiarrítmico. Entre los 86 pacientes sometidos a cirugía de FA concomitante con otra cirugía cardíaca, 97,5% estaban en RS con o sin fármacos antiarrítmicos y 73% estaban en RS y libres de terapia con fármacos antiarrítmicos. La incidencia de complicaciones mayores entre los 112 pacientes que sólo se sometieron a cirugía de FA fue del 10,7%. La incidencia de complicaciones mayores entre los 86 pacientes que se sometieron a cirugía conjunta de FA y cardíaca fue de 13,9%. Sin embargo, hemos de tener en cuenta que en esta serie, los pacientes no fueron sometidos a un seguimiento riguroso preestablecido.

3.4.2. Nuevas técnicas de ablación quirúrgica

A pesar de su eficacia, la expansión del procedimiento de Cox-Maze se vio limitada por la complejidad del procedimiento, la dificultad de la técnica y los riesgos de la misma. Con el fin de superar estas limitaciones, diferentes grupos quirúrgicos optaron por sustituir las lesiones clásicas de esta técnica por lesiones lineales de ablación mediante el uso de fuentes de energía unipolar o bipolar (76,77).

3.4.3. Ablación quirúrgica aislada de la FA mediante video-toracoscopia

Aunque la experiencia de la cirugía aislada de la FA se inició hace más de dos décadas, el interés de la técnica se ha renovado en los últimos años, con el desarrollo y evolución de métodos mínimamente invasivos. La mayor serie reportada de cirugía aislada de FA

fue descrita por el Dr. James Cox y corresponde al trabajo que incluyó los 112 pacientes sometidos al procedimiento de Cox-Maze III, descrito previamente (78). De ellos, el 88% estaba libre de tratamiento anticoagulante en el último seguimiento.

Con la introducción de nuevas técnicas en el procedimiento de ablación, como la fuente de energía de radiofrecuencia bipolar y los nuevos sistemas de crioablación, ha resurgido un interés en el desarrollo de procedimientos mínimamente invasivos para el tratamiento quirúrgico aislado de la FA. La intervención quirúrgica consistente en la realización de una esternotomía y de una lesión Cox-Maze biauricular completa se denomina Cox-Maze IV. Esta técnica ha evolucionado hacia estrategias menos invasivas, como son el abordaje a través de una pequeña incisión inframamaria derecha. Los resultados obtenidos con esta nueva intervención quirúrgica son similares a los obtenidos con la técnica de Cox-Maze pero reduciéndose el tiempo de clampaje (79).

La técnica de ablación quirúrgica de la FA mediante cirugía mínimamente invasiva asistida por video-toracoscopia con exclusión de la orejuela izquierda fue descrita por primera vez en 2005 (80). Wolf y col. emplearon una pinza de clampaje bipolar para el aislamiento de las VVPP en corazón latiente en 27 pacientes. Tras un seguimiento mínimo de 3 meses en 23 pacientes, 21 de ellos (91%) estaban en RS, de los cuales 65% se encontraban sin fármacos antiarrítmicos mientras que 4 de ellos sufrieron algún tipo de complicación mayor. Más recientemente, un total de 50 pacientes con FA predominantemente paroxística fueron sometidos al aislamiento de todas las VVPP mediante una fuente de energía epicárdica a través de un abordaje endoscópico (81). Al final del seguimiento el 79.5% de los pacientes se encontraban en RS. Un 25% de los pacientes mantenían el tratamiento con amiodarona, 5% con propafenona y 50% continuaban bajo anticoagulación oral (ACO). El porcentaje de ausencia de recurrencias de FA sintomáticas y re-intervenciones fue del 49%. En la serie se describió una muerte

tardía y hasta un total de 4% de complicaciones mayores, incluyendo la parálisis diafragmática. Edgerton y col. (82) describieron una técnica mínimamente invasiva para el aislamiento de las VVPP que incluía la denervación parcial. Incluyeron un total de 74 pacientes que se sometieron al aislamiento de VVPP bilateral asistido por video-toracoscopia con confirmación del bloqueo y denervación autonómica parcial. A los seis meses de seguimiento, 84% de los pacientes con FA paroxística y el 57% de los pacientes con FA persistente o persistente de larga evolución estaban libres de recurrencia arrítmica. Hubo una muerte, un hemotórax, un caso de insuficiencia renal transitoria y un caso de plexopatía braquial transitoria. Un segundo estudio más amplio de este grupo incluyó 114 pacientes y observó que el 72%, 46,9% y 32% de los pacientes con FA paroxística, persistente, y persistente de larga evolución estaban libres de FA y sin FAA tras un seguimiento de 195 días (83). Un nuevo estudio de aislamiento de VVPP mediante cirugía mínimamente invasiva con ablación de los ganglios autonómicos en 45 pacientes describió un porcentaje libre de recurrencia arrítmica del 65% a los 12 meses de seguimiento. No hubo ninguna muerte, sólo un caso de lesión del nervio frénico, y dos casos de derrame pleural (84).

La principal limitación de este abordaje consiste en la dificultad de completar la línea hasta el anillo mitral. Ello se debe a que la visualización de la pared posterior del anillo mitral está limitada en el corazón latiente, a que existe un riesgo significativo de lesionar la arteria circunfleja y a la poca fiabilidad del seno coronario como referencia epicárdica para la localización del anillo mitral (85). Todo ello conduce a un incremento del riesgo de que la ablación sea incompleta, con la posibilidad de aparición de flutter auricular izquierdo a lo largo del seguimiento (86-88).

Con el fin de hacer frente a estas limitaciones, se introdujo la técnica de la Lesión de Dallas, que incluye la creación de otras líneas accesorias: de las VVPP derechas hacia el

anillo mitral, en el trígono, de las VVPP izquierdas a la orejuela izquierda, y finalmente, una lesión que une el aislamiento bilateral de ambas venas. (89-91). Tras 6 meses de seguimiento en 30 pacientes sometidos a esta nueva técnica quirúrgica (92), 90% de los pacientes con FA persistente y 75% de los pacientes con FA persistente de larga evolución estaban en RS. La terapia con fármacos antiarrítmicos se continuó en el 22% de los pacientes con FA persistente y en el 53% de los pacientes con persistente de larga evolución.

Sin embargo, a la hora de analizar los resultados de la ablación quirúrgica de la FA, hemos de tener en cuenta que no existen hasta la fecha estudios randomizados que comparen el tratamiento quirúrgico con los procedimientos de ablación percutánea de FA.

JUSTIFICACIÓN DEL PROYECTO

JUSTIFICACIÓN DEL PROYECTO

La Fibrilación Auricular es la arritmia clínica más frecuente, y provoca un incremento de la morbilidad y mortalidad cardiovascular, por lo que parece deseable un abordaje temprano dirigido a evitar las complicaciones. A pesar de las recomendaciones actuales, diversos estudios demuestran que hasta el 50% de los casos (93) no reciben un tratamiento correcto. Por todo ello pensamos que es necesario, en primer lugar, un análisis crítico de las estrategias de tratamiento de la FA en los diferentes niveles asistenciales para así identificar los errores más comunes en la práctica habitual del tratamiento de la FA, y, en segundo lugar, establecer un programa de formación en el tratamiento de la FA en los diferentes niveles asistenciales. Todo ello contribuiría a conocer la práctica clínica habitual y a mejorar y unificar los criterios de tratamiento de esta arritmia.

El manejo no invasivo del control del ritmo cardíaco se logra, además de mediante fármacos antiarrítmicos, mediante la cardioversión eléctrica. A lo largo de los años, se han desarrollado nuevos fármacos antiarrítmicos y estrategias intervencionistas para el control del ritmo cardíaco, lo que ha generado modificaciones en las indicaciones del tratamiento dirigido a perseguir el mantenimiento del RS en pacientes con FA. Sin embargo, se desconoce el impacto de las nuevas directrices del tratamiento de la FA en la práctica de CVE. Por ello, resulta de utilidad analizar las características de los pacientes sometidos a CVE en la actualidad y sus indicaciones y eficacia en comparación con los años previos.

Por otra parte, en los últimos años, la ablación percutánea de la FA se ha convertido en un procedimiento cada vez más frecuente en pacientes con FA sintomática y refractaria a tratamiento médico, con un porcentaje de éxito superior al tratamiento farmacológico

antiarrítmico. Sin embargo, existe mucha disparidad en aspectos periprocedimentales y de selección de pacientes que pudieran tener repercusión en los resultados de la ablación.

Las guías clínicas recomiendan excluir la presencia de trombo en la aurícula izquierda (normalmente dentro de la orejuela) para reducir el riesgo de episodios tromboembólicos durante el procedimiento de ablación mediante la realización de una ecocardiografía transesofágica previa al procedimiento de ablación. Sin embargo, se desconoce la verdadera utilidad de este procedimiento diagnóstico en función de la estratificación del riesgo tromboembólico de los pacientes.

Por otro lado, los estudios que analizan la eficacia de la ablación percutánea de la FA proceden de equipos con gran experiencia y de personal que trabaja en instituciones especializadas. Dado que se trata de un procedimiento complejo que pudiera tener complicaciones graves, resulta necesario definir la sistemática de la técnica así como analizar la tasa real de complicaciones, con el fin de poder establecer las directrices que permitan llevar a cabo dicho procedimiento de forma segura y eficaz en los diferentes centros.

Asimismo, la mayoría de los estudios que revelan la superioridad de la ablación frente al tratamiento antiarrítmico incluyen pacientes con los factores de riesgo clásicos para el desarrollo de la FA, como son la HTA, diabetes mellitus, o la presencia de cardiopatía estructural. Sin embargo, son escasos los trabajos que analizan la eficacia de la ablación en grupos de pacientes sin estos factores de riesgo, en los que el mecanismo fisiopatológico de la FA pudiera ser diferente, y, por tanto, el abordaje dirigido al aislamiento eléctrico de las venas pulmonares pudiera no ser eficaz. Es el caso del deporte de resistencia de alta intensidad, que se ha asociado a una mayor incidencia de

FA, y cuyo mecanismo fisiopatológico pudiera ser diferente, lo que hipotéticamente condicionaría un tratamiento distinto al de aquellos pacientes con cardiopatía estructural o HTA.

Por otra parte, diversos estudios clínicos prospectivos y multicéntricos han confirmado la superioridad de la AC en comparación con los fármacos antiarrítmicos. Sin embargo, un importante porcentaje de los pacientes incluidos en los estudios ha requerido más de un procedimiento para conseguir la mejoría clínica. Adicionalmente, se han descrito una serie de factores de mala respuesta al tratamiento de ablación percutánea, como son la dilatación auricular izquierda o la hipertensión arterial. Asimismo, una de las principales limitaciones del tratamiento percutáneo es el riesgo incrementado de arritmias post-ablación como consecuencia de la realización de líneas de ablación incompletas.

En 2006, Wolf y col. describieron la técnica de la ablación quirúrgica de la FA por radiofrecuencia asistida mediante video-toracoscopia. Esta técnica consiste en el aislamiento de las venas pulmonares mediante la aplicación de radiofrecuencia desde un acceso epicárdico, junto con la ablación de los ganglios de la aurícula izquierda y la exclusión de la orejuela izquierda. Se ha descrito un porcentaje de éxito entre el 70-90% y está indicado en pacientes con FA sintomática y refractaria a tratamiento médico, sólo después del fracaso de la ablación percutánea de la FA.

Sin embargo, no existen estudios randomizados que comparen la eficacia de la ablación quirúrgica frente a la ablación percutánea.

Un análisis crítico de los tratamientos empleados en la práctica clínica habitual en los pacientes con FA, así como la evaluación de nuevos enfoques

diagnósticos y terapéuticos podría mejorar el resultado del tratamiento de la FA y disminuir sus complicaciones.

HIPÓTESIS Y OBJETIVOS

HIPÓTESIS DE TRABAJO Y OBJETIVOS

En este proyecto se analizan los resultados de diferentes estrategias de tratamiento de la FA en el ámbito asistencial. Este trabajo se dividió en dos subproyectos, orientados a describir la práctica clínica habitual en el tratamiento de la FA, la eficacia de la instauración de diferentes protocolos terapéuticos, y los resultados y complicaciones de diferentes abordajes terapéuticos.

Para ello, se analizó el manejo de la FA desde todas sus opciones terapéuticas, tanto a nivel no invasivo, como es el abordaje farmacológico y mediante CVE, como a nivel intervencionista, mediante la AC y la ablación quirúrgica.

Subproyecto 1

En este subproyecto, en primer lugar se evaluó la eficacia de la implementación de un protocolo asistencial común para el tratamiento farmacológico de la FA en diferentes niveles asistenciales y se describe la práctica de la CVE en el tratamiento de la FA en Cataluña. En segundo lugar, se describe la metodología y resultados del tratamiento de ablación percutánea de la FA abordando tres aspectos de gran relevancia en la práctica clínica diaria que no están totalmente aclarados en la literatura, como son la necesidad de la ETE previa a la ablación, el impacto de la instauración de un protocolo de anticoagulación y sedación, o el resultado de la ablación en poblaciones específicas (como es el caso de los deportistas).

Por tanto, las hipótesis del presente subproyecto consisten en:

1. La implementación de un protocolo común en el tratamiento de la FA en los diferentes niveles asistenciales podría mejorar los resultados del tratamiento de la arritmia.

2. La CVE es una estrategia terapéutica cuya utilidad real y eficacia en la práctica clínica habitual puede haber variado a lo largo de los años por el desarrollo concomitante de otras modalidades terapéuticas (nuevos fármacos antiarrítmicos y la ablación).

3. La utilidad de la ETE para descartar la presencia de trombos intracavitarios previo al procedimiento de AC de la FA podría variar según el riesgo tromboembólico de los pacientes.

4. La aplicación sistemática de un protocolo de anticoagulación y sedación consciente en pacientes con FA sintomática y refractaria a tratamiento médico podría tener repercusión en los resultados y las complicaciones en el procedimiento de AC de FA.

5. Los resultados de la AC de la FA en deportistas sin los factores de riesgo clásicos de FA podrían ser diferentes a los del resto de la población con FA.

Subproyecto 2.

La hipótesis correspondiente a este segundo subproyecto es que la ablación quirúrgica de la FA podría ser un procedimiento seguro y eficaz en pacientes con FA y presencia de factores predictores de mala respuesta al tratamiento de ablación percutánea o

antecedentes de un procedimiento fallido de ablación percutánea de la FA. Para ello, se compara la eficacia de la ablación percutánea de la FA respecto a la ablación quirúrgica.

OBJETIVOS

Subproyecto 1

- Analizar la eficacia de la implementación de un protocolo común en el tratamiento farmacológico de la FA en diferentes niveles asistenciales.
- Comparar la evolución a lo largo de los años de la eficacia, indicaciones y características de los pacientes sometidos a CVE para el tratamiento de la FA.
- Evaluar la utilidad de la ETE para descartar la presencia de trombos intracavitarios previo al procedimiento de ablación de la FA e identificar los factores de riesgo de trombos intracavitarios.
- Evaluar la eficacia y seguridad de la aplicación sistemática de un protocolo de sedación y anticoagulación en pacientes con FA sintomática y refractaria a tratamiento médico sometidos a la AC de FA.
- Analizar la eficacia de la AC de la FA en deportistas de resistencia de alta intensidad.

Subproyecto 2.

- Comparar la eficacia y seguridad de la ablación quirúrgica de la FA frente a la AC en pacientes con recurrencia de la FA tras un primer procedimiento de ablación percutánea y en pacientes con baja probabilidad de éxito de la AC por la existencia previa de factores predictores de mala respuesta.

ARTÍCULOS PUBLICADOS

Impacto de la instauración de un protocolo común en los distintos niveles asistenciales de un área sanitaria para la mejora del tratamiento de la fibrilación auricular

Impact of Implementing Common Guidelines at Different Care Levels in a Healthcare Area on the Improvement of Atrial Fibrillation Treatment

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Introduction and objectives. Atrial fibrillation (AF) is treated in different settings by different specialists. The objective of the study was to analyze the impact of the implementation of a practice guideline about AF treatment common to the different levels of health attention on the adequacy of AF treatment and on corrective interventions.

Methods. The study was performed in 2 periods, before and after the implementation of a practice guideline common to all health care levels. In each period, patients with AF who consulted to any of the health care attention levels of a sanitary area were included. Data referring to treatment and compliance of guidelines before and after the visit were recorded prospectively.

Results. 293 patients were included in the first period and 267 in the second one. After the guideline implementation, adequacy before the visit, both of antiarrhythmic treatment and of antithrombotic prophylaxis were superior than in the first period (80% vs 71%; *P*=.009; and 81% vs 67%; *P*<.001, respectively). The percentage of improvement in case of a previous inadequacy of antithrombotic prophylaxis was significantly better in the second period than in the first one (35% vs 9%; *P*<.001), but the percentage of corrective interventions on antiarrhythmic treatment was similar in both periods.

Conclusions. The implementation of a common practice guideline in the different levels of health care attention is useful to improve adequacy of AF treatment, although there is still some reluctance to change an inadequate antiarrhythmic treatment.

Key words: *Atrial fibrillation. Adequacy treatment. Treatment protocol. Levels of health care.*

Impacto de la instauración de un protocolo común en los distintos niveles asistenciales de un área sanitaria para la mejora del tratamiento de la fibrilación auricular

Introducción y objetivos. La fibrilación auricular (FA) se trata en múltiples ámbitos asistenciales. El objetivo del estudio fue analizar el impacto de la instauración de un protocolo de tratamiento de la FA común a todos ellos en la adecuación del tratamiento y en las intervenciones correctoras en caso de inadecuación.

Métodos. El estudio se realizó en 2 períodos, antes y después de la elaboración y difusión de un protocolo de tratamiento de la FA común para los distintos ámbitos de atención sanitaria de un hospital de tercer nivel y de un centro de atención primaria relacionado. En cada período se incluyó a todos los pacientes adultos con FA que consultaron en ellos. Se registraron el tratamiento de la FA y la adecuación de éste a las guías clínicas vigentes antes y después de la visita.

Resultados. Se incluyó a 293 pacientes en el primer período y a 267 en el segundo. La adecuación antes de la visita fue superior en el segundo período (tratamiento antiarrítmico del 80 frente al 71%; p = 0,009; profilaxis antitrombótica del 81 frente al 67%; p < 0,001). El porcentaje de intervenciones correctoras en caso de profilaxis antitrombótica inadecuada fue superior en el segundo período (el 35 frente al 9%; p < 0,001), pero este porcentaje no cambió en el tratamiento antiarrítmico.

Conclusiones. La elaboración y difusión de un protocolo de tratamiento de la FA común a los distintos ámbitos asistenciales es útil para la mejora de la adecuación del tratamiento de la FA, pero persiste la reticencia a cambiar un tratamiento antiarrítmico inadecuado.

Palabras clave: *Fibrilación auricular. Adecuación del tratamiento. Protocolo de tratamiento. Ámbitos asistenciales.*

INTRODUCTION

Atrial fibrillation (AF) is the most frequent arrhythmia in clinical practice and its prevalence is expected to increase due to the increased survival in the general

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ABBREVIATIONS

AF: atrial fibrillation

population and of patients with comorbidities that predispose to the development of AF.[1,2] The wide range of clinical manifestations and seriousness of presentation[1,3] means patients with AF are attended in many different healthcare settings by a variety of specialists.

Atrial fibrillation is a potentially serious condition given that it doubles mortality and has a high level of morbidity.[1,3-7] However, AF-related complications can largely be prevented or efficiently controlled by early, adequate treatment of arrhythmia.[7-9] Similarly, the earlier therapy is begun, the more likely it is that sinus rhythm can be restored and maintained.[7,9] Consequently, adequate treatment in each healthcare setting is crucial to the subsequent optimal evolution of the patient.

However, treatment of AF and prophylaxis for complications often vary according to the specialist responsible for each patient despite the availability of clinical guidelines and consensus documents.[10-13] Furthermore, these are applied differently in different settings. In a recent study, we determined the inadequacy of some aspects of AF treatment in half the patients with this arrhythmia and the reluctance of specialists to rectify inadequacies in most cases.[14] These findings have been corroborated elsewhere.[15-19]

The objective of the present study is to evaluate the impact of implementing a common AF treatment protocol in different settings within a healthcare area, on improving treatment and increasing specialists' commitment to rectifying preexisting inadequacies.

METHODS

Settings

The study was conducted in an urban, tertiary hospital and a primary care clinic (PCC) in the catchment area. The contexts in which patients were included were the following: *a)* family physician clinics in the PCC; *b)* PCC and hospital outpatient cardiology clinics; *c)* hospital emergency room (ER); and *d)* conventional hospital wards.

Patients attending ER and subsequently admitted were included in ER setting when evaluating before the visit, and in the hospital setting at discharge, as final treatment depends on the physicians on the wards.

Different healthcare settings are independent and autonomous in their treatment of these patients and face no restrictions in the application of treatments recommended in the clinical guidelines below (electric cardioversion, antiarrhythmic drugs, anticoagulants, antiplatelet treatment).

Periods

The study was conducted in 2 periods, as follows:

Period 1 or preintervention. We included all adult patients (>18 years) with antecedents of AF demonstrated by electrocardiogram attending any of the healthcare settings mentioned during 14 consecutive days in June 2004 whether their reason for attending was directly AF-related or not. We excluded patients first diagnosed with AF at this consultation (first episodes), as they did not receive treatment prior to AF and we could not therefore evaluate treatment adequacy before the visit or the change in treatment if it were inadequate.

Period 2 or postintervention. We included all adult patients (>18 years) with antecedents of AF demonstrated by electrocardiogram attending clinic in any of the healthcare settings mentioned during 14 consecutive days in June 2005 (the same period as in 2004), whether the reason for consultation was AF-related or not. We again excluded first episodes.

In the 2 periods, all patients were treated according to the criteria of the physician responsible and followed the care routines established at the time of the study. The same specialists were responsible for patients in the 2 periods, although there were changes among the interns who collaborated in attending patients.

Intervention

Between the 2 periods, we designed a protocol for action in the face of AF agreed by physicians from all the healthcare settings involved through the participation of 2 or 3 representatives from each. The protocol covered both treatment of different types of AF and procedures for referral between fields. To create this, the physicians responsible based themselves on the current clinical guidelines specified below[10-13] and adapted them to the realities of the healthcare area.

The protocol was publicized in 2 ways: *a)* a pocket-sized brochure summarizing the protocol was distributed to all physicians working in the healthcare settings involved, both interns (n=81) and specialists (n=53), and *b)* in each setting, clinical sessions were led by 2 of the physicians responsible for preparing the protocol. In the sessions, they explained AF treatment, data obtained on adequacy in the first period, the reason for preparing the agreed protocol and described the protocol. Although sessions were aimed at the same physicians who had received the summary, only 70% attended.

Variables Studied

In the 2 periods, we conducted a personal interview with each patient and/or their close family, and reviewed clinical records.

We obtained the following data on each patient:

– Age
– Gender
– Social-family support (good, partial, none)
– Quality of life/degree of dependence (Barthel index, Annex 1)
– Arterial embolism risk factors (number and type)
– AF classification (paroxystic, persistent, permanent)
– Reason for visit (see text)
– Antiarrhythmic treatment. Type of treatment and adequacy according to current clinical guidelines (see text)
– Prophylactic treatment for arterial embolism. Type of treatment and adequacy according to current clinical guidelines (see text)

Reasons for attending clinic were classified in 2 subgroups: *a)* directly AF-related, and *b)* non AF-related.

Treatment was considered adequate when it corresponded to that in clinical guideline recommendations current at the time of the study, even though they might differ on certain points. In the first period, we accepted: "Guidelines of the Spanish Society of Cardiology on Cardiac Arrhythmias," "Guidelines for the treatment of atrial fibrillation in hospital emergency services," "ACC/AHA/ESC guidelines for the management of patients with atrial fibrillation."[10-12] In the second period, we also accepted the more recent "7th Consensus of the American College of Chest Physicians."[13] This was not available for inclusion in the first period evaluation but could be included in the second period and in the preparation of the protocol.

Evaluation of adequacy of treatment was conducted before and after the study visit. We considered treatment inadequate when it was not specified in guidelines for the use it was being given, when it was not the first choice treatment and there was no justifiable reason for not using the first choice treatment, or when there was a contraindication to its use. However, we did consider adequate, prophylactic treatment for arterial embolism, in patients theoretically indicated for anticoagulation, according to guidelines, but not receiving it because of a medical or social contraindication detailed in their clinical records.

In the first and second periods, the physicians responsible for the patients were only informed about the existence of an epidemiologic study which some of their patients had been included in. They were asked to give permission for inclusion, but, to avoid bias, were not informed in advance about the exact nature of data gathered or about the period when analysis would be conducted.

Data on the variables studied were gathered by interns (n=8) and of specialists in family and community medicine (n=2), internal medicine (n=3, including 2 subspecialists in ER), and cardiology (n=1). All data was recorded by interns under the supervision of the specialists, who then judged the adequacy or inadequacy of treatment based on the specified clinical guidelines. The same specialists were involved in data collection in the 2 periods.

Statistical Analysis

Values are expressed as mean (SD) for continuous variables and absolute values or percentages for discontinuous variables. For comparisons we used the Student's *t* test and one-way ANOVA with Bonferroni correction for normally distributed continuous variables and χ^2 and the Fisher test for qualitative variables. A *P* value less than .05 was considered significant. Calculations were with software SPSS 12.0.

RESULTS

We included 293 patients in the first period and 267 in the second. Table 1 shows the settings patient came from and percentages of patients with AF versus total number of visits in each setting, as well as clinical-epidemiologic characteristics of patients included. In the first period, 2 patients admitted to ER or in-hospital died: 1 of an AF-related cause (antiarrhythmic treatment). In the second period, 5 patients died: 2 of AF-related causes (1 antiarrhythmic treatment, 1 anticoagulation treatment) (*P*=.27).

Antiarrhythmic Treatment

In the first period, antiarrhythmic AF treatment varied greatly in all settings (Table 2). In 71% of patients, antiarrhythmic treatment was adequate according to clinical guideline recommendations current at the time of the study. We found no differences in drug regimens between patients attending in the different settings studied. However, significant differences existed in adequacy of treatment, with greater adequacy in patients attending ER and lower adequacy in patients attending family physician clinics and in-hospital (*P*=.007).

In 31 patients, antiarrhythmic treatment drugs were modified at the study visit. Treatment was most frequently changed following medical attention in ER (*P*<.001 vs other settings). The principal reasons for attending clinic that led to modification of antiarrhythmic treatment were directly AF-related: complications of the illness or treatment and symptoms caused by AF.

After the visit, overall adequacy of antiarrhythmic treatment rose from 71% to 73% (nonsignificant). The increased percentage of adequate antiarrythmic treatments was not significant in any setting. We continued to record significantly greater inadequacy of antiarrhythmic treatment in primary care (Table 3).

The principal reasons for inadequate antiarrhythmic treatment before and after the visit (Tables 2 and 3,

TABLE 1. **Settings of Provenance and Clinical-Epidemiologic Characteristics of Patients Included***

	Family Physician P1/P2	Outpatient Cardiologist P1/P2	ER P1/P2	Hospital P1/P2	Total P1/P2
Total visits	4534/7150	457/676	1284/1496	377/351	6652/9673
Patients with AF, % of total visits	126 (2.8)/85 (1.2)‖	69 (15)/52 (7.6)‖	83-59† (6.5-4.6)/ 106-83† (7-5.5)	15-37† (4-10.3)/ 24-42† (6.8-12)‖	293 (4.4)/ 267 (2.8)
Age, years (SD)	75 (9)/75 (10)	69 (13)/69 (13)	77 (10)/76 (12)	70 (15)/75 (10)	74 (11)/74 (12)
Gender M:W	58:68/39:46	41:28/23:30	37:46/42:65	7:8/12:12	143:150/116:153
Barthel	95 (14)/92 (15)	98 (5)/91 (14)§	88 (16)/80 (24)§	85 (18)/81 (21)	93 (14)/86 (20)
Reason for consultation					
Related	12/8	45/26†t	36/39§	9/7	102/80§
AF symptoms	1/2	3/2	9/11	0/1	13/16
AF control	11/5	42/24	0/0	0/0	53/29
AF complication	0/1	0	20/21	7/5	27/27
Secondary effect	0/0	0	7/7	2/1	9/8
Not related	114/77	24/27†t	47/68§	6/17	191/189§
Classification					
Paroxystic	83/23‖	23/14	20/25	4/2	130/64‖
Persistent	1/8§	10/4	3/3	0/3	14/18
Permanent	42/54‖	36/35	60/9	11/19	149/187‖

*P1 indicates period 1; P2, period 2.
†Initial-discharge. The difference between the initial number of patients and the number at discharge is because 24 patients visited initially in ER were admitted and, therefore, discharged from the hospital. Moreover, 2 patients died in the first period and 5 in the second.
‡$P<.05$.
§$P<.01$.
‖$P<.001$.

respectively) were: *a)* digoxin prescribed as the only drug and as first choice to control heart rate in patients with moderate or high physical activity (guideline Class IIb recommendation only in patients in repose); *b)* digoxin in patients with paroxysmal AF (Class III recommendation both to control heart rate, with Level of Evidence B, and for cardioversion or prophylaxis of new episodes, with Level of Evidence A); *c)* amiodarone for chronic control of heart rate in patients with permanent AF (this does not appear as a guideline recommendation) and *d)* other, includeding:

– Amiodarone as first choice therapeutic for chronic treatment in patients without structural cardiomyopathy with paroxysmal AF and very isolated episodes (<1/year), clinically well-tolerated (antiarrhythmic treatment in these cases is a Class IIb recommendation with level of evidence C, and amiodarone is the second choice drug)
– β-blockers in patients with chronic obstructive pulmonary disease and bronchial hyper-reactivity (Class III recommendation, level of evidence C)
– Combined calcium antagonists and β-blockers in patients with history of bradycardia

After implementing the protocol (period 2), we also found substantial clinical variety in antiarrhythmic drug regimens before the visit although differences arose when compared with the settings of inclusion (Table 4). Overall adequacy increased significantly with respect to the previous year (80% vs 71%; $P=.009$). This was reflected in all healthcare settings although it was not significant in individual cases (Figure 1A). Family physician clinics continued to record a lower level of adequacy.

In the second period, antiarrhythmic treatment was modified in 35 patients. Treatment was most frequently modified in ER and in-hospital ($P<.001$ vs other settings), and reasons for attending clinic leading to changes were the same as in the first period. The percentage of corrective interventions to remedy previous inadequacy was similar to the previous period, both overall and in individual settings (Figure 2A). Reasons for inadequacy were also similar, both before and after the visit, although the frequency of each changed (Tables 4 and 5, respectively).

Antithrombotic Prophylaxis

In the first period, 53% of patients received anticoagulation treatment before medical attention, and 30% received antiplatelet treatment (4% received both). Overall adequacy of arterial embolism prophylaxis was 67% before the study visit and we found no significant differences between settings (Table 2). After the visit, overall adequacy was 70% (nonsignificant increase) with no significant differences between settings.

The principal reasons for inadequacy of antithrombotic prophylaxis before and after the visit (Tables 2 and 3, respectively), were: *a)* no anticoagulation in patients with AF and high risk of arterial embolism without contraindication (non-fulfillment of Class I recommendation and Level of Evidence A); *b)* no

TABLE 2. **Drug Regimen Before Visit in the First Period***

	Total	Family Physician	Outpatient Cardiologist	ER	Hospital	*P*
Antiarrhythmic drugs before visit						
Digoxin	116 (40%)	48 (38%)	23 (33%)	39 (47%)	6 (40%)	NS
Amiodarone	62 (21%)	28(22%)	15 (22%)	14 (17%)	5 (33%)	NS
β-blockers	25 (9%)	14 (11%)	7 (10%)	4 (5%)	0 (0%)	NS
Calcium antagonists	16 (5%)	5 (4%)	5 (7%)	4 (5%)	2 (13%)	NS
Class Ic antiarrhythmic drugs	21 (8%)	11 (9%)	6 (9%)	3 (4%)	1 (7%)	NS
Without treatment	65 (22%)	25 (20%)	14 (20%)	26 (31%)	1 (7%)	NS
Adequacy of antiarrhythmic treatment before visit						.007
Yes	207 (71%)	78 (62%)	51 (74%)	69 (83%)	9 (60%)	
No	86 (29%)	48 (38%)	18 (26%)	14 (17%)	6 (40%)	
Causes of inadequate antiarrhythmic treatment						
Digoxin to control HR	34 (12%)	18 (14%)	7 (10%)	5 (6%)	4 (27%)	NS
Digoxin for prophylaxis in Paroxysmal AF	30(10%)	24 (19%)	4 (6%)	2 (2%)	0	<.001
Amiodarone for chronic control of HR	18 (6%)	3 (2%)	6 (9%)	7 (8%)	2 (13%)	NS
Other	11 (4%)	5 (4%)	3 (4%)	2 (2%)	1 (7%)	NS
Antithrombotic prophylaxis before visit						
Anticoagulation	154 (53%)	59 (47%)	46 (67%)	37 (45%)	12 (80%)	.004
Antiplatelet treatment	88 (30%)	40 (32%)	21 (30%)	20 (24%)	7 (47%)	NS
Without treatment	62 (21%)	27 (21%)	9 (13%)	26 (32%)	0	NS
Adequacy of antithrombotic prophylaxis before visit						NS
Yes	197 (67%)	77 (61%)	52 (75%)	56 (68%)	13 (87%)	
No	96 (33%)	49 (39%)	17 (25%)	27 (32%)	2 (13%)	
Causes of inadequate antithrombotic prophylaxis						
No anticoagulation when this is indicated	74 (25%)	42 (33%)	14 (20%)	17 (20%)	1 (7%)	.029
Neither anticoagulation nor antiplatelet treatment when these are indicated	5 (5%)	6 (5%)	0	9 (11%)	0	.033
Anticoagulation not indicated	3 (1%)	1 (0.3%)	1 (1.4%)	0	1 (7%)	NS

*AF indicates atrial fibrillation; HR, heart rate; NS, nonsignificant.

anticoagulation or antiplatelet treatment in patients in who, due to lower risk of arterial embolism, the 2 choices of treatment are accepted (non fulfillment of Class I recommendation and Level of Evidence A); and *c)* anticoagulation in patients without medical indication (Class III recommendation and Level of Evidence C) or with medical or social contraindications.

Prophylaxis was less adequate in patients with paroxysmal AF both before the visit (58% vs 74% in permanent AF and 85% in persistent AF; *P*=.006) and after the visit (61% vs 78% in permanent AF and 85% in persistent AF; *P*=.005). Adequacy was greater in patients with a previous neurologic complication, both before the visit (83% vs 64%; *P*=.01) and after the visit (87 vs 67%; *P*<.007), although we found no relationship between adequacy of treatment and other risk factors such as advanced age (anticoagulated patients were younger, although the difference was nonsignificant), diabetes, high blood pressure or presence of heart failure. Adequacy at discharge was lower in family physician clinics than other settings (*P*=.05).

Overall adequacy of arterial embolism prophylaxis before the visit was greater in the second period than the first (81% vs 67%; *P*<.001). This was reflected in all settings although it was only significant in ER (Figure 1B). The percentage of corrective interventions in cases of previous inadequacy was also greater than in the first period (Figure 2B), both overall (35% vs 9%; *P*<.001) and in ER and outpatient cardiology. We also recorded a nonsignificant increase in family physician clinics.

The reasons for inadequacy were similar to those in the first period, both before and after the visit, although the frequency of each changed (Tables 4 and 5, respectively). In the second period, we found no relation between adequacy of arterial embolism prophylaxis and AF type, or with any of the risk factors for arterial embolism, either before or after the visit.

DISCUSSION

This study shows the value of training and of unifying criteria for AF treatment. Between the 2 periods in the

TABLE 3. **Drug Regimen After Visit in the First Period***

	Total	Family Physician	Outpatient Cardiologist	ER	Hospital	*P*
Antiarrhythmic drugs after visit						
Digoxin	106 (36%)	48 (38%)	22 (32%)	22 (39%)	14 (36%)	NS
Amiodarone	59 (20%)	28 (22%)	14 (20%)	8 (14%)	9 (23%)	NS
β-blockers	28 (10%)	14 (11%)	7 (10%)	3 (5%)	4 (10%)	NS
Calcium antagonists	18 (6%)	5 (4%)	4 (6%)	5 (9%)	4 (10%)	NS
Class Ic antiarrhythmic drugs	24 (8%)	11 (9%)	7 (10%)	5 (9%)	1 (3%)	NS
Without treatment	68 (23%)	25 (20%)	15 (22%)	17 (13%)	11 (28%)	NS
Adequacy of antiarrhythmic treatment after visit						.002
Yes	212 (73%)	78 (62%)	55 (80%)	49 (86%)	30 (77%)	
No	79 (27%)	48 (38%)	14 (20%)	8 (14%)	9 (23%)	
Causes of inadequate antiarrhythmic treatment						
Digoxin to control HR	29 (10%)	17 (13%)	5 (7%)	3 (5%)	4 (10%)	NS
Digoxin for prophylaxis in paroxysmal AF	30 (10%)	24 (19%)	5 (7%)	1 (2%)	0	<.001
Amiodarone to control HR	14 (5%)	3 (2%)	2 (3%)	5 (9%)	4 (10%)	NS
Other	10 (3%)	5 (4%)	3 (4%)	0	2 (5%)	NS
Antithrombotic prophylaxis after visit						
Anticoagulation	151 (52%)	59 (47%)	46 (67%)	26 (46%)	27 (68%)	.001
Antiplatelet	86 (30%)	40 (32%)	22 (32%)	16 (29%)	11 (29%)	NS
Without treatment	51 (18%)	26 (21%)	8 (12%)	13 (23%)	4 (10%)	NS
Adequacy of antithrombotic prophylaxis after visit						.05
Yes	204 (70%)	79 (63%)	52 (75%)	41 (73%)	33 (84%)	
No	87 (30%)	47 (33%)	17 (25%)	16 (27%)	6 (16%)	
Causes of inadequate antithrombotic prophylaxis						
No anticoagulation when indicated	69 (24%)	41 (33%)	14 (20%)	10 (18%)	4 (10%)	.01
Neither anticoagulation nor antiplatelet treatment when these are indicated	12 (4%)	6 (5%)	0	5 (9%)	1 (3%)	NS
Anticoagulation not indicated	1 (0.3%)	1 (0.8%)	1 (1.4%)	0	1 (3%)	NS

*AF indicates atrial fibrillation; HR, heart rate; NS, nonsignificant.

study, no new ideas or technological approaches were developed. We simply publicized and reinforced the application of known concepts in our context.

The benefit of implementing the protocol was twofold. In the postintervention period, initial adequacy was notably greater in all healthcare settings, reflecting the use of the consensus protocol and the training given during the year between the 2 periods analyzed. More importantly, in the second period we also found a significant increase in corrective interventions in cases previously found to be inadequate. This reflects physicians' commitment to improving the situation of patients receiving inadequate treatment.

Although the results of implementing a combined treatment protocol in different healthcare settings may seem obvious, little previous experience exists of the value of similar training programs. However, results reported elsewhere are also positive[20,21]: Zimetbaum et al[20] showed the usefulness of providing information about clinical guidelines for AF in ER on improvements in cost-effectiveness, although they did not determine intrinsic adequacy. In Spain, previous experience of programs to improve AF treatment has also been reported by Ruiz et al,[21] who achieved 90% anticoagulation in patients without contraindications. However, these researchers implemented their own protocol and no data were given about anticoagulation prior to the intervention. The present study includes scientific tests of prior status of treatment and treatments were prescribed by a number of physicians other than the researchers and those responsible for the protocol. Application of the protocol to a non-selected sample of physicians objectively increases the value of the level of acceptance.

The commitment of physicians to remedying preexisting inadequacies was evident in arterial embolism prophylaxis, but this was not the case with antiarrhythmic treatment, despite an overall improvement in the initial adequacy of antiarrhythmic treatment in the second period. The explanation may lie in the multifactorial nature of the issue. To date we have found no other study that determines the level of physicians' commitment to improving inadequacies existing before consultation. Most studies of AF treatment adequacy are descriptive and only refer to anticoagulation.[15-19,22,23] Adequacy of

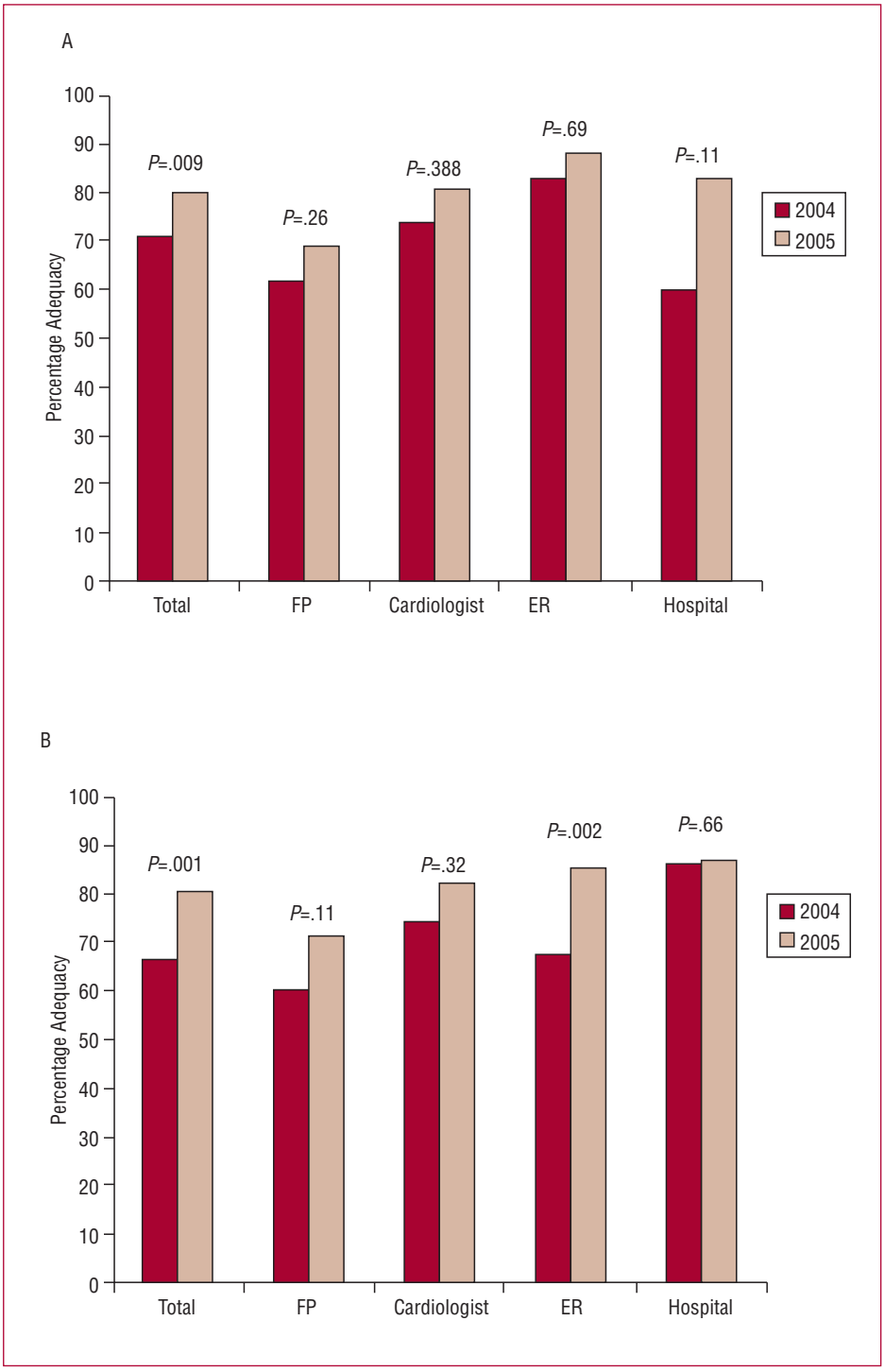

Figure 1. Comparison of adequacy of antiarrhythmic (A) and antithrombotic treatments (B) before visit between preintervention and postintervention periods. FP indicates family physician; ER, emergency room.

antiarrhythmic treatment is barely studied[24] and there may be less awareness of incorrect use. Alternatively, in cases when the principal reason for a change of treatment was a complication in treatment or illness, fear or reluctance to start a new treatment without a specific reason to do so, may be the explanations. Finally, the great improvement found in initial adequacy in the second period may have been influenced by less obvious corrective interventions.

However, despite increased adequacy in primary care before the visit, in comparison with the previous year, and at discharge, in comparison with before the visit, patients in primary care continued to be the least likely to receive anticoagulation treatment or to have it changed because of its inadequacy. Family physicians are, or should be, the doctors who best know the personal, social, and family situation of patients in order to determine whether to start and/or maintain anticoagulation treatment

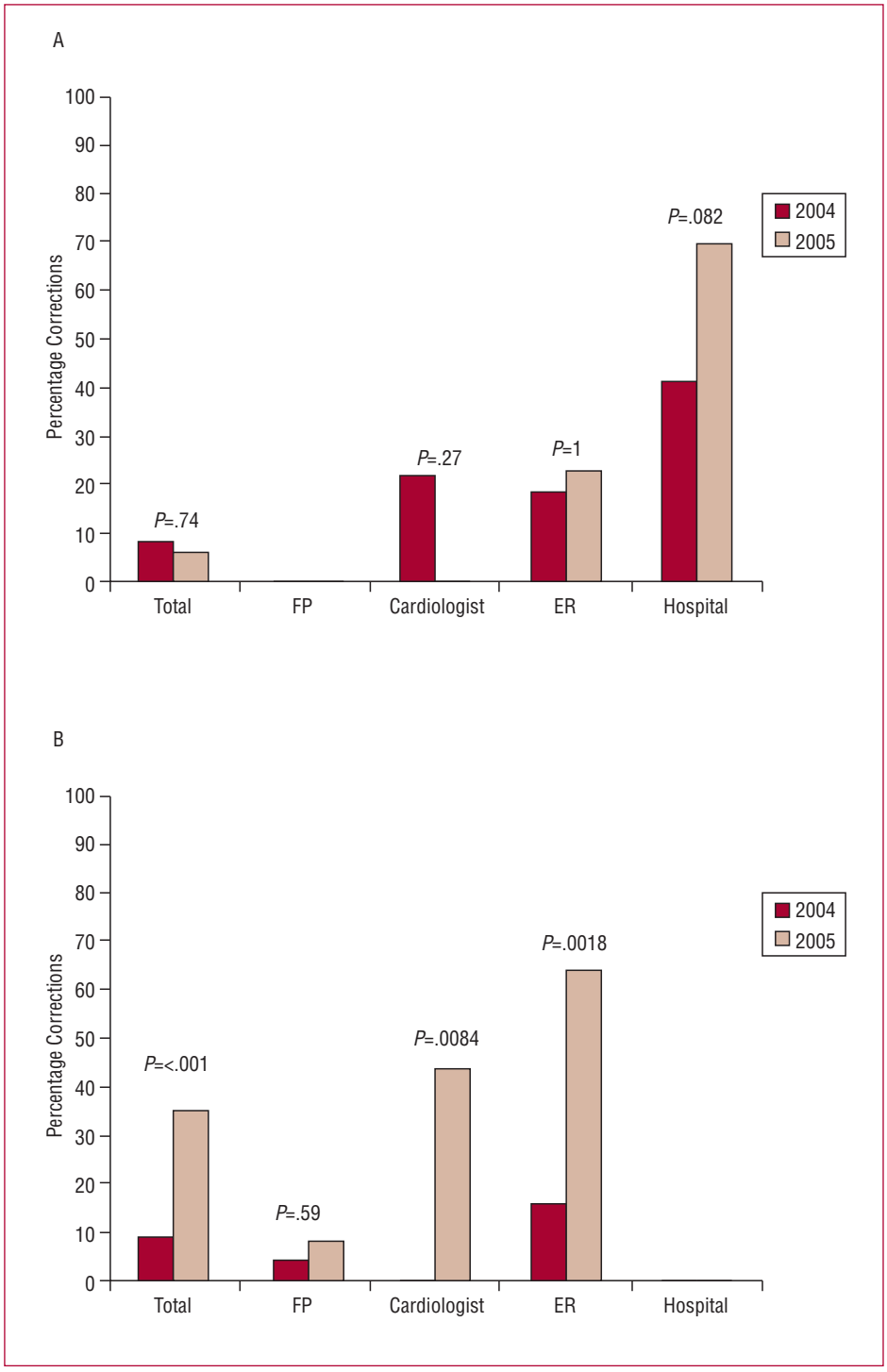

Figure 2. Comparison of percentage of correction in case of inadequacy of antiarrhythmic (A) and antithrombotic (B) treatments between preintervention and postintervention periods. FP indicates family physician; ER, emergency room.

and to control adequate follow-up and possible harmful effects or events that might justify interrupting it. The present study found increased, but nonsignificant, adequacy of treatment in primary care as did Martín et al,[22] who reported 81% adequacy in antithrombotic prophylaxis in a primary care clinic. These studies demonstrate anticoagulation treatment can be started and controlled from primary care although figures for adequacy of treatment in most studies conducted in this and other settings do not usually surpass 60%.[15-19,24] In primary care, many patients with AF attending family physician clinics are controlled by cardiologists. This may explain the lack of commitment and reluctance to change treatment on the part of family physicians, patients, or patients' families. Whatever the case may be, increased training sessions in primary care seem indicated.

To date, numerous multicenter studies have been conducted to evaluate the adequacy of coordinated

TABLE 4. **Drug Regimen Before Visit in the Second Period***

	Total	Family Physician	Outpatient Cardiologist	ER	Hospital	*P*
Antiarrhythmic drugs before visit						
Digoxin	125 (47%)	34 (40%)	22 (42%)	51 (48%)	18 (75%)	.021
Amiodarone	48 (18%)	20 (24%)	11 (21%)	13 (12%)	4 (17%)	NS
β-blockers	45 (17%)	14 (16%)	16 (31%)	14 (13%)	1 (4%)	.012
Calcium antagonists	33 (12%)	9 (11%)	10 (19%)	11 (10%)	3 (12%)	NS
Class Ic antiarrhythmic drugs	19 (7%)	8 (9%)	4 (8%)	7 (7%)	0	NS
Without treatment	55 (21%)	14 (16%)	11 (21%)	27 (25%)	3 (12%)	NS
Adequacy of antiarrhythmic treatment before visit						.017
Yes	214 (80%)	59 (69%)	42 (81%)	93 (88%)	20 (83%)	
No	53 (20%)	26 (31%)	10 (19%)	13 (12%)	4 (17%)	
Causes of inadequate antiarrhythmic treatment						
Digoxin to control HR	21 (8%)	12 (14%)	5 (10%)	3 (3%)	1 (4%)	.03
Digoxin for prophylaxis in paroxysmal AF	7 (3%)	0	1 (2%)	4 (4%)	2 (8%)	NS
Amiodarone to control HR	24 (9%)	12 (14%)	4 (8%)	6 (6%)	2 (8%)	NS
Other	3 (1%)	2 (2%)	1 (2%)	0	0	NS
Antithrombotic prophylaxis before visit						
Anticoagulation	155 (58%)	43 (51%)	40 (77%)	55 (52%)	16 (67%)	.01
Antiplatelet	68 (25%)	31 (36%)	8 (15%)	25 (24%)	4 (17%)	.032
Without treatment	44 (16%)	9 (11%)	4 (8%)	27 (25%)	4 (17%)	.001
Adequacy of antithrombotic prophylaxis before visit						NS
Yes	216 (81%)	61 (72%)	43 (83%)	91 (86%)	21 (87%)	
No	51 (19%)	24 (28%)	9 (17%)	15 (14%)	3 (12%)	
Causes of inadequate antithrombotic prophylaxis						.023
No anticoagulation when indicated	36 (13%)	20 (24%)	7 (13%)	7 (7%)	2 (8%)	.006
Neither anticoagulation nor antiplatelet treatment when these are indicated	13 (5%)	4 (5%)	2	7 (7%)	0	NS
Anticoagulation not indicated	2 (1%)	0	0	1 (1%)	1 (4%)	NS

*AF indicates atrial fibrillation; HR, heart rate; NS, nonsignificant.

treatment of AF in different centers within the same setting, whether in primary care,[9,10] ER,[12-14] or in-hospital,[15-17] but multidisciplinary analysis within a single healthcare area, as in the present study, has not been conducted. This enables us to make reliable comparisons and even design future strategies. Moreover, given that the structure of healthcare areas and settings studied is similar to other parts of Spain, the intervention we conducted could be applied elsewhere. However, the peculiarities of each area, especially the intensity and type of relationship between different settings and their capacity and autonomy for therapeutic action, could substantially influence results. In our case, improved results in ER, in-hospital and outpatient cardiology can probably be explained by closer relationships between these settings, favored by physical proximity and a certain flow of physicians from one setting to another. Future improvements in communication with primary care will depend on each hospital.

Limitations of the Study

One limitation of the present study is the inclusion of the "7th Consensus of the American College of Chest Physicians" in the second period as an accepted clinical guideline. While inclusion in this period was obligatory, as it was already current, it could have increased the range of patients considered as receiving adequate treatment. In any case, all patients believed to need antithrombotic prophylaxis as defined by the consensus document were also in need of prophylaxis according to at least one of the guideline documents accepted in the first period.

CONCLUSIONS

The present study shows that the consensus of physicians involved in attending patients with AF, following the implementation of a specific protocol derived from this consensus and adapted to all the settings,

TABLE 5. **Drug Regimen after Visit in the Second Period***

	Total	Family Physician	Outpatient Cardiologist	ER	Hospital	*P*
Antiarrhythmic drugs after visit						
Digoxin	120 (46%)	35 (41%)	23 (44%)	38 (46%)	24 (57%)	NS
Amiodarone	50 (19%)	21 (25%)	9 (17%)	15 (18%)	5 (12%)	NS
β-blockers	43 (16%)	14 (16%)	15 (29%)	10 (12%)	4 (10%)	.039
Calcium antagonists	34 (13%)	9 (11%)	9 (17%)	11 (13%)	5 (12%)	NS
Class Ic antiarrhythmic drugs	18 (7%)	8 (9%)	3 (6%)	7 (8%)	0	NS
Without treatment	49 (19%)	13 (15%)	10 (19%)	14 (17%)	12 (29%)	NS
Adequacy of antiarrhythmic treatment after visit						<.001
Yes	212 (81%)	58 (68%)	41 (79%)	73 (88%)	40 (95%)	
No	50 (19%)	27 (32)	11 (21%)	10 (12%)	2 (5%)	
Causes of inadequate antiarrhythmic treatment						
Digoxin to control HR	19 (7%)	11 (12%)	5 (10%)	2 (2%)	1 (2%)	.032
Digoxin for prophylaxis in paroxysmal AF	4 (2%)	0	2 (4%)	2 (2%)	0	NS
Amiodarone to control HR	23 (9%)	13 (15%)	3 (6%)	5 (6%)	2 (5%)	NS
Other	5 (2%)	3 (4%)	1 (2%)	1 (1%)	0	NS
Antithrombotic prophylaxis after visit						
Anticoagulation	163 (62%)	44 (52%)	43 (83%)	48 (58%)	28 (67%)	.003
Antiplatelet	73 (28%)	31 (36%)	8 (15%)	22 (26%)	12 (29%)	NS
Without treatment	27 (10%)	10 (12%)	1 (2%)	13 (16%)	3 (7%)	NS
Adequacy of antithrombotic prophylaxis after visit						<.001
Yes	228 (87%)	63 (74%)	47 (90%)	79 (95%)	39 (39%)	
No	34 (13%)	22 (16%)	5 (10%)	4 (5%)	3 (3%)	
Causes of inadequate antithrombotic prophylaxis						
No anticoagulation when indicated	25 (10%)	17 (20%)	5 (10%)	2 (2%)	1 (2%)	<.001
Neither anticoagulation nor antiplatelet treatment when these are indicated	6 (2%)	3 (4%)	0	2 (2%)	1 (2%)	NS
Anticoagulation not indicated	3 (1%)	2 (2%)	0	0	1 (2%)	NS

*AF indicates atrial fibrillation; HR, heart rate; NS, nonsignificant.

can significantly improve antiarrhythmic treatment in daily clinical practice. However, greater emphasis should be placed on specific issues, especially the commitment of all physicians to improving treatment.

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ANNEX 1. **Barthel Index**

Parameter	Patient Status	Score
Eating	Totally independent	10
	Needs help to cut meat, bread, etc	5
	Dependent	0
Washing	Independent: enters and leaves the bathroom alone	5
	Dependent	0
Dressing	Independent: can put on and take off clothes button clothes and tie shoelaces	10
	Needs help	5
	Dependent	0
Personal hygiene	Independent for washing face, hands, brushing hair, shaving, putting on makeup, etc	5
	Dependent	0
Stools	Normal continence	10
(to determine the previous week)	Occasional episodes of incontinence, or Needs help to administer suppositories or laxatives	5
	Incontinence	0
Micturition	Normal continence or is able to take care of catheter if inserted	10
(to determine the previous week)	Maximum 1 daily episode of incontinence or Needs help to take care of catheter if inserted	5
	Incontinence	0
Use of WC	Independent to go to the WC, take off and put on clothing	10
	Needs help to go to the WC, but can clean self	5
	Dependent	0
Movement	Independent to go from chair to bed	15
	Minimal physical help or supervision needed	10
	Needs great degree of help, but is capable of staying seated alone	5
	Dependent	0
Walking	Independent, walks 50 m alone	15
	Needs physical help or supervision to walk 50 m	10
	Independent in wheelchair without help	5
	Dependent	0
Stairs	Independent to go up and down stairs	10
	Needs physical help or supervision	5
	Dependent	0

Efficacy of circunferencial pulmonary vein ablation of atrial fibrillation in endurance athletes

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CLINICAL RESEARCH

Efficacy of circumferential pulmonary vein ablation of atrial fibrillation in endurance athletes

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Aims Long-term endurance sport practice has been increasingly recognized as a risk factor for lone atrial fibrillation (AF). However, data on the outcome of circumferential pulmonary vein ablation (CPVA) in endurance athletes are scarce. The aim of the study was to evaluate the efficacy of CPVA in AF secondary to endurance sport practice.

Methods and results Patients submitted to CPVA answered a questionnaire about lifetime history of endurance sport practice. Endurance athletes were defined as those who engaged in >3 h per week of high-intensity exercise for at least the 10 years immediately preceding their AF diagnosis. A series of 182 consecutive patients was included (51 ± 11 years, 65% with paroxysmal AF, 81% men, 42 ± 6 mm mean left atrial diameter); 107 (59%) patients had lone AF, and 42 of them (23% of the study population) were classified as endurance athletes (lone AF sport group). Freedom from arrhythmia after a single CPVA was similar in the lone AF sport group compared with the remaining patients ($P = 0.446$). Left atrial size and long-standing AF were the only independent predictors for arrhythmia recurrence after ablation.

Conclusion Circumferential pulmonary vein ablation was as effective in AF secondary to endurance sport practice as in other aetiologies of AF.

Keywords Atrial fibrillation • Catheter ablation • Endurance sport • Recurrence • Athletes

Introduction

Atrial fibrillation (AF) is the most common cardiac rhythm disorder in clinical practice. The estimated prevalence of AF is 0.4–1% in the general population,[1] increasing with age to 8% in those older than 80 years.[2] The recognized risk factors for developing AF include age, hypertension, structural heart disease, diabetes mellitus, and hyperthyroidism.[3] However, in a significant number of patients younger than age 60, no cardiovascular disease or any other known causal factor is present and the aetiology remains unclear. This condition is termed lone AF,[4] and may be responsible for as many as 30% of patients with paroxysmal AF seeking medical attention.[5,6] In recent years, long-term endurance sport practice has been recognized as a risk factor for AF.[7–14] On the other hand, AF ablation has emerged as an effective and safe invasive treatment of drug-refractory AF.[15–21] However, little is known about the outcome of this therapy in AF secondary to endurance sport practice.[22] The aim of the present study was to analyse the efficacy of circumferential pulmonary vein ablation (CPVA) in endurance athletes with lone AF referred to AF ablation.

Methods

Study population

A series of 182 consecutive patients submitted to a first CPVA procedure because of symptomatic and drug-refractory AF between February 2003 and October 2006 was included in the study. Patients

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were asked about their lifetime physical activity and about the occurrence of AF episodes.

Prior to the procedure, all patients underwent transthoracic echocardiography to rule out structural heart disease and to measure the cardiac chambers and left ventricular ejection fraction. Transoesophageal echocardiography was performed 1–5 days before ablation to exclude the presence of intracavitary thrombus, as was magnetic resonance angiography of the left atrium (LA) and pulmonary veins (PVs) which, when possible, merged into the navigation system to achieve better spatial resolution and anatomical definition.

Anti-arrhythmic drug therapy was stopped at least five half-lives before the ablation, except in patients receiving amiodarone, to try to unmask the potential triggers of AF, such as supraventricular tachycardias (AV nodal re-entry or accessory pathway-mediated atrioventricular reciprocating tachycardia). Patients on oral anticoagulation stopped medication 3 days prior to the procedure, and low-molecular-weight heparin was administered until the day before the ablation. All ablation procedures were performed by experienced operators. Written informed consent was obtained from all the participants. The protocol was approved by the Institutional Ethics Committee.

Definitions

Atrial fibrillation was classified as paroxysmal, persistent, or long-standing, following the definition established by AF ablation consensus.[23]

Lone AF was defined as AF presenting in individuals younger than 60 years without clinical or echocardiographic evidence of cardiopulmonary disease, including hypertension, or other identifiable cause for the arrhythmia such as hyperthyroidism or alcohol abuse.[4]

Athletes were defined as those who performed regular endurance sport activity (cycling, jogging, swimming, soccer, rowing, etc.) for at least 3 h per week for at least the 10 years immediately preceding the arrhythmia diagnosis. This cut-off point was chosen because it represents a lifetime sport practice of at least 1500 h, which, as previously described,[8] is associated with a higher risk of lone AF.

Vagally induced AF was defined as AF occurring at least 80% of the time during sleep, after heavy meals or in the hours immediately following exercise. Adrenergically induced AF was defined as AF episodes that started during waking hours at least 80% of the time and during strenuous exercise or other states of adrenergic activation.[10,24] The remaining patients were classified as having AF of unknown origin.

Circumferential pulmonary vein ablation

Catheters were introduced percutaneously through the femoral vein; a transseptal puncture was performed to access the LA. After transseptal access, a bolus of heparin was administered (5000–6000 IU, according to patient weight), followed by additional boluses to maintain an activated clotting time of 200–250 s. Ablation was performed under intravenous sedation with midazolam and analgesia with meperidin and phentanyl. Oxygen saturation and invasive arterial blood pressure were monitored throughout the procedure. A three-dimensional map was constructed using an electro-anatomical mapping system (CARTO, Biosense-Webster Waterloo, Belgium or NAVX, St Jude Corporation, St Paul, MN, USA) to support the creation and validation of radiofrequency (RF) lesions. Continuous RF lesions surrounding each ipsilateral PV were delivered as described previously.[25] Ablation lines were also deployed along the LA roof and LA posterior wall joining contralateral encircling lesions, and along the mitral isthmus. Mitral isthmus ablation was performed in all patients by creating an RF line from the inferior-lateral aspect of the left PV lesions to the mitral annulus. This line was anatomically performed, and no electrical block was assessed. Then, an RF line was created connecting contralateral PV-encircling lesions through the LA roof, and the LA posterior wall was electrically excluded by adding another ablation line, on top of the roof line, connecting the inferior aspect of the contralateral PV. The isolation of the posterior wall was confirmed by the absence of electrical activity and the inability to capture with pacing inside the whole encircled LA posterior region. All patients got ablation lines, regardless of AF type.

Radiofrequency was delivered through an 8 mm or irrigated tip thermocouple-equipped catheter, using a target temperature of 55°C at a maximum output of 60 W for the 8 mm tip catheter and 48°C at 40 W for the irrigated tip catheter.

The endpoint was a reduction of local electrogram to <0.15 mV.[19]

Follow-up

Patients were followed up at the outpatient clinic at 1, 4, and 7 months after the ablation procedure and every 6 months thereafter. Routine 24 or 48 h Holter monitoring was performed before each appointment, and a 12-lead electrocardiogram was obtained at each visit. Patients were asked to report to the emergency room or our arrhythmia unit for an ECG if any symptom suggestive of recurrence occurred between scheduled visits.

After the ablation procedure, all patients received anti-arrhythmic treatment for at least 1 month to protect against early recurrences and continued oral anticoagulation for a minimum of 2 months to maintain an international normalized ratio between 2.0 and 3.0. Additionally, magnetic resonance angiography was repeated at 3–6 months after the procedure to evaluate the presence of PV stenosis.

Arrhythmia recurrence was defined as a documented AF or atrial flutter episode of >30 s. Arrhythmic episodes within the first 3 months after the CPVA (healing period) were not considered in the evaluation of final success rates because they are often described as transient recurrences related to atrial inflammatory processes following RF lesions.[26]

The endpoint of the study was freedom from arrhythmia recurrence after a single CPVA procedure, without anti-arrhythmic medication.

A minimum follow-up of 3 months was required.

Statistical analysis

Continuous variables were expressed as mean $\pm$ SD. Comparisons were made using Student's *t*-test or χ^2 analysis as appropriate. The relationship between baseline variables and time to recurrence during follow-up was evaluated using survival Cox analysis methodology; relationships with $P < 0.10$ were included as covariates in the multivariable analysis. Predictors of arrhythmia recurrence were assessed with a Cox regression model using a backward stepwise procedure with criteria of $P < 0.05$ for inclusion and $P > 0.10$ for removal from the model. A two-sided *P*-value ≤ 0.05 was considered statistically significant. Analyses were performed using the SPSS 12.0 statistical package (SPSS Inc., Chicago, IL, USA).

Results

Patient characteristics

A series of 182 consecutive patients with symptomatic and drug refractory AF was included in the study. Their baseline characteristics are shown in *Table 1*. The majority (81%) of patients were male, younger than 75 years with a mean age of 51 ± 11 years, and without a markedly dilated LA. A total of 120 (66%) patients had paroxysmal AF; AF was persistent in 39 patients (21%), and the remaining 23 patients (13%) had long-standing AF.

Lone AF was diagnosed in 107 (58%) patients; 42 of these patients (23% of the total study population) were identified as endurance athletes and included in the lone AF sport group.

Table 1 Clinical and echocardiographic parameters at baseline

Baseline characteristics of patients	*n* = 182
Age (years)	51 ± 11
Male gender	148 (81%)
Hypertension	59 (32%)
Type of AF	
Paroxysmal	120 (66%)
Persistent	39 (21%)
Long-standing	23 (13%)
Structural heart disease	32 (18%)
Lone AF	107 (59%)
Endurance athletes[a]	64 (35%)
Lone AF sport group[b]	42 (23%)
AF origin	
Vagal	64 (35%)
Adrenergic	5 (3%)
Unknown	113 (62%)
AF duration (years)	6.1 ± 5.0
Echocardiography	
LAD (mm)	41.0 ± 5.9
LVEDD (mm)	51.4 ± 5.2
LVESD (mm)	32.9 ± 5.8
LVEF (%)	60.7 ± 10.3

Data are expressed as mean ± SD or number (%) of patients. AF, atrial fibrillation; LAD, anteroposterior left atrial diameter; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction.
[a]>3 h/week >10 years when arrhythmia was diagnosed (with or without any other risk factors for AF).
[b]>3 h/week >10 years when arrhythmia was diagnosed and without any other risk factors for AF (i.e. athletes with lone AF).

The clinical and echocardiographic characteristics of the lone sport AF group vs. patients with lone AF and no history of endurance sport practice and the remaining patients (the control group) are given in *Table 2*. In the lone AF sport group, there was a higher proportion of male patients, and the left ventricular end-systolic diameter was smaller than in the control group.

When we analyse baseline characteristics of the lone AF and lone AF sport groups, there are no statistically significant differences, except for a higher proportion of male patients in the lone AF sport group ($P = 0.031$).

Outcomes after circumferential pulmonary vein ablation

The mean follow-up was 18.69 ± 11.7 months.

Ablation was performed using 35.7 ± 14.8 min of RF with total fluoroscopic and procedural durations of 26.0 ± 9.3 and 122.3 ± 33.1 min, respectively. The procedural duration of ablation comprised the time between the vascular puncture and the withdrawal of the catheters (skin-to-skin time). The complications rate in the lone AF sport group was comparable with the control group (7.1 vs. 4.3%; $P = 0.45$). Overall, four patients (2.2%) suffered a transient cerebrovascular ischaemia, which was resolved under heparin with normal computed tomography scanning; three patients (1.6%) showed transient inferior myocardial ischaemia during the procedure, secondary to air embolism, resolved with sublingual NTG within a few minutes and without consequences; and two patients (1.1%) had cardiac tamponade during transseptal puncture, resolved by pericardiocentesis.

The probability of remaining free from arrhythmia at 1-year follow-up after a single CPVA procedure, based on Kaplan–Meier estimates, was similar in the lone AF sport group and controls: 59 and 48%, respectively, log-rank test $P = 0.44$ (*Figure 1*). On the other hand, the probability of remaining free from arrhythmia at 1-year follow-up after a single CPVA procedure was similar in the lone AF sport group compared with other patients with lone AF and no history of endurance sport activity (59 vs. 47%, log-rank test $P = 0.532$) (*Figure 2*).

Table 2 Clinical and echocardiographic characteristics of control group, lone AF sport group, and patients with lone AF and no history of endurance sport practice

	Control group	Athletes (lone AF sport group)	Lone AF	*P*-value[a]	*P*-value[b]
LAD (mm)	41.0 ± 6.2	41.1 ± 4.4	39 ± 6	0.883	0.174
LVEDD (mm)	51.7 ± 5.3	50.0 ± 4.3	51 ± 4.46	0.233	0.288
LVESD (mm)	33.5 ± 6.0	30.4 ± 4.7	32.5 ± 4.37	0.027	0.060
LVEF (%)	60.1 ± 10.6	62.9 ± 8.9	61.7 ± 8.5	0.152	0.610
Age (years)	52.1 ± 10.8	48.5 ± 11.0	47.3 ± 10.5	0.057	0.585
Paroxysmal AF	90 (64%)	31 (74%)	48 (74%)	0.251	0.603
Vagal AF	48 (34%)	16 (38%)	19 (36%)	0.650	0.545
Hypertension	60 (43%)	0 (0%)	0 (0%)	<0.001	
Male gender	111 (79%)	39 (93%)	50 (77%)	0.0427	0.031
Structural heart disease	32 (23%)	0 (0%)	0 (0%)	<0.001	

AF, atrial fibrillation; LAD, left atrial anteroposterior diameter; LVEDD, left ventricle end-diastolic diameter; LVESD, left ventricle end-systolic diameter; LVEF, left ventricle ejection fraction.
[a]*P*-value: control group vs. lone AF sport group.
[b]*P*-value: lone AF sport group vs. lone AF (without history of sport practice) group.

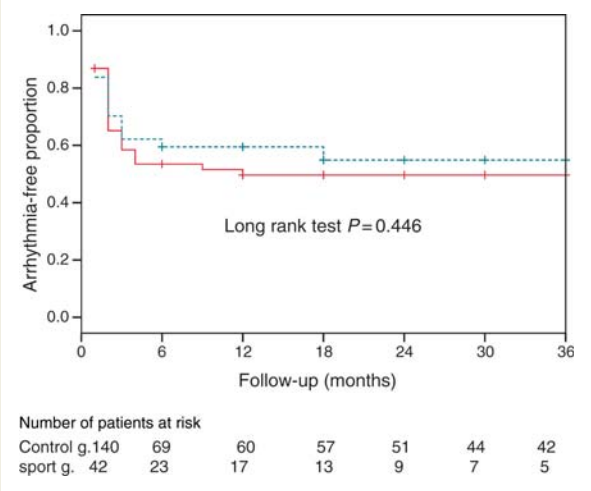

Figure 1 Kaplan–Meier curves for long-term freedom from recurrent arrhythmias after a single ablation procedure in the lone AF sport group (dashed line) and the control group (solid line).

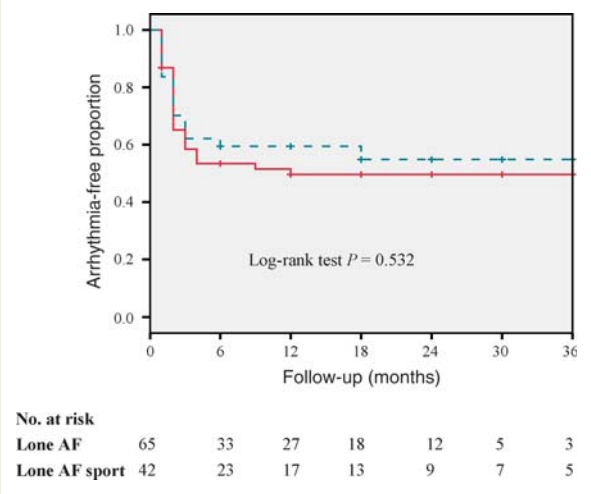

Figure 2 Kaplan–Meier curves for long-term freedom from recurrent arrhythmias after a single ablation procedure in the lone AF sport group (dashed line) and patients with lone AF and no history of exercise activity (solid line).

Table 3 shows the relationship between each baseline variable and arrhythmia recurrence. In the Cox regression multivariable analysis, after adjusting for the type of AF (paroxysmal, persistent, or long-standing), age, HTA, LA dimension, EF, LV dimensions, presence of structural cardiac disease, and regular sport practice, only LA anteroposterior diameter and long-standing AF were independent predictors of arrhythmia recurrence (*Table 4*). The ejection fraction was a predictor of AF recurrence in the univariable analysis. However, it had no independent predictive value for recurrence in the multivariable analysis.

Table 3 Relationship between each baseline variable and arrhythmia recurrence after a single ablation procedure

	Hazard ratio (95% CI)	*P*-value
Age (years)	1.004 (0.983–1.025)	0.742
Male gender	1.048 (0.598–1.838)	0.869
Hypertension	1.181 (0.743–1.877)	0.482
Paroxysmal AF	0.535 (0.344–0.831)	0.005
Structural heart disease	0.931 (0.501–1.729)	0.821
AF duration (months)	1.00 (0.997–1.003)	0.940
LAD (mm)	1.057 (1.013–1.104)	0.011
LVEDD (mm)	1.014 (0.962–1.069)	0.609
LVESD (mm)	1.036 (0.997–1.077)	0.070
LVEF (%)	0.974 (0.953–0.996)	0.020
Sport practice	0.821 (0.475–1.419)	0.479

AF, atrial fibrillation; LAD, left atrial anteroposterior diameter; LVEDD, left ventricle end-diastolic diameter; LVESD, left ventricle end-systolic diameter; LVEF, left ventricle ejection fraction.

Table 4 Final model of the Cox regression for arrhythmia recurrence after a single ablation procedure

	Hazard ratio (95% CI)	*P*-value
AF		
Paroxysmal	1 (—)	—
Persistent	1.819 (0.990–3.340)	0.054
Long-standing	2.297 (1.090–4.839)	0.029
LAD (mm)	1.069 (1.018–1.122)	0.007

Ablation was repeated in 67 patients of this series (37%), achieving a 72% overall probability of freedom from arrhythmia recurrence at 1 year without anti-arrhythmic drugs. There were no statistically significant differences in the proportion of redo procedures between the lone AF sport group (40.5%) and the control group (37.3%) ($P = 0.587$) and between the lone AF (36.4%) and the lone AF sport group ($P = 0.540$). The majority of these patients had AF recurrences (62%), atrial flutter was present in 12%, and the remaining patients had AF and atrial flutter recurrences (26%). All patients showed reconduction into the prior PV-encircling areas.

The Kaplan–Meier probability of remaining arrhythmia-free after repeated ablations was higher in the lone AF sport group (81%) at 1 year compared with the control group (63%, $P = 0.051$) (*Figure 3*).

Discussion

The main finding of the present study is that the probability of remaining free of arrhythmia recurrences after a single CPVA

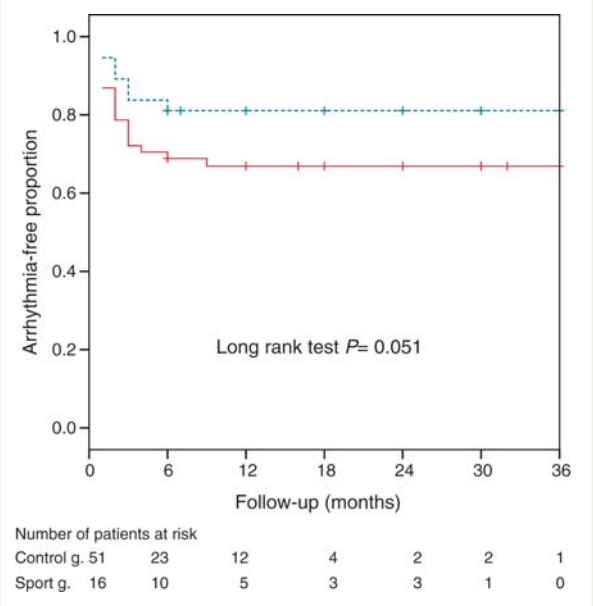

Figure 3 Kaplan–Meier curves for long-term freedom from recurrent arrhythmias after repeated ablation procedures in the lone AF sport group (dashed line) and the control group (solid line).

was similar in athletes compared with the control group. Furthermore, LA diameter and long-standing AF were the only independent predictors of recurrence.

Recent studies have shown that the prevalence of AF is higher in individuals who regularly engage in endurance sports than in control populations.[7–13] Additionally, Heidbüchel *et al.*[27] reported that a history of endurance sport activity is associated with the development of AF after ablation of atrial flutter. In contrast with these previous studies, Pelliccia *et al.*[28] reported that the incidence of lone AF among competitive athletes was uncommon and similar to that observed in the general population. However, the study was performed in young athletes at the moment of highest activity. Studies supporting the association have been performed in middle-aged individuals, after many years of sport practice. The most recent and largest epidemiological study[14] supports that this association is not a matter of selection because despite adjustment for multiple potentially confounding lifestyle factors and health conditions, vigorous exercise activity was associated with an increased risk of developing AF.

The pathophysiological mechanisms responsible for increased AF risk in individuals who practice an endurance sport remain unclear. However, it is well known that the athlete's heart is characterized by increased LA size and left ventricular mass, adaptations that may create the substrate for developing AF. Another proposed mechanism is increased vagal tone, resulting in a short refractory atrial period.[29] Experimental animal models have demonstrated that AF can be induced by acetylcholine,[30] and that increasing vagal tone shortens the atrial refractory period, which, combined with atrial stimulation, induces AF.[31]

In the present study, we did not find differences in LA or LV size between the lone AF sport group and the control group. We think the explanation could be that exercise training leads to LA and LV enlargement similar to that seen in patients with other causes of AF, such as increased afterload in hypertension.

It is worth mentioning that our data showed that a high proportion of men with AF submitted to the ablation procedure are engaged in regular endurance sport practice (35%). This proportion is significantly higher than that of males of the same age in the general population of Catalonia (15.4%), according to the data from the REGICOR study.[32] This finding is in agreement with previous studies[7–14] and further supports the association between long-term endurance sport practice and AF.

We included highly symptomatic patients younger than 75 years and without a markedly dilated LA. Therefore, this selection procedure may explain the high proportion of lone AF among our patients. Nevertheless, we think that it represents the clinical practice, as our findings are consistent with the previous ablation studies which show that 50–60% of patients do not have structural heart disease.[33–35]

Circumferential pulmonary vein ablation is established as an effective and safe treatment of AF, with success rates ranging from 30 to 85%.[20] To date, one small study by Furlanello *et al.*[22] has demonstrated high efficacy of repeated ablation procedures in a population of elite athletes; however, no data comparing endurance athletes and a control population are available. Theoretically, the effectiveness of this procedure in athletes, who are usually a younger population, could be associated with higher success rates than in the general population with AF on the basis of age. On the other hand, the pathophysiological mechanisms of AF in endurance athletes could be responsible for reducing the success of CPVA.

In the present study, we observed no difference in the effectiveness of CPVA between a population of endurance athletes with lone AF and other patients with AF after a first CPVA procedure, and found that endurance sport practice is not a predictor of the results of the ablation procedure.

Data obtained after repeated ablation procedures probably reflect a selection bias and should be interpreted with caution, since repeated ablation procedures were not performed in patients with a low probability of success.

Earlier studies reported LA anteroposterior diameter prior to the ablation procedure, paroxysmal vs. persistent AF, early recurrence of AF, age, and hypertension as independent predictors of AF recurrences.[25,35,36] Our study confirmed LA diameter and long-standing AF as the most powerful predictors of AF recurrence after CPVA; in addition, persistent AF showed a trend towards a higher probability of recurrence ($P = 0.054$).

Study limitations

One limitation of the study is the follow-up method of scheduled 24 or 48 h Holter recordings. If asymptomatic arrhythmias or non-documented symptomatic episodes occurred between routine follow-up visits, recurrence after ablation might have been missed in these patients, as previous studies have demonstrated.[37] This could have affected athletes differently than the control group, since athletes are typically well trained in monitoring heart rate and are more used to detecting pulse abnormalities. Theoretically, asymptomatic arrhythmia episodes could have been more

frequently detected among athletes. However, this potential bias is unlikely to be significant, since our data showed a trend towards fewer recurrence episodes among athletes. Another limitation is that both study groups included endurance athletes because athletes with any other identified risk factor, such as hypertension, were included in the control group. However, the main purpose of the study was to analyse the efficacy of the CPVA in 'purely' endurance sport related arrhythmia. Finally, the number of athletes with lone AF is relatively small. Therefore, further studies including a larger number of patients are required to confirm our results.

Conclusions

Circumferential pulmonary vein ablation seems to be as effective in endurance athletes as in other aetiologies of AF.

Conflict of interest: none declared.

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Usefulness of transesophageal echocardiography before circumferential pulmonary vein ablation in patients with atrial fibrillation: is it really mandatory?

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Usefulness of transoesophageal echocardiography before circumferential pulmonary vein ablation in patients with atrial fibrillation: is it really mandatory?

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Aims Transoesophageal echocardiography (TEE) is recommended prior to circumferential pulmonary vein ablation (CPVA) in patients with atrial fibrillation (AF) to identify left atrial (LA) or left atrial appendage (LAA) wall thrombi. It is not clear whether all patients undergoing CPVA should receive pre-procedural TEE. We wanted to assess the incidence of LA thrombus in these patients and to identify factors associated with its presence.

Methods and results Consecutive patients referred for CPVA from 2004 to 2009 underwent TEE within 48 h prior to the procedure. Of 408 patients included in the study, 6 patients (1.47%) had LA thrombi, persistent AF, and LA dilation. Compared with patients without thrombus, these six patients had larger LA diameter ($P = 0.0001$) and more frequently were women ($P = 0.002$), had persistent AF ($P = 0.04$), and had underlying structural cardiac disease ($P = 0.014$). The likelihood of presenting LA thrombus increased with the number of these four risk factors present ($P < 0.001$). None of the patients with paroxysmal AF and without LA dilation had LA thrombus. A cut-off value of 48.5 mm LA diameter yielded 83% sensitivity, 92% specificity, and a 10.1 likelihood ratio to predict LA thrombus appearance.

Conclusion The incidence of LA thrombus prior to CPVA is low. Persistent AF, female sex, structural cardiopathy, and LA dilation were associated with the presence of LA thrombus. Our data suggest that the use of TEE prior to CPVA to detect LA thrombi might not be needed in patients with paroxysmal AF and no LA dilation or structural cardiopathy.

Keywords Atrial fibrillation • Thrombus • Transoesophageal echocardiography • Ablation

Introduction

Catheter ablation has been shown to be successful in the treatment of atrial fibrillation (AF) and is now an accepted clinical standard of care. However, the AF ablation procedure itself has an inherent risk of stroke, which may be caused by mobilization of left atrial appendage (LAA) thrombus induced by restoration of atrial contraction or even by catheter manipulation during navigation in the left atrium. Therefore, the presence of left atrial (LA) thrombus is an established contraindication for catheter ablation of AF.[1] Nonetheless, the use of transoesophageal echocardiography (TEE) to assess atrial thrombus prior to AF ablation is variably employed. Recent data suggest that pre-ablation TEE is routinely employed in up to 72% of centres performing catheter ablation of AF.[2] The Heart Rhythm Society Consensus Statement on catheter ablation of AF recommends pre-ablation TEE to exclude LA thrombus in patients with persistent AF who present in AF; no specific recommendation is made for patients with paroxysmal AF.[1]

Despite these recommendations, there is scarce data about the real incidence of LA thrombus identified by TEE prior to AF ablation.[3,4] Concern has been raised about the intrinsic risk of TEE and the cost-effectiveness of routinely performing pre-ablation TEE in

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all persistent AF patients.[5] Finally, these recommendations imply incremental demands on already busy echo laboratories. Therefore, we aimed to determine the incidence of LA thrombus in patients undergoing catheter ablation of AF and the existence of any clinical predictors that could be used in risk stratification of these patients to improve the efficacy of TEE in this setting.

Methods

We prospectively included consecutive patients with symptomatic and drug-refractory AF referred for catheter ablation of AF between July 2004 and April 2009 in our university hospital. All patients had a complete clinical record and physical examination and all underwent transthoracic echocardiography (TTE) and TEE within 48–72 h before the ablation procedure. We excluded patients who did not undergo the TEE in our centre.

Atrial fibrillation was classified as paroxysmal, persistent, or long-standing persistent, according to AF ablation consensus.[1] Antiarrhythmic drug therapy was stopped at least five half-lives before the ablation, except in patients receiving amiodarone.

A magnetic resonance angiography of the left atrium and pulmonary veins was performed 1–5 days before ablation to integrate the images with the real-time catheter-based electroanatomic mapping and to achieve better spatial resolution and anatomical definition during ablation.

The study was approved by our hospital's ethics committee and written informed consent was obtained from all patients.

Anticoagulation therapy

We used the recently validated $CHADS_2$ score to stratify patients for stroke risk.[6] Briefly, this index measures stroke risk by assigning one point each for congestive heart failure, hypertension, age 75 years or older, and diabetes mellitus, with two points added for a history of stroke, transient ischaemic attack, or systemic embolism. Accordingly, patients with a $CHADS_2$ score ≥ 2 were treated with warfarin to maintain an international normalized ratio (INR) between 2.0 and 3.0 for at least 4 weeks before the ablation, with cessation of warfarin 3 days prior to the procedure and bridging therapy with enoxaparin (1 mg/kg every 12 h) from 3 days before until the night prior to the ablation procedure. Patients with CHADS score <2 were treated with anticoagulation or antiplatelet agents, at their physician's discretion.

Transthoracic and transoesophageal echocardiographic studies

A standard two-dimensional (2D) TTE and TEE were performed 48–72 h before the ablation procedure with a commercially available system (Sonos 7500 & IE33, Philips, Andover, MA, USA). Left atrial anteroposterior diameter was determined with M-mode scans from the long-axis parasternal view with special attention to perpendicular cursor placement as guided by 2D echo.[7] Transoesophageal echocardiography was performed with a 5 MHz multiplane transducer at the same session to investigate the presence of intracardiac thrombus. Multiple planes of the LA appendage, including a continuous sweep from 0° to 180° with short- and long-axis views of the LA appendage, were obtained from the mid-oesophagus. All images were stored and reviewed digitally off-line by two experienced echocardiographers. If a patient's rhythm during the echo scan was AF, the mean value of five measurements was performed with every echocardiographic parameter.

Circumferential pulmonary vein ablation

Catheters were introduced percutaneously through the femoral vein; a transseptal puncture was performed to access the left atrium. After transseptal access, a bolus of heparin was administered (5000–6000 IU, according to patient weight), followed by additional boluses to maintain an activated clotting time of 250–300 s. Ablation was performed under intravenous sedation with midazolam and analgesia with meperidine and phentanyl. Oxygen saturation and invasive arterial blood pressure were monitored throughout the procedure. A three-dimensional map was constructed using an electroanatomical mapping system (CARTO®, Biosense-Webster or NAVX®, St Jude Corporation) to support the creation and validation of radiofrequency lesions.

Since 2006, a 20 -mm, decapolar circular mapping catheter with a deflectable loop (Lasso®, Biosense-Webster Lasso, or Inquiry Optima®, St Jude Medical) was placed at the ostium of each pulmonary vein for mapping.

Continuous radiofrequency lesions surrounding each ipsilateral pulmonary vein were delivered as described previously.[8] Ablation lines were also deployed in most patients along the LA roof and LA posterior wall. Radiofrequency was delivered through an 8 mm or irrigated tip thermocouple-equipped catheter, using a target temperature of 55°C at a maximum output of 60 W and 45°C at 40 W, respectively.

Mitral isthmus ablation was performed by creating a radiofrequency line from the inferior lateral aspect of the left pulmonary vein lesions to the mitral annulus. This line was anatomically performed and no electrical block was assessed. A radiofrequency line was then created to connect contralateral pulmonary veins-encircling lesions through the LA roof. During the first 4 years, LA posterior wall was electrically excluded by adding another ablation line, on top of the roof line, connecting the inferior aspect of the contralateral pulmonary veins. The isolation of the posterior wall was confirmed by the absence of electrical activity and the inability to capture with pacing inside the whole encircled LA posterior region.

The endpoint was a reduction of local electrogram to <0.15 mV[9] and the establishment of a bidirectional conduction block between the LA and pulmonary veins.

Follow-up

When LA or LAA thrombus was detected, the ablation procedure was deferred for at least 2 months and TEE was repeated after optimum anticoagulation therapy. The subsequent ablations were performed if no residual thrombus was found.

Patients were followed up at the outpatient clinic at 1, 4, and 7 months and every 6 months thereafter. Routine 24 or 48 h Holter monitoring was performed before each appointment and a 12-lead electrocardiogram was obtained at each visit. Patients were asked to report for an electrocardiogram if any symptom suggestive of recurrence occurred between scheduled visits. Arrhythmia recurrence was defined as a documented AF or atrial flutter episode of more than 30 s. Arrhythmic episodes within the first 3 months after the circumferential pulmonary vein ablation (CPVA) ('healing period') were not considered in the evaluation of final success rates because they are often described as transient recurrences related to atrial inflammatory processes following radiofrequency lesions.[10]

After the ablation procedure, all patients continued oral anticoagulation for a minimum of 2 months to maintain an INR between 2.0 and 3.0. Thrombo-embolic episodes were defined by clinical and imaging criteria.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation (SD) or median and interquartile range (25–75%) as appropriate. Discrete variables are expressed as cases (%). Differences between patients with and without LA thrombus were evaluated by Mann–Whitney *U* test for unpaired data or Fisher's exact test as appropriate. A sum score was performed to build a model to predict LA thrombus, based on the significant variables identified by univariate analysis. The likelihood of LA thrombus was then calculated with χ^2 test. Receiver operator characteristic (ROC) curve analysis was performed to identify an optimal cut-off point of LA size to predict thrombus presence using likelihood ratio statistics, this value was defined as the value for which the sum of sensitivity and specificity was maximized. The area under the ROC (AUROC) value was calculated as a measure of the test's accuracy. A value of $P < 0.05$ was considered statistically significant. Analyses were performed using the SPSS 15.0 statistical package (SPSS Inc., Chicago, IL, USA).

Results

Baseline characteristics of the 408 patients included in the study are shown in *Table 1*. Mean age was 52 ± 11 years, 78% were male, and 67% of the patients received oral anticoagulation therapy. Atrial fibrillation was paroxysmal in 237 (59%), persistent in 116 (28%), and long-standing in 51 (13%).

Table 1 Clinical and echocardiographic parameters at baseline (n = 408)

Age (years)	52 ± 11
Male sex	317 (78)
HTA	161 (40.5)
Structural cardiopathy	72 (19.3)
Ischaemic	16 (4.1)
Valvular	19 (4.8)
Hypertrophic cardiomyopathy	15 (3.8)
Idiopathic	9 (2.3)
ARVD	1 (0.3)
Hypertensive	9 (2.3)
Non-compacted	2 (0.5)
Infiltrative	1 (0.3)
Number of previous CPVA procedures	1.28 ± 0.55
Type of AF	
Paroxysmal	237 (59)
Persistent	116 (28)
Long-standing	51 (13)
OAC therapy	273 (67)
AF duration (months)	64 ± 60
LA diameter (mm)	41 ± 6
LV EDD (mm)	52 ± 5
LVESD (mm)	34 ± 6
LV EF (%)	58 ± 10.
Sinus rhythm at the time of TEE	186 (45.5)

Data are expressed as mean ± SD or number (%) of patients. AF, atrial fibrillation; HTA, hypertension; OAC, oral anticoagulation therapy; LA, left atrial; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; LVEF, left ventricular ejection fraction; LV EF, left ventricular ejection fraction; TEE, transoesophageal echocardiography.

Characteristics of patients with left atrial thrombus

Transoesophageal echocardiography revealed LA thrombus in six patients (1.47%); 4 (67%) were LAA thrombus cases and 2 (33%) were LA thrombus.

Five of these six patients had been anticoagulated with warfarin for at least 4 weeks prior to the procedure (mean 36 months); bridging with enoxaparin was performed 3 days prior to the procedure. The only non-anticoagulated patient had a history of cerebral arteriovenous malformation and was treated with aspirin 100 mg/day.

$CHADS_2$ score was <2 in five patients and 2 in the remaining patient. A previous ablation procedure had been performed in one patient and TEE did not identify LA or LAA thrombus at that time. Atrial fibrillation was persistent or long-standing in all of the patients with thrombus and all of them had LA dilation (mean LA anteroposterior diameter 52.16 ± 5.6).

Follow-up of patients with left atrial thrombus

Ablation procedure was cancelled in all six patients and oral anticoagulation was continued to maintain INR 2.0–3.0. A second TEE was performed in all patients at least 2 months (mean 5 months) later; in all cases the thrombus had disappeared. Catheter ablation was then performed in two patients without complications. Another two patients had surgical AF ablation by means of video-assisted bilateral pulmonary vein isolation procedure. One of the remaining two patients underwent AV node catheter ablation and pacemaker implantation, and the other was eventually treated with a rate control strategy.

Predictors of left atrial thrombus

The univariate analysis revealed that patients with thrombus were more often female, had a larger LA diameter, had more persistent or long-standing AF and more often had structural heart disease (*Table 2*). No significant differences regarding AF duration, age or cardiac rhythm at the time of TEE were observed.

From the ROC curves (*Figure 1A* and *B*), a cut-off value of 48.5 mm LA diameter had 83% sensitivity, 92% specificity, and a likelihood ratio of 10.1 to predict LA thrombus appearance. A cut-off LA diameter value of 41.5 mm had 100% sensitivity to predict thrombus appearance, although only 50% specificity. Left atrial diameter values of 40, 45, and 50 mm had 100, 83, and 77% sensitivity, and 38.4, 71, and 94.3% specificity, respectively, to predict presence of LA/LAA thrombus.

Figure 2 shows LA thrombus prevalence stratified by number of risk factors (female sex, structural cardiopathy, LA enlargement, and persistent long-standing AF). Left atrial thrombus prevalence was 0, 0.73, 6.38, and 33.33% of patients with 0–1, 2, 3, and 4 risk factors, respectively (χ^2 55.76, $P < 0.001$).

Table 2 Characteristics of patients with and without left atrial thrombus

	No LA thrombus ($n = 402$)	LA thrombus ($n = 6$)	*P*-value
Age	53 (46,60)	55 (44.5,57.5)	0.961
Male sex	316 (79)	1 (17)	0.002
HTA	157 (39)	4 (67)	0.227
Structural cardiopathy	67 (16.6)	5 (83.3)	0.001
Ischaemic	14 (3.5)	2 (33.3)	
Hypertrophic	12 (3)	3 (50)	
Valvular	19 (4.8)	0	
Idiopathic	9 (2.14)	0	
ARVD	1 (0.25)	0	
Hypertensive	9 (2.14)	0	
Non-compacted	2 (0.5)	0	
Infiltrative	1 (0.25)	0	
Type of AF			0.004
Paroxysmal	237 (60)	0 (0)	
Persistent	113 (28)	3 (50)	
Long-standing	48 (12)	3 (50)	
OAC therapy (%)	268 (67)	5 (83)	0.668
AF duration (months)	64 ± 61	56 ± 14	0.807
LA diameter (mm)	42 (38,45)	54 (46.5,54.5)	0.0001
LVEDD (mm)	52 (50,55)	54 (44.5,55.5)	0.599
LVESD (mm)	34 (30,37	32 (25.5,35)	0.33
LVEF(%)	60 (55,65)	66 (57,68.5)	0.625
SR at the time of TEE	183 (45.5)	3 (50)	0.692

Data are expressed as median (P_{25},P_{75}) or number (%) of patients. AF, atrial fibrillation; LA, left atrial; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; LVEF, left ventricular ejection fraction; HTA, hypertension; OAC, oral anticoagulation therapy; SR, sinus rhythm; TEE, transoesophageal echocardiography.

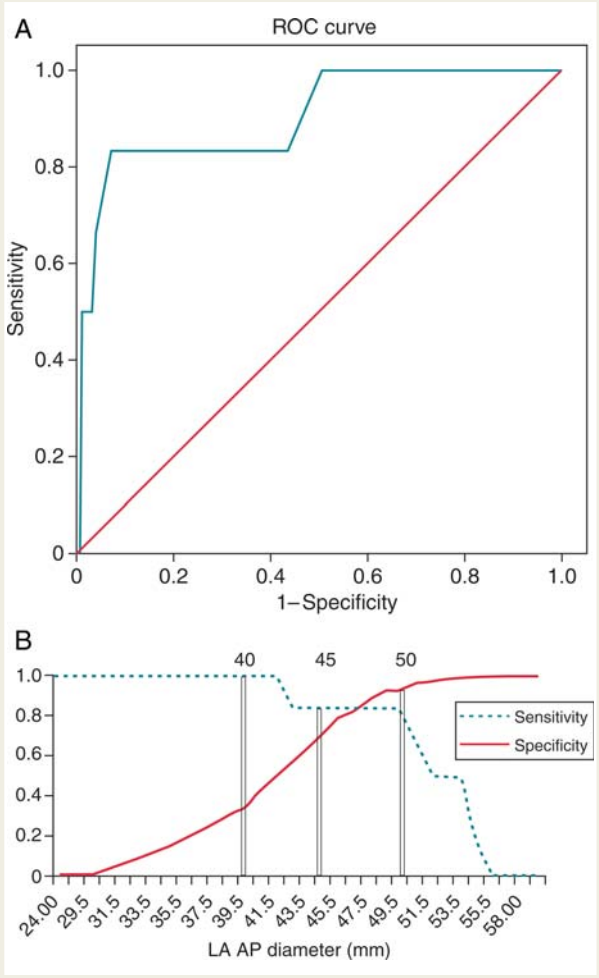

Figure 1 (*A*) Receiver-operating characteristic (ROC) analysis for LA anteroposterior diameter, as used in predicting LA or LAA thrombus. (*B*) Sensitivity (dashed line) and specificity (solid line) values according to LA anteroposterior diameter. An anteroposterior diameter of the LA larger than 48.5 mm predicted thrombus appearance with an 83.3% of sensitivity and a 91.8% of specificity. LA diameter values of 40, 45, and 50 mm had 100, 83, and 77% sensitivity, and 38.4, 71, and 94.3% specificity, respectively..

Thrombo-embolic complications

In the group of patients without thrombus, seven patients (1.71%) suffered a periprocedural transient cerebrovascular ischaemia, which was resolved under heparin with unremarkable computed tomography (CT) scanning. We did not find any correlation between the rate of thrombo-embolic complications and the type of catheter used (i.e. irrigated vs. 8 mm) for the ablation.

There were no cases of acute cerebrovascular ischaemia in the group of patients with thrombus. One patient suffered a thrombo-embolic episode 1 month after TEE revealed thrombus disappearance and the ablation procedure had been performed. Although she was treated with anticoagulant therapy, she had a subtherapeutic INR value (1.6) at the time of the embolic episode.

Discussion

The main findings of the present study were that among patients with AF undergoing CPVA: (i) the prevalence of LA/LAA thrombi was low (1.47%,); (ii) atrial fibrillation type (persistent or long-standing persistent AF), female sex, presence of structural cardiopathy, and a dilated LA diameter were associated with higher risk of LA thrombus; (iii) all the patients with LA/LAA thrombus had persistent or long-standing AF and a dilated LA. Therefore, our data suggest that we might avoid TEE prior to catheter ablation in patients with paroxysmal AF, no structural cardiopathy and a non-dilated left atrium.

Few studies have analysed the predictors of LA thrombus in patients undergoing CPVA. Scherr *et al.*[3] found that incidence of LA thrombus was 1.6% in CPVA patients, which is consistent with our data; they reported that a $CHADS_2$ score ≥ 2 and a large LA diameter were independent predictors of LA thrombus, while type of AF or rhythm at the time of TEE were not. Puwanant *et al.*[4] have recently described that the prevalence of LA/LAA

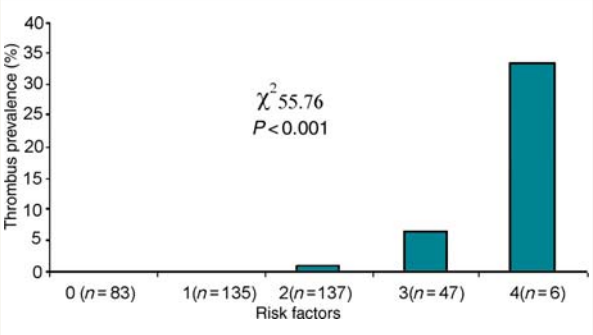

Figure 2 Bar graph displaying LA thrombus prevalence stratified by the number of risk factors (female sex, structural cardiopathy, LA anteroposterior diameter, and type of AF). Left atrial thrombus was present in 0, 0.73, 6.38, and 33.33% of patients with 0–1, 2, 3, or 4 risk factors, respectively (χ^2 55.76, $P < 0.001$).

thrombus in this population is low (0.6%), and the most powerful predictors of LA/LAA thrombus are an impaired left ventricular function (<35%) and a history of congestive heart failure. In a more recent study, McCready *et al.*[11] reported that the incidence of thrombus in patients undergoing AF ablation was 1.9%; hypertension, advanced age, and cardiomyopathy were independently associated with thrombus. Similarly, Yamashita *et al.*[12] detected LA thrombus in 2.9% of patients. In this study, persistent AF, advanced age, and structural heart disease were independent positive predictors of LA thrombus prior to LA ablation.

A multicentre national survey describing practice at 11 Canadian teaching hospitals,[13] found no differences in the thrombo-embolic events rate in patients with non-dilated LA diameter and paroxysmal AF either undergoing a TEE routinely or according to selection criteria prior to catheter ablation; indeed, the incidence of thrombo-embolic events was very low (0.49%).

Gula *et al.*[14] developed a model to assess the efficacy and costs of routine use of TEE prior to AF ablation using simulations. They concluded that routine TEE use might detect LA thrombi and prevent stroke in some patients with an incremental cost-effectiveness ratio of $226 608 per quality adjusted life year. However, in high-risk patients the cost-effectiveness ratio was much lower ($2232 per quality adjusted life year). Therefore, they also suggested that TEE might not be warranted in a subgroup of patients with low risk.

Contrary to these studies, previously reported rates of LA thrombus in patients with AF undergoing external electrical cardioversion are high, with an incidence that ranges from 6 to 18%.[15–19] The discrepancies in the atrial thrombus incidence data may have been related to patient selection criteria. Studies that assess the presence of LA thrombus before a cardioversion procedure include a markedly higher risk population whereas patients submitted to CPVA have a lower prevalence of significant comorbidities. However, despite the differences in thrombus incidence, all of these trials have shown a high rate of thrombus resolution after adequate therapeutic anticoagulation,[20,21] which emphasizes the importance of careful anticoagulation treatment and monitoring in these patients.

In the present study, all patients with thrombus had received anticoagulant therapy for at least 4 weeks prior to the TEE and the follow-up TEE studies confirmed thrombi disappearance. Therefore, thrombus resolution might be explained by a longer and a closer INR monitoring of oral anticoagulation therapy in this group of patients. In addition, LA thrombus could also result from the withdrawal of oral anticoagulant therapy prior to catheter ablation, identifying a vulnerable period between stopping oral anticoagulation and commencing subcutaneous low-molecular-weight heparin. However, previous studies[4] have identified LA/LAA thrombus despite a close monitoring of INR in these patients and continuation of anticoagulation until the time of CPVA, revealing that oral anticoagulation therapy does not fully preclude thrombus formation in high-risk patients undergoing CPVA.

There are conflicting data about association of embolic events and presence of LA thrombus. Previous studies[22] have described that LA thrombus can predict embolic episodes in patients with AF. However, other studies have not found a significant association between LA thrombus and embolic events.[23,24] In our study, only one patient with LA thrombus suffered a thrombo-embolic episode during follow-up. However, it happened 1 month after TEE had revealed thrombus disappearance and the ablation procedure had been performed; moreover, the patient had a subtherapeutic INR value (1.6) at the time of the embolic episode.

Recently, CT has also been used to identify LA and LAA thrombus in patients with AF referred for pulmonary vein isolation.[25–30] In a cohort of 1221 patients undergoing catheter ablation of AF, Khan *et al.*[31] found zero incidence of LA or LAA thrombus in paroxysmal AF patients with normal ejection fraction, suggesting that pre-screening with CT is likely to be sufficient in paroxysmal AF patients with normal left ventricular function and TEE could be avoided. However, CT requires relatively large doses of radiation, is not available in most centres and is expensive. In addition, time and experience are required for accurate interpretation.

Study limitations

This is an observational single centre study and the number of patients with thrombus was relatively small, thus limiting the power of statistical analysis for finding predictors of LA thrombus. Additionally, because data on INR levels from 4 weeks prior to ablation and TEE were not available, the extent to which potentially subtherapeutic INR was responsible for the LA thrombi found in this study could not be ascertained.

Conclusions

The incidence of LAA thrombus prior to CPVA is low. Persistent AF, female sex, presence of structural cardiopathy, and a dilated left atrium were associated with the presence of LA and LAA thrombus. We did not observe LA thrombus in patients with paroxysmal AF referred to CPVA. Our data suggest that the use of TEE for detecting LAA thrombi in male patients with paroxysmal AF, no structural cardiopathy and a non-dilated left atrium might not be needed. Randomized and multicentre studies are warranted to definitely answer the question regarding the need of the TEE in all patients undergoing AF ablation.

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Conflict of interest: none declared.

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Evolución de la mejora en los resultados y las complicaciones de la ablación por catéter de la fibrilación auricular: aprendizaje, técnicas y metodología

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Artículo original

Evolución de la mejora en los resultados y las complicaciones de la ablación por catéter de la fibrilación auricular: aprendizaje, técnicas y metodología

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Protocolo
Complicaciones
Curva de aprendizaje

RESUMEN

Introducción y objetivos: Los resultados y las complicaciones del procedimiento de ablación de fibrilación auricular varían ampliamente entre los diferentes centros. Nuestro objetivo es analizar los resultados y las complicaciones derivadas de este procedimiento en nuestro centro e identificar los factores predictores de éxito y de seguridad.
Métodos: Entre 2002 y 2009 se realizó un total de 726 procedimientos de ablación de fibrilación auricular. Basándonos en la aplicación sistemática de un protocolo de anticoagulación y sedación consciente desde enero 2008, podemos establecer dos estrategias de ablación que constituyen dos grupos bien diferenciados: grupo A, constituido por 419 procedimientos realizados antes de enero 2008, y grupo B, formado por 307 procedimientos realizados después.
Resultados: El 60,9% de los pacientes no presentaron recurrencia arrítmica tras varios procedimientos durante un seguimiento medio de 8,7 meses. Con un único procedimiento, la tasa total de éxito fue del 41%, significativamente mayor entre los pacientes del grupo B (el 51,6 frente al 35,2% de éxito en el grupo A; p = 0,001). Hubo un total de 31 complicaciones mayores (4,2%); 26 en el grupo A (6,2%) y 5 en el grupo B (1,6%) (p = 0,002). La protocolización del procedimiento fue un factor predictor de la ausencia de complicaciones (odds ratio = 0,406; intervalo de confianza del 95%, 0,214-0,769; p < 0,006).
Conclusiones: La aplicación sistemática de un protocolo de anticoagulación y sedación consciente se asocia a la mejora de los resultados y la reducción de las complicaciones en el procedimiento de ablación de fibrilación auricular. Otros factores no evaluados en este estudio, como la curva de aprendizaje de los operadores y la progresiva mejora tecnológica, pueden haber influido en los cambios observados.

Improved Outcomes and Complications of Atrial Fibrillation Catheter Ablation Over Time: Learning Curve, Techniques, and Methodology

Keywords:
Catheter ablation of atrial fibrillation
Protocol
Complications
Learning curve

ABSTRACT

Introduction and objectives: The outcomes of atrial fibrillation ablation procedures vary widely between different centers. Our objective was to analyze the results and complications of this procedure in our center and identify factors predicting the efficacy and safety of atrial fibrillation ablation.
Methods: In total, 726 atrial fibrillation ablation procedures were performed in our center between 2002 and 2009. Beginning in January 2008, a protocol for anticoagulation and conscious sedation was systematically applied. Outcomes and complications could therefore be compared in 2 well-differentiated groups: group A included 419 procedures performed prior to 2008 and group B included 307 procedures completed after 2008 using the new protocol.
Results: During an average follow-up of 8.7 months, 60.9% of patients were arrhythmia-free after one or repeat procedures. After only 1 procedure, the success rate was 41% and significantly higher in group B (51.6% vs 35.2% in group A; *P*=.001). There were 31 major complications (4.2%), 26 in group A (6.2%) and 5 in group B (1.6%) (*P*=.002). The implementation of the new protocol was an independent predictor of the absence of complications (odds ratio=0.406; 95% confidence interval, 0.214-0.769; *P*<.006).

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Conclusions: Systematic application of an anticoagulation and conscious sedation protocol is associated with improved results and fewer complications of atrial fibrillation ablation. Factors not evaluated in the present study, such as operator experience and ongoing improvements in atrial fibrillation ablation technology, could have influenced these findings.

Full English text available from: www.revespcardiol.org

Abreviaturas

AI: aurícula izquierda
FA: fibrilación auricular
HNF: heparina sódica no fraccionada
RF: radiofrecuencia
SAOS: síndrome de apnea obstructiva del sueño
VP: venas pulmonares

INTRODUCCIÓN

En la última década, la ablación con catéter de la fibrilación auricular (FA) se ha convertido en un procedimiento habitual de práctica clínica. Paralelamente a la progresiva curva de aprendizaje de los operadores, con los años se ha producido una notable mejora tecnológica y la sistematización de la técnica[1–3]. Sin embargo, hay pocos datos en la literatura acerca de los beneficios derivados de la modificación de la técnica juntamente con la adquisición de experiencia de los operadores y la evolución de la tecnología.

Debido a la rápida expansión de las indicaciones de la ablación y la demanda creciente de la ablación de la FA[4–8], resulta obligado tratar de identificar y establecer un procedimiento seguro, así como analizar la tasa de complicaciones reales que se da en cada centro.

El objetivo del presente estudio es analizar los resultados y las complicaciones sufridas por los pacientes sometidos a la ablación percutánea de las venas pulmonares (VP) en nuestro centro los últimos 7 años, para así identificar los posibles factores predictores de éxito en el tratamiento de la FA y las potenciales fuentes de complicaciones.

MÉTODOS

Entre octubre de 2002 y diciembre de 2009, se realizaron en nuestro centro 726 procedimientos de ablación percutánea de las VP mediante un sistema de cartografía tridimensional no fluoroscópica (CARTO® o NAVX®) en un total de 542 pacientes.

Se sometió sistemáticamente a todos los pacientes a un ecocardiograma transesofágico en las 48 h previas a la ablación, para descartar la presencia de trombos intracavitarios. Asimismo se realizó una tomografía computarizada (TC) o resonancia magnética (RM) de la aurícula izquierda (AI) y de las VP en un 74,2% de los procedimientos, con el fin de integrar las imágenes con el sistema de cartografía electroanatómica y adquirir mejores resolución espacial y definición anatómica durante el procedimiento de ablación.

Se suspendió la anticoagulación oral los 3 días previos a la ablación, con el consiguiente inicio de heparina de bajo peso molecular el día antes del procedimiento.

Desde enero de 2008, todos los procedimientos se realizaron según un protocolo de anticoagulación y sedación consciente (tabla 1). Los pacientes sometidos a este régimen de anticoagulación y sedación protocolizada constituyeron el grupo B, mientras que los pacientes pertenecientes al grupo sometido a la ablación de VP antes de 2008 constituyeron el grupo A.

Todos los pacientes firmaron el consentimiento informado antes del procedimiento y el estudio fue aprobado por el comité ético de nuestro centro.

Procedimiento de ablación

El procedimiento de ablación percutánea se llevó a cabo a través de un acceso venoso femoral, con monitorización de la saturación arterial de oxígeno y monitorización invasiva de la presión arterial. Tras una doble punción transeptal, se accedió a la AI, donde se situó el catéter de ablación y, desde el año 2006, el catéter circular (Lasso®, Biosense-Webster Lasso, o Inquiry Optima®, St. Jude Medical) para registro y estimulación. A continuación, se administró heparina sódica no fraccionada (HNF) según la estrategia establecida. Se realizó un mapa tridimensional de la AI y las estructuras adyacentes mediante sistema de navegación

Tabla 1
Protocolo de anticoagulación y sedación consciente aplicado sistemáticamente en los procedimientos de ablación de la fibrilación auricular realizados desde enero de 2008

Protocolo de anticoagulación periprocedimiento
Dosis inicial, administrada justo después de la realización de la punción transeptal
a. < 75 kg: 5.000 UI HNF
b. > 75 kg: 6.000 UI HNF
Control del ACT cada 10 min hasta alcanzar ACT > 200 s
Si el ACT es:
a. 150-200 s, administrar 3.000 UI HNF, con nuevo control de ACT a los 10 min
b. 201-250 s, administrar 2.000 UI HNF, con nuevo control de ACT a los 30 min
c. 250 s, no administrar HNF, con nuevo control de ACT a los 30 min
Protocolo de anticoagulación tras el procedimiento
En las siguientes 6 h, reiniciar anticoagulación, administrando HBPM a dosis de 1 mg/kg/12 h, a la vez que se reinicia warfarina hasta lograr dosis óptimas de anticoagulación (INR > 2). Mantener anticoagulación oral durante al menos 2 meses. Su interrupción podrá realizarse en ausencia de un riesgo > 1 según la escala CHADS
Sedación consciente
Al inicio
Dolantina 25 mg + midazolam 1 mg en bolo ± fentanilo 30 µg
Justo antes de la punción transeptal
Fentanilo, < 65 kg: 30 ml/h perfusión; ≥ 65 kg: 40 ml/h (300 µg/120 ml SSF = 2 amp./120 ml SSF)
Justo antes de la aplicación de radiofrecuencia
Fentanilo 75 µg (5 ml) bolo ± midazolam 1-2 mg adicional bolo en casos necesarios

ACT: tiempo de coagulación activado; amp.: ampolla; HBPM: heparina de bajo peso molecular; HNF: heparina no fraccionada; INR: razón normalizada internacional; SSF: suero salino fisiológico.

Tabla 2
Características basales de los pacientes y diferencias entre subgrupos atendiendo a la realización de la ablación antes y después de enero de 2008

Características basales de pacientes	Total (n = 542)	Grupo A (< 01/08) (n = 270)	Grupo B (> 01/08) (n = 272)	p
Edad	53,1 ± 10,7	52,4 ± 11	54 ± 10	0,086
Sexo masculino	77%	76,6%	77,6%	0,792
Tipo arritmia				
Paroxística	51,3%	52,4%	49,8%	0,547
Persistente	31,2%	27,4%	36,7%	0,023
Persistente larga evolución	13,4%	14,7%	11,6%	0,317
Flutter izquierdo	4%	5,5%	1,9%	0,035
Duración mínima (meses)	62,3 ± 60,9	65,2 ± 59,8	56,7 ± 62,7	0,173
HTA	42,2%	42,7%	41,6%	0,791
Ausencia de cardiopatía	78,8%	77,2%	78,6%	0,710
Taquimiopatía	7,3%	6,9%	7,9%	
Cardiopatía valvular	4,9%	5,9%	3,3%	
AI (mm)	42 ± 5,6 (25-59 mm)	41,6 ± 5,4	42,7 ± 5,8	0,025
FE	58,3 ± 9,7 (15-84%)	58,4 ± 10	58,1 ± 9,3	0,768
DTDVI (mm)	52,7 ± 5,4	52,4 ± 5,3	53,1 ± 5,5	0,170
DTSVI (mm)	34,1 ± 6,2	33,7 ± 5,8	34,7 ± 6,6	0,151
SAOS[a]	19,4%	18,1	21,5	0,411
IMC	27,8 ± 3,7	27,7 ± 3,4	28,6 ± 4,8	0,284
Sobrepeso/obesidad	79,5%	79,7%	78,4%	0,605
Deportistas de alto rendimiento[b]	15,7%	13,9%	18,1%	0,244

AI: aurícula izquierda; DTDVI: diámetro telediastólico de ventrículo izquierdo; DTSVI: diámetro telesistólico de ventrículo izquierdo; FE: fracción de eyección; HTA: hipertensión arterial; IMC: índice de masa corporal; SAOS: síndrome de apnea obstructiva del sueño.
[a] Pacientes con alto riesgo según el cuestionario de Berlín que presentan un índice de apnea-hipopnea > 10 o pacientes portadores de aparatos de ventilación no invasiva con presión positiva de la vía aérea o presión positiva coninua de la vía aérea nocturna al inicio del estudio[5].
[b] Deportistas de alto rendimiento: pacientes con práctica deportiva vigorosa, regular y prolongada, al menos 3 h/semanales durante > 2 años[7].

CARTO® (Biosense Webster) o NavX® (St. Jude Medical). Además, siempre que fue posible, se integraron las imágenes de RM o de TC para optimizar la reconstrucción anatómica. La radiofrecuencia (RF) se aplicó con un catéter de ablación de 8 mm o de punta irrigada de 3,5 mm a una temperatura objetivo de 55 o 45 °C y una salida máxima de 60 o 40 W respectivamente. Se realizaron lesiones continuas de RF cercando las VP homolaterales a nivel astral. Además, se realizaron líneas de ablación en la pared posterior, el techo de la AI y el istmo mitral y se procedió a la ablación de las áreas con alta fragmentación de los electrogramas locales en algunos subgrupos de pacientes, lo que se determinó en función del tipo de FA o el tamaño auricular. Por otra parte, la participación de nuestro centro en estudios aleatorizados contribuyó también a variar la metodología empleada respecto a la realización de las líneas o ablación de los electrogramas fragmentados en determinados grupos de pacientes.

El objetivo del procedimiento era la disminución del voltaje de los electrogramas locales de las VP < 0,15 mV en los pacientes en quienes no se utilizó catéter circular o la desaparición de los potenciales de VP en el catéter circular y la comprobación del bloqueo bidireccional entre la AI y las VP. El bloqueo de la línea del techo se comprobó por la presencia de dobles potenciales y la activación caudocraneal de la pared posterior. El aislamiento de la pared posterior se comprobó por la desaparición de potenciales y la falta de captura auricular con captura local. No se procedió a comprobar sistemáticamente el bloqueo del istmo mitral en los pacientes sin antecedentes de *flutter* izquierdo.

En el grupo A se administró midazolam y fentanilo durante el procedimiento, a juicio del operador, mientras que la sedación en el grupo B respondió a una estrategia sistemática consistente en dolantina, midazolam y fentanilo (tabla 2).

Con respecto a la estrategia de la anticoagulación en el grupo A, se limitó a la administración de un bolo inicial de HNF, monitorizando de manera variable el tiempo de coagulación activado (ACT) y administrando cantidades de heparina variables, a juicio del operador; se aceptaron anticoagulaciones < 250 ms. Sin embargo, en el grupo B se administró un bolo inicial de 5.000 o 6.000 UI de HNF, según el peso del paciente, seguido de una monitorización regular y establecida del ACT y la administración de heparina según la dosis establecida hasta alcanzar valores comprendidos entre 250 y 300 ms.

Seguimiento

Tras la ablación, siguiendo las directrices acordadas por el grupo de expertos de la *Heart Rhythm Society/European Heart Rhythm Association/European Cardiac Arrhtymia Society*[4,5], la anticoagulación tras la ablación se mantuvo en todos los pacientes durante al menos 3 meses, y se interrumpió o se continuó según las recomendaciones actuales basadas en la escala de riesgo $CHADS_2$. Interrumpir o mantener el tratamiento antiarrítmico durante el seguimiento se realizó a criterio del cardiólogo. El seguimiento de los pacientes se llevó a cabo con visitas cada 3-6 meses durante al menos 1 año. Cada visita incluyó la realización de un ECG de superficie y un Holter-ECG de 48 h. Entre los 6 y los 9 meses, se llevó a cabo un ecocardiograma transtorácico y una TC o RM de las VP a fin de descartar complicaciones diferidas.

Se definió la recurrencia arrítmica como cualquier episodio de taquiarritmia auricular con una duración > 30 s registrado más allá de los primeros 3 meses de la ablación. Se consideró el periodo correspondiente a los primeros 3 meses tras la ablación como el periodo de blanqueo o ventana, de modo que los eventos arrítmicos que tuvieron lugar en ese periodo no se contabilizaron como recurrencias[4].

Se registraron las complicaciones clínicamente relevantes relacionadas con el procedimiento de ablación. Las complicaciones mayores se definieron como las que supusieron riesgo vital, causaron daño permanente o requirieron intervención terapéutica y prolongación de la estancia hospitalaria[9].

Análisis estadístico

Las variables continuas se expresan como media ± desviación estándar y las variables categóricas, como porcentajes. Las diferencias en las características basales de los pacientes halladas entre los procedimientos realizados antes y después de la fecha de la protocolización de la anticoagulación y sedación, así como entre los procedimientos exitosos y los no exitosos y entre los libres de complicaciones y con complicaciones clínicamente relevantes, se analizaron usando los estadísticos χ^2 y t de Student, aplicando un valor de $p < 0,05$ como valor estadísticamente significativo. Para determinar el éxito de la técnica, se analizó la supervivencia libre de recurrencia arrítmica mediante el método de Kaplan-Meier, empleando el modelo de regresión de Cox para el análisis multivariable de todos los factores significativos. Finalmente, para determinar la existencia de factores predictores independientes de complicaciones, se forzó la introducción de todos los factores significativos del análisis univariable mediante el modelo de regresión logística binaria, estimando la *odds ratio* (OR) y tomando $p < 0,05$ como valor estadísticamente significativo.

RESULTADOS

Desde octubre de 2002 hasta diciembre de 2009, se realizaron 726 procedimientos de ablación de VP mediante sistema de cartografía no fluoroscópica en un total de 542 pacientes. Las características basales de la población se muestran en la tabla 2. El 77% de los pacientes eran varones, con una media de edad de 53 años; el 21,2% tenía cardiopatía estructural y el 42,2%, hipertensión. El diámetro AP medio de la AI fue de 42 mm y la fracción de eyección del ventrículo izquierdo estaba conservada en la mayoría de los pacientes. El 51,3% de los pacientes presentaban FA paroxística; el 31,3%, FA persistente; el 13,4%, FA persistente de larga evolución, y un 4%, *flutter* auricular izquierdo. Requirieron al menos un segundo procedimiento 153 pacientes (el 28,2% del total de pacientes), lo que representa un total de 184 reablaciones.

Resultados de la ablación

La probabilidad general de éxito con sólo un procedimiento de ablación tras un seguimiento máximo de 24 meses fue del 41,1% (el 51,6% de los pacientes del grupo B frente al 35,2% del grupo A; p = 0,001), y se elevó al 60,9% tras repetir el procedimiento. Del total de recurrencias, el 75,3% presentaba de forma predominante FA y el 24,7%, *flutter* auricular atípico. En la tabla 3 se muestran las características de los pacientes con y sin recurrencias arrítmicas tras la primera ablación. Tal y como se aprecia en las curvas de supervivencia representadas tras un primer procedimiento, los pacientes con FA no paroxística (fig. 1A), hipertensión arterial (fig. 1B), AI dilatada (fig. 1C) y síndrome de apnea obstructiva del sueño (SAOS) (fig. 1D) presentaron más recurrencias arrítmicas durante el seguimiento. La tabla 4 muestra las variables predictoras de recurrencia, y la hipertensión arterial y el SAOS resultaron ser factores predictores de recurrencia independientes tras un primer procedimiento de ablación. Tener dilatada la AI (> 44 mm) y una FA no paroxística mostraron una tendencia a favor de las recurrencias, pero no alcanzaron la significación estadística en el análisis multivariable. La presencia de cardiopatía estructural o la realización de la línea mitral no fueron predictores independientes de recurrencia.

Complicaciones de la ablación

Hubo un total de 61 complicaciones clínicamente relevantes (8,4%): 48 pertenecientes a procedimientos del grupo A (11,45%) y 13 a procedimientos del grupo B (4,2%), con diferencia estadísticamente significativa (p = 0,002) (tabla 5). En total, 31 (4,2%) fueron clasificadas como graves o mayores, y resultaron significativamente más frecuentes en los procedimientos del grupo A (26; 6,2%) que en el B (5; 1,6%; p = 0,002), y 30 (4,1%) fueron clasificadas como complicaciones menores, sin diferencias estadísticamente significativas entre los grupos (22 en el grupo A, el 5,2%, y 8 en el grupo B, el 2,6%; p = 0,129). Las diferencias

Tabla 3
Diferencias en las características basales entre los pacientes con y sin recurrencias tras un primer procedimiento

Resultados de la ablación (procedimiento) 24 meses de seguimiento máximo	Recurrencia arrítmica (58,9%)	No recurrencia arrítmica (41,1%)	p
Grupo A/B	64,8% grupo A frente a 48,4% grupo B	35,2% grupo A frente a 51,6% grupo B	0,001
Edad (años)	53,6 ± 10,8	52,4 ± 10,8	0,267
Sexo	59% varones frente a 58,4% mujeres	41% varones frente a 41,6% mujeres	0,917
HTA	66,7% HTA frente a 52,5% normotensos	33,3% HTA frente a 47,5% normotensos	0,003
AI dilatada (> 44 mm)	69% AI dilatada frente a 52,9% AI no dilatada	31% AI dilatada frente a 47,1% AI no dilatada	0,003
FE (%)	58,1 ± 9,6	58,7 ± 9,3	0,584
Cardiopatía estructural	68,1% CP frente a 56,3% no CP	31,9% CP frente a 43,7% no CP	0,042
FAPx	54,8% FAPx frente a 65% FA no Px	45,2% FAPx frente a 35% FA no Px	0,031
Duración arritmia (meses)	64,2 ± 50,7	59,9 ± 61,4	0,463
SAOS	77,1% SAOS frente a 55,3% no SAOS	22,9% SAOS frente a 44,7% no SAOS	0,001
IMC	28,1 ± 3,4	27,3 ± 4	0,166
Tiempo EEF (min)	144 ± 51,7	147,6 ± 49,3	0,542
Tiempo RF (s)	2.689 ± 1.195	2.686 ± 1.184	0,984
LT	61,1% LT frente a 47,8% no LT	38,9% LT frente a 52,2% no LT	0,066
LM	65,2 LM frente a 47% no LM	34,8% LM frente a 53% no LM	0,003

AI: aurícula izquierda; CP: cardiopatía; EEF: estudio electrofisiológico; FAPx: fibrilación auricular paroxística; FE: fracción de eyección; HTA: hipertensión arterial; IMC: índice de masa corporal; LM: línea mitral; LT: línea del techo; RF: radiofrecuencia; SAOS: síndrome de apnea obstructiva del sueño.
Grupo A: antes de enero de 2008; Grupo B: después de enero de 2008.

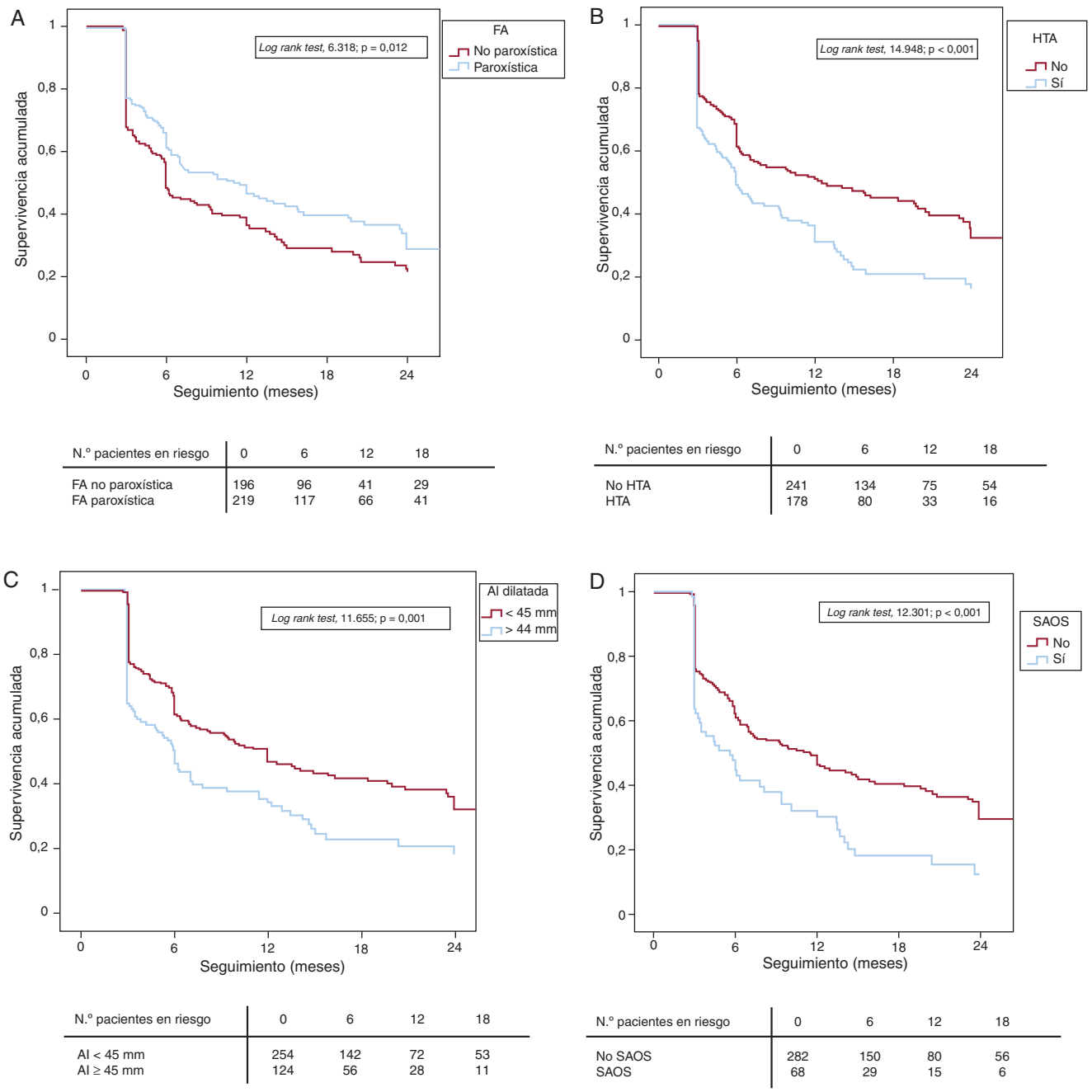

Figura 1. A: análisis de la supervivencia (Kaplan-Meier); seguimiento libre de recurrencia arrítmica tras un primer procedimiento de ablación, atendiendo al tipo de fibrilación auricular. B: análisis de la supervivencia (Kaplan-Meier); seguimiento libre de recurrencia arrítmica tras un primer procedimiento de ablación entre pacientes hipertensos y normotensos. C: análisis de la supervivencia (Kaplan-Meier); seguimiento libre de recurrencia arrítmica tras un primer procedimiento de ablación entre los pacientes con diámetro de aurícula izquierda > 44 o < 45 mm. D: análisis de la supervivencia (Kaplan-Meier); seguimiento libre de recurrencia arrítmica tras un primer procedimiento de ablación en los pacientes con y sin síndrome de apnea obstructiva del sueño. AI: aurícula izquierda; FA: fibrilación auricular; HTA: hipertensión auricular; SAOS: síndrome de apnea obstructiva del sueño.

Tabla 4
Análisis multivariable: factores independientes predictores de recurrencia arrítmica

Variables	HR	IC95%	p
HTA	1,502	1,102-2,046	0,010
SAOS	1,420	1,008-2,001	0,045
AI dilatada	1,293	0,945-1,769	0,108
FA paroxística	0,841	0,624-1,133	0,256

AI: aurícula izquierda; FA: fibrilación auricular; HR: *hazard ratio;* HTA: hipertensión arterial; IC95%: intervalo de confianza del 95%; SAOS: síndrome de apnea obstructiva del sueño.

observadas entre subgrupos se debieron principalmente a una reducción de las complicaciones embólicas (coronarias y cerebrovasculares), tal y como se aprecia en la tabla 5. Registramos un total de 9 embolias coronarias de aire (1,2%), todas transitorias y con completa resolución de la clínica anginosa y la elevación del segmento ST en el ECG con nitroglicerina endovenosa. De ellas, 8 (1,9%) tuvieron lugar con anterioridad a la aplicación del protocolo especificado (grupo A) y 1 (0,3%) después (grupo B). Igualmente registramos un total de 9 accidentes isquémicos cerebrales transitorios (AIT). El resto de las complicaciones mayores, a excepción de los taponamientos pericárdicos (7; 1%),

Tabla 5
Diferencias en las complicaciones de la ablación de las venas pulmonares según la protocolización del procedimiento (grupo A: procedimientos realizados antes de enero de 2008, sin protocolización; grupo B: procedimientos realizados después de enero de 2008, protocolizados)

Complicaciones	Totales (n = 726)	Grupo A (n = 419)	Grupo B (n = 307)	p
Mayores	31 (4,3)	26 (6,2)	5 (1,6)	0,002
AIT	9 (1,2)	8 (1,9)	1 (0,3)	0,087
Embolia coronaria	9 (1,2)	8 (1,9)	1 (0,3)	0,087
Taponamiento pericárdico	7 (1)	6 (1,4)	1 (0,3)	0,248
Rotura subvalvular mitral	1 (0,1)	0	1 (0,3)	0,423
TEP	1 (0,1)	1 (0,2)	0	0,392
Seudoaneurisma femoral	4 (0,5)	3 (0,7)	1 (0,3)	0,642
Menores	30 (4,1)	22 (5,2)	8 (2,6)	0,129
Punción transeptal complicada	23 (3,2)	16 (3,8)	7 (2,3)	0,290
Pericarditis	3 (0,4)	3 (0,7)	0	0,267
Esofagitis	2 (0,3)	1 (0,2)	1 (0,3)	0,825
Estenosis VP asintomática	2 (0,3)	2 (0,5)	0	0,511
Totales	61 (8,4)	48 (11,4)	13 (4,2)	0,002

AIT: accidente isquémico transitorio; TEP: tromboembolia pulmonar; VP: venas pulmonares.
Los datos expresan n (%).

a pesar de su gravedad, fueron excepcionales. Hubo un total de 4 seudoaneurismas femorales (0,6%), los cuales requirieron la reparación quirúrgica de la arteria. Mención especial merece una rotura del aparato subvalvular mitral por atrapamiento del catéter circular durante la cartografía electroanatómica de la AI, que requirió reparación quirúrgica urgente de la válvula mitral, y una perforación cardiaca por desgarro de la unión venoauricular de la VP superior izquierda durante la cartografía, que requirió pericardiocentesis urgente y sutura quirúrgica del desgarro. En cuanto a las complicaciones menores, no hubo diferencias en la interrupción del procedimiento debido a complicación de la punción transeptal con punción pericárdica o aórtica (sin taponamiento) (el 3,8% en el grupo A y el 2,3% en el grupo B; p = 0,29). Registramos 3 pericarditis con derrame pericárdico no severo asociado (0,4%), 2 (0,3%) esofagitis (clínica de disfagia transitoria con dolor retroesternal urente asociado, sin evidencia de fístula esofagicoauricular), y 2 pacientes (0,3%) presentaron estenosis significativas de VP (definida como reducción a menos del 50% del calibre vascular de al menos una VP), aunque sin repercusión clínica. Los únicos factores relacionados de manera estadísticamente significativa con mayor prevalencia de complicaciones totales fueron la protocolización del procedimiento, el empleo de catéter circular (ambos protectores) y el sexo femenino (tabla 6); la protocolización del procedimiento (OR = 0,406; intervalo de confianza del 95% [IC95%], 0,214-0,769; $p < 0,006$) y el sexo masculino (OR = 0,503; IC95%, 0,275-0,919; $p < 0,026$) resultaron predictores independientes de la ausencia de complicaciones. A pesar de que los procedimientos del grupo B fueron discretamente más largos (162 ± 48 min en el grupo B frente a 131 ± 45 min en el grupo A; $p < 0,001$) y tuvieron tiempos de aplicación de RF más largos (3.221 ± 984 ms en el grupo B frente a 2.307 ± 1.062 ms en el grupo A; $p < 0,001$), estos factores no resultaron predictores de complicaciones.

Tabla 6
Características diferenciales entre los procedimientos que presentan complicaciones. Análisis univariable

	Complicaciones (%)		
Variable analizada	Sí	No	p
Empleo de catéter circular	3,1	7,8	0,019
Protocolización del procedimiento	4,2	10,5	0,002
Sexo masculino	6,8	11,8	0,040
HTA	8,3	7,9	0,850
SAOS	8,1	9	0,771
Antecedentes de ACV	12,9	8,4	0,382
Cardiopatía	4,8	9,2	0,067
Línea mitral	5,9	6,3	0,842
Línea del techo	5,3	9,2	0,094
FA paroxística	7,6	8,3	0,750
AI dilatada	7,1	9,9	0,201

ACV: accidente cerebrovascular; AI: aurícula izquierda; FA: fibrilación auricular; HTA: hipertensión arterial; SAOS: síndrome de apnea obstructiva del sueño.

DISCUSIÓN

Debido a la prevalencia creciente de FA en nuestra población, y con el fin de dar respuesta a las exigencias crecientes en el tratamiento de ablación de la FA, cada vez son más los laboratorios que se inician en esta técnica. La ablación de FA es un procedimiento complejo, y sus complicaciones, aunque infrecuentes, pueden ser graves. Los resultados presentados en las distintas series varían ampliamente y dependen fundamentalmente de la experiencia del centro y el tipo de FA. En este sentido, a pesar de las elevadas tasas de éxito publicadas para la FA paroxística, superiores al 80% en las series publicadas inicialmente por grupos pioneros, son inferiores al 70% cuando se revisan series más recientes[10–12]. Del mismo modo, si comparamos para un mismo grupo las primeras series publicadas con series posteriores, los resultados también varían ampliamente (de tasas de éxito a 6 meses < 60% a tasas libres de recurrencia al año > 90%)[10,13] debido a la curva de aprendizaje y el avance tecnológico acompañante. Esto mismo ocurre en la FA persistente, de modo que, dependiendo del centro, la técnica empleada y la metodología para la detección de las recurrencias, las tasas de éxito oscilan entre un 50 y 75%[12,14]. En nuestra serie, el éxito total de la ablación es del 60,9%, algo menor que lo publicado por algunos de estos grupos. Posiblemente, este mayor porcentaje de recurrencias en nuestro grupo se deba a la aceptación de recurrencia arrítmica con un criterio muy riguroso, en el que cualquier episodio arrítmico registrado a partir del tercer mes de seguimiento (periodo de blanqueo) de más de 30 s de duración se considera como tal, independientemente de que sea sintomático o no o de que el paciente esté tomando fármacos antiarrítmicos, ligado a la

realización de Holter de 48 h (ocasionalmente de 7 días) a los 3, 6 y 12 meses, y finalmente a la recomendación insistente que damos a los pacientes de obtener registros ECG en caso de sufrir síntomas que indiquen arritmia. En nuestra institución, todos los procedimientos incluidos en la serie se realizaron mediante cartografía no fluoroscópica de la AI, con ayuda de las imágenes tridimensionales previamente adquiridas con TC o RM, especialmente útil en el caso de anatomías complejas, empleando en más del 80% de los casos un catéter de ablación irrigado y con el objetivo principal de lograr el aislamiento eléctrico de las VP mediante la aplicación de RF a nivel de la unión venoauricular. Según estudios previamente publicados, en los pacientes hipertensos, con AI dilatada, FA no paroxística y con SAOS, la ablación de las VP resulta menos efectiva[15–22]; mientras que en nuestra serie la hipertensión arterial y el SAOS han sido los más potentes predictores de recurrencia independientes. Paralelamente, observamos que los pacientes con ablación lineal del istmo mitral presentaron un mayor número de recurrencias. Probablemente su realización incompleta, sin comprobación del bloqueo, podría haber resultado proarrítmica. Por este motivo, en la gran mayoría de los procedimientos realizados en los últimos 2 años, la línea mitral no ha sido realizada. Por otra parte, en nuestro estudio el empleo de catéter circular para cartografiar la AI se asoció con una reducción de las complicaciones totales; sin embargo, dado que su empleo en el grupo A del estudio es muy minoritario y se introdujo sistemáticamente en el grupo B, podría haber un efecto tiempo y el beneficio real en la reducción de las complicaciones podría no ser tan claro.

A pesar de que las complicaciones han ido disminuyendo de acuerdo con la curva de aprendizaje de los operadores y gracias a los avances tecnológicos, sigue habiendo complicaciones mayores y representan en nuestra serie el 4,2%, lo que supone una frecuencia similar a la recogida en el último registro mundial sobre los métodos, la eficacia y la seguridad de la ablación por catéter de la FA[23].

La mayoría de las complicaciones aparecen durante o inmediatamente después del procedimiento. El taponamiento cardiaco sigue siendo la más frecuente complicación con potencial riesgo vital, en la mayoría de los casos relacionada con el procedimiento de punción transeptal. En nuestra serie esta complicación no disminuyó significativamente con el tiempo, probablemente en relación con la incorporación de un nuevo operador en los últimos 2 años de la serie, pues es indiscutible la importancia de la curva de aprendizaje. En el presente estudio, de las 61 complicaciones, el 79% se compone de las derivadas de la punción transeptal (con o sin taponamiento) y eventos embólicos tanto cerebrales como coronarios. A partir de la instauración de un protocolo de anticoagulación y sedación consciente durante el procedimiento, se observó una reducción de las complicaciones tromboembólicas (de 8 antes a 1 después de su instauración sistemática). Previamente a la protocolización del procedimiento, se realizaba la aplicación de un bolo inicial de HNF, monitorizando de manera variable el ACT y administrando dosis de HNF variables a juicio del operador, lo que conllevaba aceptar niveles de anticoagulación subóptimos (< 250 s). Según este protocolo, el objetivo es mantener durante todo el procedimiento niveles de ACT > 250 ms.

Por otra parte, es de especial importancia la manipulación cuidadosa de las vainas y los sistemas de irrigación continua para evitar tanto la formación de trombos como la introducción de aire en el sistema, ya que ello puede ser causa de gran parte de los eventos cardioembólicos, fundamentalmente coronarios. En este sentido, resulta primordial la formación del personal de enfermería en la vigilancia de los niveles de anticoagulación y los sistemas de irrigación y la detección precoz de complicaciones.

La reducción significativa de complicaciones con el paso de los años responde sin duda a varios factores. Por una parte, la sistematización de la anticoagulación durante el procedimiento ha contribuido a conseguir unos niveles óptimos y estables de anticoagulación, lo que podría explicar la reducción significativa de las complicaciones embolicas a partir de 2008. Por otra, con los años el análisis de las complicaciones y la búsqueda exhaustiva de sus potenciales causas han contribuido a la formación tanto del personal médico como del personal de enfermería. La curva de aprendizaje ha supuesto una atención exhaustiva a la manipulación de los catéteres, saber reconocer las potenciales fuentes de complicaciones y, por lo tanto, evitar su aparición.

Asimismo, junto con la protocolización de la anticoagulación, en 2008 se inició un protocolo de sedación consciente a todos los pacientes. Este protocolo, definido gracias a las recomendaciones de los compañeros del servicio de anestesiología, posiblemente sea un factor adicional de la reducción de las complicaciones, gracias a un mayor confort del paciente y, por ello, mayores estabilidad del catéter y seguridad del procedimiento.

Limitaciones del estudio

Dado que se trata de un estudio prospectivo y no aleatorizado, no es posible detectar qué porcentaje de la mejora en resultados y complicaciones deriva de los tres factores implicados: aprendizaje, mejora tecnológica y protocolización. Por otra parte, en la evaluación del éxito resulta primordial el método de monitorización empleado en el seguimiento para registrar las recurrencias arrítmicas, debido a que a menudo no hay buena correlación entre los síntomas percibidos por el paciente y los episodios de arritmia persistentes. Sin embargo, la monitorización de los resultados fue igual en ambos grupos. Por último, hay aspectos técnicos de los procedimientos, tales como la realización de la línea mitral, la línea del techo o el empleo del catéter circular, cuyas limitaciones derivadas tanto de su realización no estandarizada ni protocolizada como de la falta de datos especialmente en los procedimientos iniciales, han sido reiteradamente comentadas en el texto, y son necesarios estudios aleatorizados que analicen el valor predictor de tales factores.

CONCLUSIONES

El procedimiento de ablación de las VP ha experimentado una mejora significativa en la tasa de resultados y complicaciones con el paso de los años.

La aplicación sistemática de un protocolo de anticoagulación y sedación consciente se asocia a la mejora de los resultados y la reducción de las complicaciones en el procedimiento de ablación de FA. Otros factores no medidos en este estudio, como la curva de aprendizaje de los operadores y la progresiva mejora tecnológica, pueden haber influido en los cambios observados.

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CONFLICTO DE INTERESES

Ninguno.

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Trends in the use of electrical cardioversion for atrial fibrillation: influence of major trials and guidelines on clinical practice

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RESEARCH ARTICLE Open Access

Trends in the use of electrical cardioversion for atrial fibrillation: influence of major trials and guidelines on clinical practice

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Abstract

Background: The purpose of the present study was to assess the trends in the use of ECV following published studies that had compared rhythm and rate control strategies on atrial fibrillation (AF), and the recommendations included in the current clinical practice guidelines.

Methods: The REVERCAT is a population-based assessment of the use of electrical cardioversion (ECV) in treating persistent AF in Catalonia (Spain). The initial survey was conducted in 2003 and the follow-up in 2010.

Results: We observed a decrease of 9% in the absolute numbers of ECV performed (436 in 2003 *vs.* 397 in 2010). This is equivalent to 27% when considering population increases over this period. The patients treated with ECV in 2010 were younger, had a lower prevalence of previous embolism, a higher prevalence of diabetes, and increased body weight. Underlying heart disease factors indicated, in 2010, a higher proportion of NYHA ≥ II and left ventricular ejection fraction <30%. We observed a reduction in the number of ECV performed in 16 of the 27 (67%) participating hospitals. However, there was an increase of 14% in the number of procedures performed in tertiary hospitals, and was related to the increasing use of ECV as a bridge to AF ablation. Considering the initial number of patients treated with ECV, the rate of sinus rhythm at 3 months was almost unchanged (58% in 2003 *vs.* 57% in 2010; p = 0.9) despite the greater use of biphasic energy in 2010 and a similar prescription of anti-arrhythmic drugs.

Conclusions: Although we observed a decrease in the number of ECVs performed over the 7 year period between the two studies, this technique remains a common option for treating patients with persistent AF. The change in the characteristics of candidate patients did not translate into better outcomes.

Keywords: Atrial fibrillation, Electrical cardioversion, Rhythm control, Rate control, Follow-up

Background

The REVERCAT study (*REgistre sobre la cardioVERSió elèctrica a CATalunya*; Registry of Electrical Cardioversion in Catalonia) is a multi-center study involving 27 participating hospitals. The recording of characteristics of electrical cardioversion (ECV) was intended to evaluate the use of the technique in patients with atrial fibrillation (AF) in current clinical practice in Catalonia (Spain). The initial study was conducted at the start of 2003. The current re-evaluation was conducted early in 2010 and, over these past 7 years, there have been a few studies published, and subsequent guidelines generated, which described the lack of a clear benefit of rhythm control *vs.* rate control strategies in patients with AF [1-3]. The purpose of the present study was to compare the frequency and characteristics of patients treated with ECV between the years 2003 and 2010; the objective being to assess the impact of major clinical trials and recommendations included in the current clinical practice guidelines.

Methods

The REVERCAT study was set-up to record, prospectively, all patients with persistent AF who were

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considered candidates for ECV. There were 27 participating hospitals which are representative of the whole of Catalonia (an Autonomous Community in NE Spain) (Table 1).

The area of Catalonia is 31,930 km^2 and the population was 6,506,000 inhabitants in 2003 and 7,512,000 inhabitants in 2010, all of whom have the right to health-care provision under the publicly-funded National Health Service. The hospitals participating in the present study attend to approximately 90% of this population. The initial registry was set-up between 1st February and 30th October 2003. The present study was conducted between 1st February and 30th October 2010, the purpose being to assess the changes in the use of ECV in clinical practice in Catalonia. The patients included in the study to have ECV applied were all those who met the criteria of being ≥18 years of age, with AF duration >7 days, and with no precipitating conditions including hyperthyroidism, fever, cardiac surgery and pericarditis. Successful ECV was considered when sinus rhythm (SR) was achieved, and excluded patients with immediate relapse. A clinical and ECG follow-up was performed at 3 months post-ECV. Patients were considered to have maintained SR at 3 months if there had not been a relapse of persistent AF and, as well, the ECG at 3 months of follow-up showed SR. The information recorded included clinical data, treatment, echocardiography data, and procedure variables. We compared all these variables in the two surveys conducted 7 years apart. The principal investigator in each hospital was the same in both surveys in 21 of the 27 participating hospitals.

Table 1 List of investigators and centers participating in the REVERCAT study

Clinical Investigator[a]	Affiliation
X Sabaté	H.U. de Bellvitge, Hospitalet de Llobregat
R Serrat	H del Mar
A Sualís	H de Mataró
F Planas	H. de Badalona
G Vazquez	H. Comarcal de la Selva, Blanes
J Escudero	H Mútua de Terrassa
X Abardia/C Barberà	Clínica Ponent, Lleida
L Guillamon	H. Parc Taulí, Sabadell
L Mont/N Calvo	H. Clínic, Barcelona
J Sadurní	H. General de Vic
S Pons	H de Barcelona
A Descalzi	H. Comarcal Alt Penedés, Vilafranca del Penedés
N Batalla	H. Sagrat Cor, Barcelona
E Sanz/S Serrano	H.U. Joan XXIII, Tarragona
J Pérez-Rodon	H.G.U. Vall d' Hebrón, Barcelona
E Rodríguez-Font	H. Sta Creu i Sant Pau, Barcelona
F Freire	H. de Palamós, Palamós
M Vilaseca	H de Calella, Calella
C Romero	H. Sant Boi de Llobregat
I Duran	H.U. Sant Joan de Reus
J Tomàs	H.U. Arnau de Vilanova, Lleida
I Lechuga	H. Verge de la Cinta, Tortosa
R Villuendas	H. Germans Trias i Pujol, Badalona
A Jaber	H. de Terrassa
I Romeo	H. d'Igualada
R Canals	H. Comarcal de Mollet
M Paz	H de Figueras

[a]Collaborators in Pubmed.

The study received approval from the Institutional Review Boards (Clinical Ethics Committee) of each participating hospital on the understanding that the data were coded on entry into the registry and that patient privacy was respected. Written informed consent was obtained from the patient for publication of this report.

Statistical analyses

Qualitative variables are expressed in percentages, and the differences assessed using the chi-squared test. Quantitative variables are presented as means ± standard deviation (SD) and the differences between means evaluated using the Student *t*-test. Statistical significance was accepted at p values <0.05. All analyses were performed with the SPSS statistical software package (version 18).

Results

There were 397 ECVs performed in 2010 compared to 436 in 2003. These were consecutive patients meeting the inclusion criteria and having ECV performed over the same period of the year-of-study (February to October). This represents a 9% reduction in the number of procedures which, when taking into account the increase in the catchment population between 2003 and 2010, represents a reduction of 27%.

The clinical characteristics are summarized in Table 2. The patients treated with ECV in 2010 had a lower mean age, a lower prevalence of prior embolism, a higher prevalence of diabetes and a higher mean body weight compared to those treated with ECV in 2003.

With respect to the underlying heart disease, in 2010 we observed a higher proportion of NYHA ≥ II, lower mean ejection fraction, and a higher prevalence of EF <30% than in 2003.

There was a reduction in the numbers of patients in whom ECV was applied in 16 of 27 (67%) participating hospitals. However, the distributions of the treatment indicated a higher number of ECV procedures in tertiary-care hospitals (mainly university-associated)

Table 2 Comparisons of the clinical and echocardiographic characteristics of patients included in the two surveys (2003 *versus* 2010) of electrical cardioversion

Characteristic	2003 survey (n = 436)	2010 survey (n = 397)	P
	Mean ± SD or n (%)	Mean ± SD or n (%)	
Age; years	65 ± 11	64 ± 11	0.03
Age; >70 years	170 (39)	119 (30)	0.008
Male gender	296 (68)	285 (72)	0.19
Weight; kg	78.2 ± 13	80.9 ± 14	0.01
Height; cm	167 ± 9	168 ± 9	0.14
Body surface area; m^2	1.86 ± 0.19	1.90 ± 0.19	0.006
Hypertension	222 (51)	222 (56)	0.14
Diabetes mellitus	57 (13)	75 (19)	0.04
Previous embolism	46 (12)	29 (7)	0.02
NYHA Class ≥ II	135 (31)	175 (44)	0.0001
Left atrial size	45.4±6.3	45.4±6.8	0.95
Left atrial dilatation (>50mm)	61 (14)	67 (17)	0.42
Left ventricular hypertrophy	113 (26)	119 (30)	0.21
LVEF (%)	58 ± 14	56 ± 14	0.02
LVEF <30%	8 (2)	19 (5)	0.05
Previous electrical cardioversion	65 (15)	87 (22)	0.009
Duration of AF >1 year	48 (11)	59 (15)	0.35
Anti-arrhythmic drugs	327(78)	296 (76)	0.39
Amiodarone:	268 (64)	247 (62)	
Ic:	39 (9)	32 (9)	
Sotalol:	9 (2)	5 (1)	
Others:	11 (3)	12 (3)	
ACE inhibitor/ARB	197 (45)	197 (50)	0.12

**AF*: atrial fibrillation; *LVEF*: left ventricular ejection fraction; *Ic*: flecainide, propafenone; *ACE*: angiotensin-converting enzyme; *ARB*: angiotensin receptor blockers.

compared to district general hospitals between 2003 and 2010. In 2003 the district hospitals accounted for 57% of procedures compared to 43% in the tertiary hospitals. In 2010 the district hospitals performed 47% of the procedures compared to 53% in tertiary hospitals (p = 0.004). Between 2003 and 2010, we observed an absolute decrease of 23% (p = 0.004) in the number of ECVs performed in district hospitals (247 in 2003 *vs.* 189 in 2010). Conversely, there was an absolute increase in the use of ECV in tertiary hospitals of 14% (p = 0.004) in 2010 (189 in 2003 *vs.* 208 in 2010). There were 7 patients in 2003 in whom ECV was applied as a bridge to AF ablation. In 2010 the number increased to 36; 3 centers performing AF ablations in 2003, and 5 centers in 2010. Overall, the numbers of AF ablations performed in the two periods of the study were 30 in 2003 and 129 in 2010.

The ECV success rates were similar in 2003 and 2010 (86% in 2003 *vs.* 89% in 2010; p = 0.21), despite the more frequent use of biphasic energy in 2010 (16% in 2003 *vs.* 88% in 2010; p = 0.0001) (Table 3).

The use of anti-arrhythmic drugs pre-ECV and at discharge from hospital was also similar in both surveys (pre-ECV 73% in 2003 *vs.* 68% in 2010; p = 0.26; at discharge 78% in 2003 *vs.* 76% in 2010; p = 0.39). Amiodarone was the preferred drug in both studies. It was used in 64% of patients in 2003 *vs.* 62% of patients in 2010 (p = 0.62), independently of underlying left ventricular ejection fraction. Dronedarone was not available in Spain until the end of the 2010 study.

With respect to anticoagulation treatment, the conventional use of coumarins at least 3 weeks pre- and 1 month post-ECV was the most common pattern (2003 59% *vs.* 2010 61%; p = 0.75). The rate of patients requiring chronic anticoagulant therapy prior to the decision to perform ECV was similar (27% in 2003 *vs.* 30% in 2010; p = 0.67), whereas the use of transesophageal echocardiography with short patterns of anticoagulation (5% in 2003 *vs.* 7% in 2010; p = 0.65) and other patterns (9% in 2003 *vs.* 2% in 2010, p = 0.28) were very low in both surveys.

The rate of SR was similar in both surveys at 3 months of follow-up (67% in 2003 *vs.* 64% in 2010; p = 0.21). If we considered the patients with and without anti-arrhythmic drugs at discharge from hospital, the rates of SR at 3 months were also similar. The patients receiving anti-arrhythmic medications in 2003 accounted for 70% of the total compared to 68% in 2010 (p = 0.30). Patients

Table 3 Electrical cardioversion procedure characteristics in both surveys (2003 *versus* 2010)

Characteristic	2003 survey (n = 436)	2010 survey (n = 397)	P
	Mean ± SD or n (%)	Mean ± SD or n (%)	
Use of biphasic energy	70 (16)	349 (88)	<0.001
Successful ECV (overall)	374 (86)	355 (89)	0.21
- Monophasic energy	313 (85)	42 (87)	0.69
- Biphasic energy	61 (89)	313 (90)	0.90
Number of shocks (overall)	1.73 ± 0.9	1.5 ± 0.9	0.0001
- Monophasic shocks	1.76 ± 0.9	1.70 ± 0.83	0.90
- Biphasic shocks	1.61 ± 0.86	1.45 ± 0.78	0.07
Energy delivered (overall) (J)	239 ± 90	165 ± 63	0.0001
- Monophasic shocks	253 ± 77	234 ± 81	0.11
- Biphasic shocks	166 ± 95	154 ± 51	0.48

**ECV*: electrical cardioversion; *J*: Joules.

not receiving anti-arrhythmic medications in 2003 accounted for 58% of the total compared to 55% in 2010 (p = 0.59). Of those treated with ECV, the rate of patients in whom the SR was restored and maintained at 3 months was almost unchanged in the two periods of the study (58% in 2003 *vs.* 57% in 2010; p = 0.9).

Discussion

To the best of our knowledge this is the first population-based study that analyzed the treatment of AF over time, specifically the use of ECV. Also, this was an opportunity to observe the impact in clinical practice of new evidence reflected in guideline recommendations. We observed that between 2003 and 2010 there was a reduction in the number of ECVs performed and a change in the characteristics of patients treated i.e. this finding may be related to a lower use of the rhythm control strategy compared to rate control in the population with the current characteristics . However, ECV continues to be used frequently in clinical practice.

The AFFIRM and RACE trials [1,2] demonstrated no differences in terms of morbido-mortality when comparing rate *vs.* rhythm control strategies in patients with AF. Also the AF-CHF trial [4], focusing on patients with heart failure or left ventricular dysfunction, observed no difference in cardiovascular mortality. Prior to this evidence, it was accepted in clinical practice that the relief of symptoms as well as prevention of embolism and avoidance of cardiomyopathy (theoretically adding to the maintenance of SR) could be reasons for restoration of SR. These consensus opinions are reflected in the guidelines from the ESC/AHA/ACC 2001 [5]. Subsequent to these publications, the concept became accepted that anticoagulation should not be stopped despite the restoration of SR in patients with criteria for anticoagulation. Thus, in the 2006 ESC/AHA/ACC guidelines, the avoidance of long-term anticoagulation was not considered a reason for ECV [3]. The recent ESC 2010 guidelines [6] were published in the course of the conduct of the present study, as were the ACCF/AHA/HRS 2011 guidelines [7] which were published soon after the study's completion. These guidelines support anticoagulation maintenance (if the patient fulfills the criteria for anticoagulation) despite the patient achieving SR. Thus, guidelines limit the recommendations for ECV to patients with clear symptoms related to AF, without any intention to reduce morbido-mortality. Theoretically, this would imply a reduction in the number of ECVs performed. However, there is scant information regarding the influence of these guidelines on the use of ECV [8] and, perhaps more importantly, the characteristics of patients who are candidates for treatment with ECV. Our initial survey was begun in early 2003, a short time after the publication of the AFFIRM and RACE studies in December 2002, the findings of which are consistent with our findings in 2010. Although we observed a considerable decrease in the number of ECVs performed, this technique remains a common option for treating patients with AF. This may be related to the impression that, when the data from these trials are analyzed according to the patient's actual rhythm, the benefit of SR over AF becomes apparent [9]. A more profound analysis of AFFIRM study reveals several limitations that preclude the assumption that attempting to restore SR is not worthwhile i.e. the study had a low percentage of SR patients in the rhythm control group, low efficacy and increased risk of death of AAD, a high percentage of SR patients in the rate control group, lower use of beta-blockers in rhythm control group, and exclusion of patients with severe symptoms who would, potentially, most benefit from SR. Strictly, the study should not be interpreted as a comparison of SR *vs.* AF and, indeed, may reflect the ineffectiveness of the rhythm control methods used.

From our results we may deduce a change in the indications for ECV. Current patients are more symptomatic for heart failure, and with higher disease burden. We also noted that in the 2003 survey the patients were less symptomatic for heart failure, were older and with higher prevalence of previous embolism. This would suggest that, currently, the avoidance of long-term anticoagulation is not considered an indication for a rhythm control strategy in slightly symptomatic patients with criteria for anticoagulation. Although other factors may be contributing to these findings, the suggestion is that such publications may have had a significant influence on our standard clinical practice.

We note a reluctance towards the use of transesophageal echocardiogram (TEE) in the ECV procedure in both of our surveys that had been conducted 7 years apart. The publication of the ACUTE study [10] in 2001 negated the expectations that TEE could reduce embolisms and complications related to anticoagulation, as well as improve the efficacy of ECV because of the shorter time-lapse between the indication and the ECV. Both of our evaluations reflect the few occasions in which this technique may be useful in standard clinical practice. Conversely, we observed almost a complete substitution of monophasic energy (the more frequent option in 2003) for biphasic energy which was used in 2010, and which had been recommended in the 2006 guidelines. The use of biphasic source results in fewer skin lesions and greater rate of reversion to SR for the same amount of energy administered [11,12]. Also, maximum biphasic energy shock is useful, especially in patients with greater body surface area [13]. The slightly higher efficacy of ECV in our 2nd survey of 2010 would be attributable to the use of biphasic energy. However,

the more frequent use of biphasic energy and the change in patients' characteristics did not result in a higher rate of SR at 3 months of follow-up. Biphasic energy could benefit a patient with a profile of higher probability of AF relapse due to higher body mass index [14]. The use of anti-arrhythmic drugs was relatively high and similar in both surveys. Although its use was related to better rates of SR at 3 months of follow-up, its efficacy was relatively low. The introduction of new anti-arrhythmic drugs with higher efficacy and less adverse effects should help to improve these outcomes in the near future. Around half of the patients had been treated with ACE inhibitors/angiotensin receptor blockers (most of them for hypertension), without significant differences between both registries. The benefit of these drugs in the prophylaxis of AF relapse post-ECV has been clear in the published studies [15,16] and this is reflected in the 2001 and 2006 ESC/AHA/ACC guidelines as well as the 2010 ESC guidelines, which do not recommend its use.

Of interest is the change in the number of ECVs performed in tertiary (referral) hospitals *versus* district (general) hospitals. Overall, in the district hospitals we observed a clear decrease in the number of ECVs performed while, in tertiary hospitals, there was an increase. The introduction of catheter ablation may explain these findings, with the use of ECV as a bridge to ablation. As mentioned earlier, this reflects the interest in the rhythm control strategy if there are appropriate therapeutic measures that impact on effective SR maintenance.

Our study has some limitations. One of them is the lack of information on the total number of patients with AF attended-to in our clinics. In consequence, we cannot strictly affirm that there has been a decrease in the proportion of patients treated with rhythm *vs.* rate control strategy. However, if we assess the increasing prevalence of AF [17,18] related, above all, to aging we may deduce a decrease in the proportion of patients with AF treated with the rhythm control strategy; the proportion probably being higher than that indicated by the decrease in the number of ECV that we observed. In our population the mean age increased from 45.8 to 47 years and the number of people >60 years of age increased by 14% during this period. Another limitation of our study is the lack of information on symptoms strictly related to AF. Symptoms described in our study only related to heart failure. A scale of symptoms related to AF had been proposed in 2007 by the EHRA [19] and was included in the 2010 ESC guidelines. As such, it had not been available at the time of our first survey performed in 2003. However, we believe that the attempt to relieve, or improve, symptoms of heart failure may be considered when an ECV is indicated, as had been assessed in our survey.

Conclusions

In conclusion, we observed that ECV technique continues to be used widely as treatment for patients with AF; albeit applied to candidate patients with different characteristics.

Abbreviations

ECV: Electrical cardioversion; AF: Atrial fibrillation; SR: Sinus rhythm.

Competing interest

None

Authors' contributions

JMA: conception and design, analysis and interpretation of data, drafting the manuscript. XV: conception and design, acquisition of data. CR: conception and design, acquisition of data. SP: acquisition of data. RV: acquisition of data. NC: acquisition of data. JPR: acquisition of data. XS: acquisition of data. All authors read and approved the final manuscript.

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Atrial fibrillation catheter ablation versus surgical ablation treatment (FAST): A 2-Center Randomized Clinical Trial

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Atrial Fibrillation Catheter Ablation Versus Surgical Ablation Treatment (FAST) : A 2-Center Randomized Clinical Trial

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Atrial Fibrillation Catheter Ablation Versus Surgical Ablation Treatment (FAST)

A 2-Center Randomized Clinical Trial

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Background—Catheter ablation (CA) and minimally invasive surgical ablation (SA) have become accepted therapy for antiarrhythmic drug–refractory atrial fibrillation. This study describes the first randomized clinical trial comparing their efficacy and safety during a 12-month follow-up.

Methods and Results—One hundred twenty-four patients with antiarrhythmic drug–refractory atrial fibrillation with left atrial dilatation and hypertension (42 patients, 33%) or failed prior CA (82 patients, 67%) were randomized to CA (63 patients) or SA (61 patients). CA consisted of linear antral pulmonary vein isolation and optional additional lines. SA consisted of bipolar radiofrequency isolation of the bilateral pulmonary vein, ganglionated plexi ablation, and left atrial appendage excision with optional additional lines. Follow-up at 6 and 12 months was performed by ECG and 7-day Holter recording. The primary end point, freedom from left atrial arrhythmia >30 seconds without antiarrhythmic drugs after 12 months, was 36.5% for CA and 65.6% for SA ($P=0.0022$). There was no difference in effect for subgroups, which was consistent at both sites. The primary safety end point of significant adverse events during the 12-month follow-up was significantly higher for SA than for CA (n=21 [34.4%] versus n=10 [15.9%]; $P=0.027$), driven mainly by procedural complications such as pneumothorax, major bleeding, and the need for pacemaker. In the CA group, 1 patient died at 1 month of subarachnoid hemorrhage.

Conclusion—In atrial fibrillation patients with dilated left atrium and hypertension or failed prior atrial fibrillation CA, SA is superior to CA in achieving freedom from left atrial arrhythmias after 12 months of follow-up, although the procedural adverse event rate is significantly higher for SA than for CA.

Clinical Trial Registration—URL: http://clinicaltrials.gov. Unique identifier: NCT00662701.

(*Circulation*. 2012;125:23-30.)

Key Words: ablation ■ atrial fibrillation ■ surgery

Catheter ablation (CA) has become an established invasive procedure in patients with atrial fibrillation (AF) refractory to antiarrhythmic drugs (AADs).[1–4] The efficacy of CA may vary considerably, depending on the strategy and technology used and the stage of the electroanatomic disease.[1–7] For paroxysmal AF, >70% single-procedure efficacy is considered achievable, whereas for (longstanding) persistent AF, additional target ablation and multiple procedures are needed to achieve a reasonable result. For any AF ablation procedure, pulmonary vein (PV) isolation (PVI) is considered a mandatory cornerstone.[2,3]

Clinical Perspective on p 30

Until the rise of CA, the Cox maze surgery was the only invasive treatment for AF. Although highly effective, it was technically challenging, entailing complete open heart surgery by dedicated surgeons in selected populations.[8–10] In 2006, Wolf et al[11] described a video-assisted thoracoscopic surgical ablation (SA) consisting of PVI from the epicardial side with a bipolar radiofrequency (RF) clamp, ablation of ganglia over the left atrial (LA) surface, and excision of the LA appendage. Initial efficacy of this minimally invasive surgery has been reported to be >90% in selected populations.[11–15]

With 2 invasive percutaneous options available, there is growing debate on the relative position of CA and SA, although no direct comparative trials have been performed. In the 2010 European Society of Cardiology guidelines,[2] CA in AF patients refractory to AAD has received a Class 2A or 2B

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(Level of Evidence A/C) indication, depending on paroxysmal or (longstanding) persistent AF, whereas SA has a Class 2B (Level of Evidence C) indication only after failure of CA. To the best of our knowledge, the present study is the first prospective randomized clinical trial to provide a head-to-head comparison of CA and SA in a well-described population of AF patients.

Methods

A prospective randomized clinical trial was designed to compare CA and SA in a well-described population of patients with AF. The study was performed at St. Antonius Hospital in Nieuwegein, the Netherlands, and the Hospital Clinic in Barcelona, Spain. The protocol was in accordance with the Helsinki Declaration and was approved by the ethics committee of both hospitals and the Dutch central trial registration organization VCMO/CCMO. The trial was registered at www.clinicaltrials.gov (No. NCT00662701). Enrollment started in July 2007 and was stopped in June 2010; the last follow-up was completed in July 2011.

Protocol

Consecutive patients with drug-refractory AF referred for invasive treatment were screened for eligibility. Patients who met all criteria and were willing to participate were enrolled and randomized after providing written informed consent. The randomization process was performed and balanced in blocks of 6 patients at each individual site by drawing a preprinted randomization letter in a sealed envelope. The main randomization list was kept in a sealed envelope and was not opened until the last patient had been randomized. The inclusion criteria were documented, symptomatic paroxysmal and/or persistent AF for at least 12 months that was refractory to or intolerant of at least 1 AAD, age between 30 and 70 years, and mentally able and willing to give informed consent. Because SA is still considered to be tertiary treatment for only selected patients,[2,3] the study included patients who were considered less amenable to CA[16] on the basis of LA diameter of 40 to 44 mm with hypertension, LA diameter ≥45 mm, or failure of a prior CA for AF. Patients were excluded if they had longstanding AF >1 year, cardiac CA or a surgical cardiac procedure in the last 3 months, previous stroke or transient ischemic attack, LA thrombus, LA size >65 mm, left ventricular ejection fraction <45%, mitral or aortic valve regurgitation above grade 2, moderate to severe mitral or aortic stenosis, active infection or sepsis, pregnancy, unstable angina, myocardial infarction within the previous 3 months, AF secondary to electrolyte imbalance, thyroid disease, other reversible or noncardiovascular causes for AF, history of blood-clotting abnormalities, known sensitivity to heparin or warfarin, life expectancy of <12 months, involvement in another clinical study involving an investigational drug or device, pleural adhesions, prior thoracotomy, prior cardiac surgery, and elevated hemidiaphragm.

A preprocedural 7-day Holter was performed to establish preexisting type and burden of AF. A baseline physical examination, echocardiogram, and computed tomography/magnetic resonance imaging scan were done to exclude significant structural cardiac disease and to establish PV anatomy. In addition, a quality-of-life questionnaire was taken. During follow-up, patients were seen at the outpatient clinic at 3, 6, and 12 months. At each visit, patients were questioned for any adverse events and the existence of palpitations. A routine 12-lead ECG was taken at each visit. A blanking period of 3 months was allowed, after which AADs were discontinued. Amiodarone was encouraged to be discontinued at discharge but no later than 3 months. At 6 and 12 months, a 7-day Holter was performed to document the presence of arrhythmias. At 6 months, a follow-up computed tomography/magnetic resonance imaging scan was done to determine PV stenosis.

Procedure

After randomization and preprocedural diagnostic tests, patients were scheduled for CA or SA. The CA procedure consisted of a wide-area linear antrum ablation with documented PV isolation with decapolar circular mapping catheter as the end point.[2,3,17] Local anesthesia was achieved with lidocaine, and during the ablation, patients were given conscious sedation with diazepam combined with fentanyl at the discretion of the operator. Transseptal access was achieved by standard Brockenbrough method. At St. Antonius Hospital, a standard 4-mm single-tip RF catheter (Biosense-Webster) was used with a maximum power of 35 W, temperature of 55°C, and applications of 1 minute combined with the 3-dimensional NavX navigation (St. Jude Medical). No additional lines were performed, regardless of the type of AF. At the Hospital Clinic, a 3.5-mm irrigated-tip RF catheter (Biosense-Webster) was used in combination with 3-dimensional CARTO navigation (Biosense-Webster). Application duration per position was based on impedance changes and voltage reduction. An additional LA line could be made at the discretion of the operator. Roofline block was demonstrated during LA appendage pacing by continuous double potentials and activation around the PVs with a caudocranial pattern along the posterior wall,[18] whereas the mitral isthmus line[19] was made empirically without a critical definition for bidirectional block. Before the procedure, vitamin K antagonists were discontinued to lower the international normalized ratio to between 2.0 and 2.5 (St. Antonius Hospital) or to <2.0 with 3 days of bridging low-molecular-weight heparin (Hospital Clinic). During the procedure, intravenous heparin was given to reach an activated clotting time of >250 seconds.

In the SA group, patients were treated with video-assisted thoracoscopy under general anesthesia, according to the (modified) minimally invasive surgery protocol described by Wolf et al[11] and Edgerton et al.[12] In brief, PVI was performed from the epicardial side with a bipolar RF ablation clamp (AtriCure). At least 2 overlapping applications around each of the ipsilateral veins were made, and isolation was confirmed by the absence of PV potentials and exit block during pacing. In Barcelona, an additional application was made in the interatrial Waterston groove in the right side to isolate the ganglionic plexi from the atria. On the left side, the ligament of Marshal was cut, but no additional ablation of ganglionic plexi was pursued. At St. Antonius Hospital, in addition to PVI, the bilateral epicardial ganglia were found by high-frequency stimulation and ablated, as confirmed by the absence of a vagal response after ablation. Additional lines[15] could be made to the aortic trigone or at the LA roof or by making a posterior box lesion, all at the discretion of the operator. Sensing and pacing maneuvers verified isolation of the posterior box. The trigone line and roofline were made on an anatomic basis with aid of the Cool Rail (AtriCure) without determining conduction block. In all SA patients, the LA appendage was removed by stapling and then cutting the blind end of the appendage. All patients in the CA and SA groups were treated under either aspirin or vitamin K antagonist treatment, depending on the CHADS2 score. The international normalized ratio during the procedure was targeted to be <2.5 but >2.0 for patients with persistent AF. In both the CA and SA groups, all patients were treated with vitamin K antagonists in the first 3 months after the procedure, which were continued at the discretion of the treating cardiologist on the basis of freedom from AF and CHADS2 score. In the CA group, bridging therapy with low-molecular-weight heparin was done until the international normalized ratio was >2.0.

In both treatment groups, electric or chemical cardioversion was allowed during the treatment within the 3-month blanking period as needed to regain sinus rhythm, as a part of good clinical practice. Any cardioversion outside the blanking period during the 12-month follow-up was regarded as a failure for the efficacy end point.

End Points

The primary efficacy end point of the trial was freedom from any LA arrhythmia lasting >30 seconds during the 12-month follow-up without the use of AADs in accordance with the generally accepted consensus document of 2007.[2,3] A secondary efficacy end point was freedom from LA arrhythmia with AADs. The primary safety end point was the rate of significant adverse events (SAEs), including, among others, death, stroke, transient ischemic attack, major bleeding requiring surgery or blood transfusion or >2.0 points hemoglo-

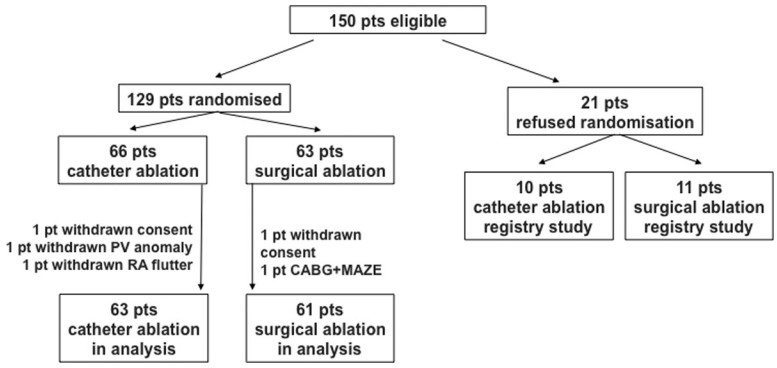

Figure 1. Patient (pt) inclusion and randomization. CABG indicates coronary artery bypass graft; PV, pulmonary vein; and RA, right atrium.

bin decrease, cardiac tamponade and/or perforation, significant/symptomatic PV stenosis >70%, pericarditis, acute coronary syndrome, myocardial infarction, diaphragmatic paresis/paralysis, persistent air leak, pneumothorax, empyema, superficial wound infections, pneumonia, and conversion to complete thoracotomy. Safety end points were also analyzed as the adverse event rate periprocedurally and during the 12-month follow-up.

Statistical Analysis

The primary efficacy analysis was based on an intention-to-treat analysis of all randomized patients who underwent their procedure. With an estimated success rate of 60% for ablation and 85% for surgery, 120 patients should have been enrolled, allowing for 5% dropout, for a power of 80% with a 1-sided Fisher exact test with a significance level of 0.025 (NCSS-PASS statistics software, www.ncss.com). The proportion of patients free from AF and other secondary LA arrhythmias at all serial ECGs and both 6- and 12-month 7-day Holter recording was calculated. Follow-up was complete for all patients, justifying the use of binary end points. Two-by-two tables with 2-sided Pearson χ^2 test and the Yates continuity correction were used to analyze the main outcome. The prespecified subgroup analyses and post hoc subgroup analyses (by center, previous ablation or LA dilatation, AF type, and preprocedural Holter result) are presented as a Forest plot depicting odds ratios with 95% confidence intervals. Tests on heterogeneity of treatment effects across the levels of the subgroups were performed. The analysis of the safety end points was descriptive by calculating rates, whereas for the overall figure, the Fischer exact test was used. All statistical analyses were performed with R, version 2.13 (www.r-project.org).

Results

Of the 150 patients eligible for inclusion, 21 refused randomization and formed a separate registry. Figure 1 provides an overview of the patient distribution. A total of 129 patients were randomized, 66 to CA and 63 to SA. In the CA group, 3 patients were withdrawn before the procedure and were excluded from analysis because of withdrawal of consent, change in diagnosis to typical right atrial flutter, and PV anatomy congenital anomaly. In the SA group, 2 patients were withdrawn and excluded from the analysis before the procedure because of withdrawal of consent and change to coronary artery bypass graft plus maze surgery. Finally, 63 patients in the CA group and 61 patients in the SA group were included in the analysis, 59 patients from St. Antonius Hospital and 64 patients from Hospital Clinic. The baseline characteristics of the population are presented in Table 1. The mean age was 56±8 years; 101 were male and 23 were female. The AF type was paroxysmal in 67% and persistent in 33%, of which 8% was continuous persistent AF of <1 year. The time since first diagnosis of AF was ≈7 years. The CHADS2 score was 0 in 60%, 1 in 30%, and >1 in 10%. Of the included patients, 67% had a prior unsuccessful CA as the inclusion criterion, and 33% had LA dilatation >40 mm as the primary inclusion criterion. The baseline 7-day Holter recording showed no AF in 48%, paroxysmal AF in 20%, and continuous AF in 32%. In the SA group, patients had slightly more paroxysmal AF, both as the initial diagnosis and in the preprocedural Holter recording, with a lower CHADS2 score and slightly more prior failed ablation as inclusion criteria.

Table 1. Baseline Characteristics of Patients

	CA N=63	SA N=61
Male	55 (87.3%)	45 (73.8%)
Age, yr	56.0±7.2	56.1±8.0
BMI, Kg/m^2	28.6±3.5	27.8±4.6
Prior MI	2 (3.2%)	0
LVEF	55.5±8.2%	57.7±6.8%
LA diameter, mm	43.2±4.8	42.5±6.5%
Prior failed CA	38 (60.3%)	45 (73.8%)
LA diameter 40–45 mm and hypertension	15 (23.8%)	8 (13.1%)
LA diameter ≥45 mm	10 (15.9%)	8 (13.1%)
AF type:		
PAF	37 (58.8%)	45 (73.8%)
PersAF	26 (41.2%)	16 (26.2%)
Years since diagnosis	6.8±5.3	7.4±6.3
Pre-procedure Holter:		
No AF	23 (40.4%)	29 (55.8%)
Paroxysmal AF	10 (17.5%)	12 (23.1%)
Continuous AF	24 (42.1%)	11 (21.2%)
Prior AAD use:		
1	28.3%	16.3%
2	41.5%	35.7%
3	15.1%	32.7%
≥4	15.1%	16.3%
Amiodarone	26 (41.3%)	30 (29.2%)
CHADS2-score:		
0	35 (58.3%)	38 (63.3%)
1	17 (28.3%)	17 (28.3%)
≥2	8 (13.4%)	4 (6.7%)

Table 2. Procedural Characteristics of CA and SA

	CA N=63	SA N=61
Total procedure time, min	163±55	188±59 (*P*=0.0177)
Flurorscopy time, min	27±11	. . .
PVI	62 (98.2%)	60 (98.3%)
PV reablated redo pts:		
1	1 (2.6%)	. . .
2	9 (23.7%)	. . .
3	3 (7.9%)	. . .
4	25 (65.8%	45 (100%)
LAA excision	. . .	60 (98.3%)
LA lines:		
Roof	30 (47.6%)	17 (27.9%)
Mitral isthmus	15 (23.8%)	. . .
Trigone		10 (16.4%)
Posterior box	. . .	10 (16.4%)
No. additional lines:		
1	17 (27.4%)	9 (14.8%)
2	14 (22.6%)	2 (3.3%)
3	. . .	8 (13.1%)
RF energy PVI	33±20 min	8.9±2.8 applications

Procedure

Table 2 shows the procedural information for the CA and SA groups. The mean procedure, fluoroscopy, and RF times in the CA ablation group were 163±55, 27±11, and 33±20 minutes, respectively. There was no significant difference in procedure and fluoroscopy times between the 2 centers. Mean SA procedure time was longer at 188±59 minutes (P=0.0177) without the need for fluoroscopy and 8.9±2.8 bipolar RF clamp applications. In all SA patients, PVI was the cornerstone of ablation, followed by ganglia ablation and LA appendage excision in the SA group. In the group with failed prior CA, all patients were found to have ≥1 PV with intact PV-LA conduction before reisolation, which were then subsequently reisolated (Table 2). In the CA group, only at the Hospital Clinic were additional lines made at the LA roof in 30 patients (47.6%), mitral annulus in 15 patients (27.4%), or both in 14 patients (22.6%). In the SA group, all PVs were always surgically ablated regardless of whether there was LA-PV conduction. In addition, various combinations of additional lines were created only at St. Antonius Hospital in 19 patients (31%). In 1 patient in both the CA and SA groups, the ablation protocol could not be performed or completed because of complications.

Efficacy of CA and SA

Table 3 lists the outcomes of CA and SA during the 12-month follow-up. No patients were lost to follow-up. At 6 months, freedom from LA arrhythmia lasting >30 seconds without AADs was seen in 44.4% in the CA group versus 67.2% in the SA group (P=0.0178). During continuation of follow-up, the difference in effect increased, further favoring SA. The primary efficacy end point of freedom from any LA arrhythmia of >30 seconds in the absence of AADs after 12 months

Table 3. Efficacy Endpoints for CA and SA

Freedom of LA Arrhythmia	CA N=63	SA N=61	*P*-Value
Overall, 12 mo	23 (36.5%)	40 (65.6%)	P=0.0022
Overall, 12 mo allowing AAD	27 (42.9%)	48 (78.7%)	P<0.0001
Overall, 6 mo	28 (44.4%)	41 (67.2%)	P=0.0178
PAF group	13/37 (35.1%)	31/45 (68.9%)	P=0.0047
PersAF group	9/25 (36%)	9/16 (56%)	P=0.3411
Prior failed CA	14/38 (36.8%)	30/44 (68.2%)	P=0.0089
LA dilation/ hypertension	9/25 (36.0%)	10/17 (58.8%)	P=0.3411
Nieuwegein	10/30 (33.3%)	18/29 (62.1%)	P=0.0513
Barcelona	13/33 (39.4%)	22/31 (70.9%)	P=0.0336

was 36.5% in the CA group and 65.6% in the SA group (P=0.0022). Thus, to increase the efficacy for freedom from LA arrhythmia by performing SA instead of CA, the number needed to treat was 3.4 (95% confidence interval, 2.3–8.7). Another 12 patients also remained free from LA arrhythmias but were not considered a success for the primary end point because they were not free from AADs during follow-up. Allowing for AAD use, CA efficacy was 42.9% and SA efficacy was 78.7% (P<0.0001). Regarding the timing of the 40 CA failures, 7 patients (17.5%) failed before the scheduled 6-month visit, 7 (17.5%) between the 6- and 12-month visits, 3 (7.5%) at the 12-month visit, and 23 (57.5%), the majority, at or around the 6-month visit. Of the 21 SA failures, 3 (14.3%) occurred before 6 months, 2 (9.5%) between the 6- and 12-month visits, 0 at the 12-month visit, and 16 (76%) at or around the 6-month visit.

Figure 2 shows the Forest plot for the subgroup analysis. The treatment effect was consistent for the 2 sites, with CA efficacy of 33.3% at St. Antonius and 39.4% at the Hospital Clinic and SA efficacy of 62.1% at St. Antonius and 70.9% at the Hospital Clinic. The use of an irrigated RF catheter or the creation of additional lines did not significantly affect the efficacy in this population. The superior efficacy of SA showed a specifically favorable trend toward paroxysmal AF patients and previously unsuccessful CA patients. All tests on heterogeneity of treatment effects performed across the levels

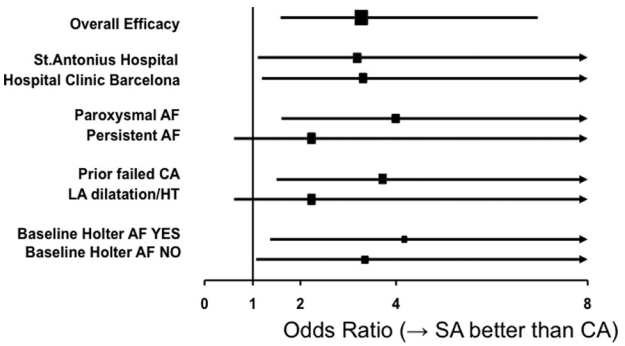

Figure 2. Forest plot of subgroup analysis for surgical ablation (SA) vs catheter ablation (CA) efficacy. AF indicates atrial fibrillation; LA, left atrium; and HT, hypertension.

Table 4. Procedural Adverse Events of CA and SA

Adverse Events	CA N=63	SA N=61	*P*-Value
Pericardial effusion/tamponade	1	1	
TIA/Stroke	1	1	
Pneumothorax	. . .	6	
Hematothorax	. . .	1	
Rib fracture	. . .	1	
Sternotomy for bleeding	. . .	1	
Pneumonia	. . .	1	
Death	. . .	. . .	
PM implant	. . .	2	
Total	2 (3.2%)	14 (23.0%)	*P*=0.001
Minor			
Groin hematoma/bleed	4 (6.3%)	. . .	

of the subgroups showed consistency of results with a significance level of >0.2.

Safety of CA and SA

Tables 4 and 5 list all adverse events, significant and minor, both periprocedurally and during the 12-month follow-up. The primary safety end point of all SAEs during 12-month follow-up was 34.4% in the SA group versus 15.9% in the CA group ($P=0.027$). The procedural adverse event rate was similar at both sites but significantly higher for SA with 23.0% (14 SAEs in 14 patients) than for CA with 3.2% (2 SAEs in 2 patients; $P=0.001$). The number needed to treat to prevent a procedural adverse event by performing CA instead of SA was therefore 5.05 (95% confidence interval, 3.3–42.5). The median duration of hospitalization was 2.0 days for CA versus 5.5 days for SA ($P<0.001$). In the SA group, 1 patient required conversion to median sternotomy for bleeding. One patient required a pacemaker implantation for sinus node dysfunction, whereas another had a pacemaker for bradycardia and nonsustained polymorphic VT. In 1 patient, the SA procedure could not be completed because of obesity and severe pulmonary hypertension, leading to severely prolonged hospitalization. Other complications included pneumothorax (n=6), hematothorax (n=1), stroke (n=1), tamponade (n=1), and rib fracture (n=1). Most of the pneumothorax cases were managed conservatively without the need for drainage or prolongation of hospitalization. In 1 patient in the CA group, PVI was not performed because of pericardial effusion after transseptal puncture with spontaneous recovery. All other patients could be treated successfully without the need for conversion to a (minimally invasive) surgical approach. In the CA group, 1 patient had a transient ischemic attack with complete convalescence; in terms of minor adverse events, 4 patients (6.6%) had a groin hematoma without a drop in hemoglobin level or need for treatment.

Table 5. Adverse Events During 12-mo Follow-Up of CA and SA

Adverse Events	CA N=63	SA N=61	*P*-Value
Stroke	1	. . .	
TIA	1	. . .	
Pneumonia	2	2	
Hydrothorax	. . .	2	
Heart failure by AF	2	. . .	
SAB causing death	1	. . .	
Pericarditis	. . .	1	
Fever unknown origin	. . .	1	
Ileus	1	1	
PV stenosis >70%	. . .	. . .	
Total	8 (12.6%)	7 (11.5%)	*P*=1.0
Minor			
Groin hematoma/bleed	2 (3.2%)	. . .	

During the 12-month follow-up, 8 SAEs (12.7%) occurred in the CA group versus 7 (11.5%) in the SA group ($P=1.0$; Table 5). Of note, 1 patient in the CA group died after 1 month of subarachnoid hemorrhage while on vitamin K antagonists. In the CA group, stroke (n=1) and transient ischemic attack (n=1) were also observed, as well as heart failure caused by AF with a high ventricular rate (n=2). In the SA group, 2 late cases of hydrothorax, one that required draining, were notable. No significant (>70%) or symptomatic PV stenosis was observed on 6-month computed tomography/magnetic resonance imaging in either group. Heterogeneity testing did not show differences in effect according to site with $P>0.2$.

Discussion

To the best of our knowledge, this is the first randomized clinical trial to directly compare CA and SA for the treatment of AF. The reported efficacy for CA varies widely, although freedom from AF of >70% is considered acceptable.[2,3] Minimally invasive SA single-center success rates have been reported to be between 75% and 92% in selected populations.[11–15] In our study, in a population of patients with failed prior CA and/or dilated atria and hypertension,[15] SA was found to be superior to CA in achieving freedom from LA arrhythmia after a 12-month follow-up, albeit at the cost of a higher adverse event rate.

Procedural Effects of SA and CA

In the present study, we evaluated the strategy of endocardial CA versus epicardial SA; the latter strategy turned out to be significantly more efficacious. Several factors may play a role in explaining this difference. A total of 67% of our population consisted of patients with AF recurrence after a failed prior procedure, which could signify a predisposition to CA failure. Moreover, in the redo patients in the CA arm, only PVs still showing LA-PV conduction were reablated, whereas in the SA arm, all PVs were always ablated. Although the difference in effect was consistent in patients with and without a prior procedure, the study was not powered to establish the significance of this factor. There was also no apparent difference between using irrigated-tip and non–irrigated-tip ablation for CA or the specific study center where treatment was performed. The efficacy difference may result from superior transmurality of the epicardial bipolar RF lesion creation in SA, resulting in more antral PVI and permanent conduction block. We did not perform a repeated electrophys-

iology study to determine whether chronic PVI was indeed achieved in either treatment group.

Some studies have shown beneficial effects of adding LA ablation lines to PVI, specifically in patients with persistent AF.[2,3,6,7,18,19] At both study sites, the cornerstone of CA was electrically confirmed PVI by wide-area ablation in the antrum. In 49% of patients, an additional LA ablation line was performed, which did not seem to affect the efficacy regardless of the underlying type of AF. The patients in the SA group tended to have a diagnosis of paroxysmal AF slightly more often, whereas baseline Holter also showed no AF or paroxysmal AF more often. Because in more advanced stages of AF additional targets such as lines or ablation with complex fractionated atrial electrograms seem mandatory,[6,7] patients in the CA group may have been undertreated compared with patients in the SA group. The present trial was not designed to study such detailed differences.

Another factor may be the difference in the extent of the lesion set of CA compared with SA. SA not only results in PVI but also targets the epicardial ganglia and comprises LA appendage excision. Several studies have demonstrated the role of these ganglia in AF initiation and maintenance, whereas ablation of ganglia alone could lead to cure of AF.[20–22] So far, no randomized clinical trials have quantified the added effect of surgical ganglia ablation to achieve freedom from AF. Elimination of LA appendage ectopy may also facilitate in obtaining freedom from AF,[23] which may have contributed to the higher efficacy of SA observed. In the SA, 31% of patients had various additional LA ablation lines at the LA roof, aortic trigone, mitral isthmus, or box lesion around the PVs. This did not appear to affect the efficacy of SA at 12 months; if anything, efficacy tended to be a little lower in patients with such lines. Of note, part of these lines were made on an anatomic basis without verifying that conduction block had indeed been established. Whether additional lesions during either CA or SA would be beneficial for specific patient populations remains to be determined[24,25]; this study was not designed or powered to answer that question.

In both the CA and SA arms, the final efficacy was considerably lower than expected during the design of the trial in 2007. The estimates of efficacy were based on historical data in the literature on CA and SA. It was obviously not possible to predict the final mix of included patients for parameters such as failed prior ablation, persistent AF, and LA diameter. In the CA group, >40% of patients finally had nonparoxysmal AF and may have been undertreated by PVI alone. In addition, 67% had already failed a prior CA, which may be a more serious predisposition to failure than anticipated. Most historical data on the efficacy of CA and SA before the consensus statement of 2007[3] are based on heterogeneous criteria of success and less thorough rhythm follow-up than performed in this trial. As is becoming more apparent in current publications, longer duration of arrhythmia follow-up may reveal lower efficacies of invasive procedures than previously reported. This is also true for SA; in many of the initial publications in selected small populations, rhythm follow-up was usually <12 months, and arrhythmia detection was less frequent and shorter than 7 days.

Safety of SA and CA

CA is considered least invasive because it involves access to the heart through a small femoral puncture hole under local anesthesia. SA is considered minimally invasive when performed through video-assisted thoracoscopic surgery, mainly distinguishing it from complete open chest Cox maze surgery. The procedure requires general anesthesia, sequential deflation of both lungs, and transthoracic access to the heart involving several collateral structures. CA for AF has been performed in increasing numbers since 1998, and several large registries have focused on safety. The update of the worldwide survey for AF ablation[4] showed major adverse events in 741 of 10.781 patients (4.54%). The adverse event rate of 3.2% of CA in the present trial seems in line with the published data. The events reported with CA seemed more transient and did not require any intervention, perhaps because all operators were highly skilled at both high-volume AF ablation centers. The adverse events seemed to center around (anti-) coagulation, with bleeding on the one hand and transient ischemic attack, stroke, and subarachnoid hemorrhage leading to death on the other hand. New anticoagulation drugs are becoming available that may provide an answer to this well-known dilemma.[26,27]

There are no large registries for minimally invasive SA that provide good insight into safety. Several smaller series have been promising in this respect.[11–15] However, the procedural SA adverse event rate of 23.0% was clearly higher than that of CA. These SA complications tended to result mostly from direct mechanical injury during the procedure. About half required additional interventions and/or prolonged hospitalization, and most resolved without leaving permanent damage. The inability to complete the SA in a patient with substantial comorbidity highlights the importance of patient selection for this elective surgical procedure. Obviously, as minimally SA techniques and tools improve and the volume and experience of operators increase, such complications may diminish over time. Although some of the SAEs, both procedural and during follow-up, may not have been directly linked to the procedure itself, it is clear that cardiologists and their patients should consider the higher event rate, before deciding on a more invasive surgical procedure for AF, even though the efficacy may be superior.

Limitations

Arrhythmia follow-up was performed with intermittent ECG, 7-day Holter, and sometimes event recording, which may underestimate absolute arrhythmia recurrence. Most patients in our study had undergone a prior unsuccessful CA as inclusion criterion. This may make the conclusion less applicable to patients with the inclusion criterion of dilated LA or to the general AF population. In the population studied, 67% had paroxysmal AF and 33% had continuous persistent AF <1 year. Although we did not observe a significant effect of AF type on efficacy, the study may have been underpowered for this factor. In the patients who had AF during the CA or SA procedure, PV ablation was simply repeated without prior measurement of actual PV-LA conduction. In both the CA and SA groups, there were differences between the sites in several of the practical procedural details. Although the efficacy of CA and

SA was consistent and similar at the sites, the trial was not powered to study the effect of such differences.

Conclusion

In AF patients with a dilated LA and hypertension or failed prior LA CA, minimally invasive SA is superior to CA in achieving freedom from LA arrhythmias after 1 year of follow-up. The procedural adverse event rate, however, is significantly higher for SA than for CA. These findings may guide physicians and patients when considering invasive AF treatment options.

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The participating institutions funded the study. AtriCure provided a partial grant to facilitate the trial. AtriCure had no part in any aspect of the trial, including design, and did not have access to any part of the data, including the collection, interpretation, conclusion, and publication.

Disclosures

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CLINICAL PERSPECTIVE

Catheter ablation (CA) and minimally invasive surgical ablation (SA) have become accepted therapy for antiarrhythmia drug–refractory atrial fibrillation (AF). This study describes the first randomized clinical trial comparing the efficacy and safety of CA and SA during 12 months of follow-up. One hundred twenty-four patients with antiarrhythmia drug–refractory atrial fibrillation with left atrial dilatation and hypertension (42 patients, 33%) or failed prior CA (82 patients, 67%) were randomized to CA (63 patients) or SA (61 patients). CA consisted of linear antral pulmonary vein isolation and optional additional lines. SA consisted of bipolar radiofrequency isolation of the bilateral pulmonary vein, ganglionated plexi ablation, and left atrial appendage excision with optional additional lines. Follow-up at 6 and 12 months was performed by ECG and 7-day Holter recording. The primary end point, freedom from left atrial arrhythmia >30 seconds without antiarrhythmia drugs after 12 months, was 36.5% for CA and 65.6% for SA ($P=0.0022$). There was no difference in effect for subgroups, which was also consistent at both sites. The primary safety end point of significant adverse events during the 12-month follow-up was significantly higher for SA than for CA (n=21 [34.4%] versus n=101 [5.9%]; $P=0.027$), driven mainly by procedural complications such as pneumothorax and bleeding. In the CA group, 1 patient died at 1 month of subarachnoid hemorrhage while on vitamin K antagonists. The results indicate that in atrial fibrillation patients with dilated left atrial and hypertension or failed prior CA, SA is superior in achieving freedom from left atrial arrhythmias after 12 months of follow-up at the cost of a higher procedural serious adverse event rate. These findings may guide physicians and patients in choosing between these invasive treatments for atrial fibrillation.

DISCUSIÓN

DISCUSIÓN

1. Evolución del tratamiento de FA:

1.1. Tratamiento farmacológico y CVE

La FA es la arritmia clínica más frecuente, y supone un incremento significativo de la mortalidad y morbilidad cardiovascular.

El tratamiento de la FA ha experimentado una evolución notoria a lo largo de los años debido a la profundización en el conocimiento de la fisiopatología de la arritmia, a la investigación de nuevos enfoques terapéuticos, así como a un marcado desarrollo de la tecnología.

El tratamiento farmacológico, mediante el control del ritmo o de la frecuencia cardíaca, está dirigido a evitar las potenciales complicaciones derivadas de la FA y requiere a menudo un abordaje multidisciplinar. Sin embargo, a pesar de la existencia de numerosos documentos de consenso y guías de práctica clínica, la estrategia de tratamiento varía entre los diferentes especialistas y entre los diferentes niveles asistenciales.

Hasta la actualidad, son escasos los estudios que han analizado la eficacia de la implantación de un protocolo de tratamiento de FA centrado en el manejo antiarrítmico y anticoagulante. Los estudios que evalúan la adecuación del tratamiento de la FA se han focalizado en el tratamiento anticoagulante, pero son pocos los trabajos que han analizado el grado de cumplimiento de las indicaciones para el tratamiento antiarrítmico en este grupo de pacientes, por lo que se desconoce la adecuación o no de su uso.

En el presente trabajo se evaluó la eficacia de la implantación de un protocolo común de tratamiento de FA en diferentes niveles asistenciales y en 2 periodos de tiempo separados por 1 año, antes y después de la implementación del protocolo. En el primer periodo de tiempo, sólo el 71% de los pacientes recibía un tratamiento antiarrítmico adecuado, porcentaje que era inferior en atención primaria. Estos datos se asemejan a los publicados en el registro europeo de manejo de FA (94), estudio observacional que incluyó prospectivamente a pacientes con FA atendidos de forma ambulatoria o bien hospitalizados en 182 hospitales, y que demostró que sólo el 67% de los pacientes con FA sintomática eran sometidos a una estrategia de control del ritmo cardíaco. Sin embargo, nuestro estudio demostró que la implementación del protocolo se asoció a una mejoría significativa en la eficacia del tratamiento antiarrítmico recibido antes de la visita en el segundo periodo en todos los niveles asistenciales (se incrementó hasta el 80%), aunque no se observaron diferencias significativas en la adopción de medidas para corregir el tratamiento antiarrítmico recibido por el paciente antes y después de esta visita.

En cuanto al tratamiento dirigido a prevenir las complicaciones tromboembólicas, hubo una mejoría en su aplicación, de modo que éste pasó de aplicarse correctamente en tan sólo un 67% de los pacientes antes de la primera visita, hasta un 81% antes de la visita en el segundo periodo. En atención primaria se observó una mejoría, aunque no significativa, en la adecuación del tratamiento anticoagulante. Estos resultados sugieren que el tratamiento anticoagulante puede ser iniciado de forma eficaz desde el nivel de atención primaria y que la formación adecuada a este nivel puede contribuir a mejorar el tratamiento de los pacientes con FA.

La adecuación en la prescripción del tratamiento anticoagulante ha sido analizada por otros autores (95-101). En el registro europeo de manejo de FA (93), y de forma similar

a nuestro estudio, sólo el 67% de los pacientes con indicación de anticoagulación recibía profilaxis tromboembólica. En un estudio previo, Ruiz y col. (102) analizaron la utilidad de un protocolo prospectivo en pacientes con FA revisados en consulta externa de cardiología para aumentar la utilización de ACO en este grupo de pacientes. De forma similar a nuestros datos, la instauración de un protocolo de tratamiento consiguió aumentar la prescripción de ACO hasta en el 90% de los pacientes. Sin embargo, no existen hasta la fecha estudios que analicen los beneficios de establecer un protocolo común de tratamiento antiarrítmico y anticoagulante entre diferentes niveles asistenciales.

El análisis de las diferentes estrategias de tratamiento antes y después de la implementación del protocolo pone de manifiesto dos importantes conclusiones. Por una parte, revela las deficiencias en el tratamiento farmacológico de la FA en la práctica clínica diaria en los diferentes niveles asistenciales, especialmente en la atención primaria. Por otro lado, demuestra el beneficio de establecer un protocolo de actuación conjunta y un programa educativo que permita aunar y mejorar el tratamiento de los pacientes con FA.

La CVE es una estrategia destinada al control del ritmo cardíaco cuya aplicación en la práctica clínica habitual no ha sido convenientemente analizada en el periodo actual. Es por ello que con el fin de conocer las características de los pacientes sometidos a CVE y evaluar el posible impacto de las guías de práctica clínica sobre el manejo de la FA, realizamos un estudio multicéntrico que incluyó a los pacientes sometidos a CVE en Cataluña en el 2010 comparándolos con una cohorte de pacientes sometidos a CVE en el 2003.

El estudio reveló una reducción absoluta del 23% en la práctica de CVE en el momento actual (247 en el 2003 frente a 189 en el 2010, p= 0,004). Además, las características de los pacientes sometidos a CVE en la actualidad eran diferentes, especialmente en lo que respecta a la presencia de una mayor morbilidad cardiovascular. Ello puede sugerir, por una parte, que en pacientes con elevada morbilidad cardiovascular se aboga por un control del ritmo cardíaco más agresivo que hace años. Por otra parte, la reducción del número de pacientes sometidos a CVE pudiera explicarse por el cada vez más habitual abordaje de control del ritmo cardíaco mediante otras estrategias, como la ablación percutánea. El hecho de que la AC se emplee preferentemente en pacientes con escasa morbilidad cardiovascular podría explicar también el aumento relativo de morbilidad cardiovascular de los pacientes sometidos a tratamientos alternativos, como es el caso de la CVE.

1.2. Ablación percutánea de FA

La ablación percutánea de la FA ha experimentado un desarrollo significativo a lo largo de los años, pasando a ser en la actualidad un procedimiento habitual en muchos de los laboratorios de Electrofisiología. La evolución en la curva de aprendizaje de los operadores, así como la mejoría progresiva de la metodología y tecnología empleada han contribuido a que dicho procedimiento se haya establecido como un tratamiento con indicación de clase I para pacientes con FA paroxística sintomática y refractaria a tratamiento antiarrítmico (43).

El procedimiento de AC de FA conlleva un riesgo de ACV debido en parte a la manipulación de los catéteres en las cavidades izquierdas. Es por ello que previo al procedimiento se recomienda la realización de un ETE con el objetivo de descartar la

presencia de trombos intracavitarios en pacientes con FA no paroxística y con una puntuación en la escala $CHADS_2 > 2$. Sin embargo, se desconoce la incidencia real de la presencia trombos en pacientes sometidos a AC así como los factores de riesgo de la formación de trombos en este grupo de pacientes. Además, las guías no establecen claras recomendaciones en cuanto a la utilidad de la ETE previa al procedimiento de ablación en pacientes con un perfil de riesgo cardioembólico bajo.

En nuestro estudio, observamos que la incidencia de trombos intraauriculares en pacientes sometidos a ablación percutánea es baja (1,47%) y que su aparición se asocia al sexo femenino, la dilatación auricular y a la presencia de cardiopatía. Ningún paciente con FA paroxística en ausencia de cardiopatía estructural y con una puntuación <2 en la escala de riesgo $CHADS_2$ presentó trombos en la aurícula.

Nuestro estudio demuestra resultados similares a los escasos trabajos publicados en la literatura, en los que la incidencia de trombos en este grupo de pacientes osciló entre un 0,49 y 2,9% (103-107). La FA persistente, la HTA y la presencia de cardiopatía estructural se han asociado con el desarrollo de trombos, mientras que el coste-efectividad de esta prueba es hasta 10 veces es mayor en pacientes que no presentan ninguno de estos factores de riesgo (108). Por tanto, los hallazgos de nuestro estudio permiten suponer que la ETE previa al procedimiento podría no ser necesaria en pacientes con FA paroxística, sin cardiopatía estructural y con una AI no dilatada.

Es importante destacar que una de las limitaciones del estudio es la falta de datos acerca del tratamiento anticoagulante y de los valores de INR en las 4 semanas previas al procedimiento, por lo que nuestros resultados deben ser corroborados en estudios randomizados con un correcto control del tratamiento anticoagulante previo a la ETE y la AC de la FA.

Además de conllevar un riesgo cardioembólico, la AC de FA es un procedimiento complejo que puede originar otras complicaciones graves, por lo que requiere la sistematización de la metodología empleada y su realización por un operador con gran experiencia. Así mismo, resulta necesario un análisis crítico de los resultados y complicaciones derivadas del procedimiento en cada centro, con el fin de identificar y evitar las potenciales fuentes de complicaciones y los predictores de mala respuesta al tratamiento.

En el presente estudio, analizamos los resultados, complicaciones y predictores de éxito de la ablación percutánea de FA en los pacientes sometidos a dicho procedimiento en nuestro centro, distinguiendo dos tipos de poblaciones que fueron definidas por la instauración de un protocolo de anticoagulación y sedación intraprocedimiento (tabla 1).

Protocolo de anticoagulación periprocedimiento:

- Dosis inicial, administrada justo después de la realización de la punción transeptal:
- a) <75 kg: 5000 UI HNF
- b) >75 kg: 6000 UI HNF
- Control ACT / 10 min hasta alcanzar ACT > 200 seg.
- Si el ACT es:

  a) 150-200 seg:3000 UI HNF, nuevo control de ACT a los 10 min.

  b) 201-250 seg: 2000 UI HNF, nuevo control de ACT a los 30 min.

  c) 250 seg: No administrar HNF, nuevo control de ACT a los 30 min.

Protocolo de anticoagulación post-procedimiento:

- Tras 6 horas, reiniciar anticoagulación, administrando HBPM a dosis de 1 mg/kg/12horas, junto con acenocumarol hasta lograr dosis óptimas de anticoagulación (INR >2).
- Mantener anticoagulación oral durante al menos 2 meses. Su interrupción podrá realizarse en ausencia de un riesgo > 1 según la escala CHADS.

Protocolo de sedación consciente durante el procedimiento:

- Al inicio: Dolantina 25 mg + Midazolam 1 mg en bolo ± Fentanilo 30 mcg.
- Justo antes de la punción transeptal:
  - < 65 kg: Fentanilo 30 ml/h perfusión
  - ≥65 kg : Fentanilo 40 ml/h (300 mcgr/120 ml SSF = 2 amp/120 ml SSF).
- Justo antes de la aplicación de radiofrecuencia: Fentanilo 75 mcg (5cc) bolo ± midazolam 1-2 mg adicional bolo en casos necesarios.

Tabla 1. Protocolo de anticoagulación y sedación intraprocedimiento.

La tasa de éxito global fue del 61%, ligeramente inferior a lo publicado en otras series (42). Esta discrepancia pudiera deberse a la heterogeneidad de la definición de recurrencia arrítmica empleada, así como a los diferentes medios de monitorización de la carga arrítmica usados durante el seguimiento en los diferentes estudios. Por otra parte, y en concordancia con trabajos previos, la HTA y el síndrome de apnea obstructiva del sueño fueron predictores de recurrencia arrítmica tras la ablación.

A partir de la instauración del protocolo de anticoagulación y sedación consciente en nuestro centro, hubo una reducción significativa de las complicaciones totales (figura 3). A pesar de que este hallazgo podría ser atribuible a la sistematización del protocolo de sedación y anticoagulación, no se puede descartar que pudiera responder a una mejoría en la curva de aprendizaje de los operadores y del personal de enfermería y a la progresiva mejoría tecnológica.

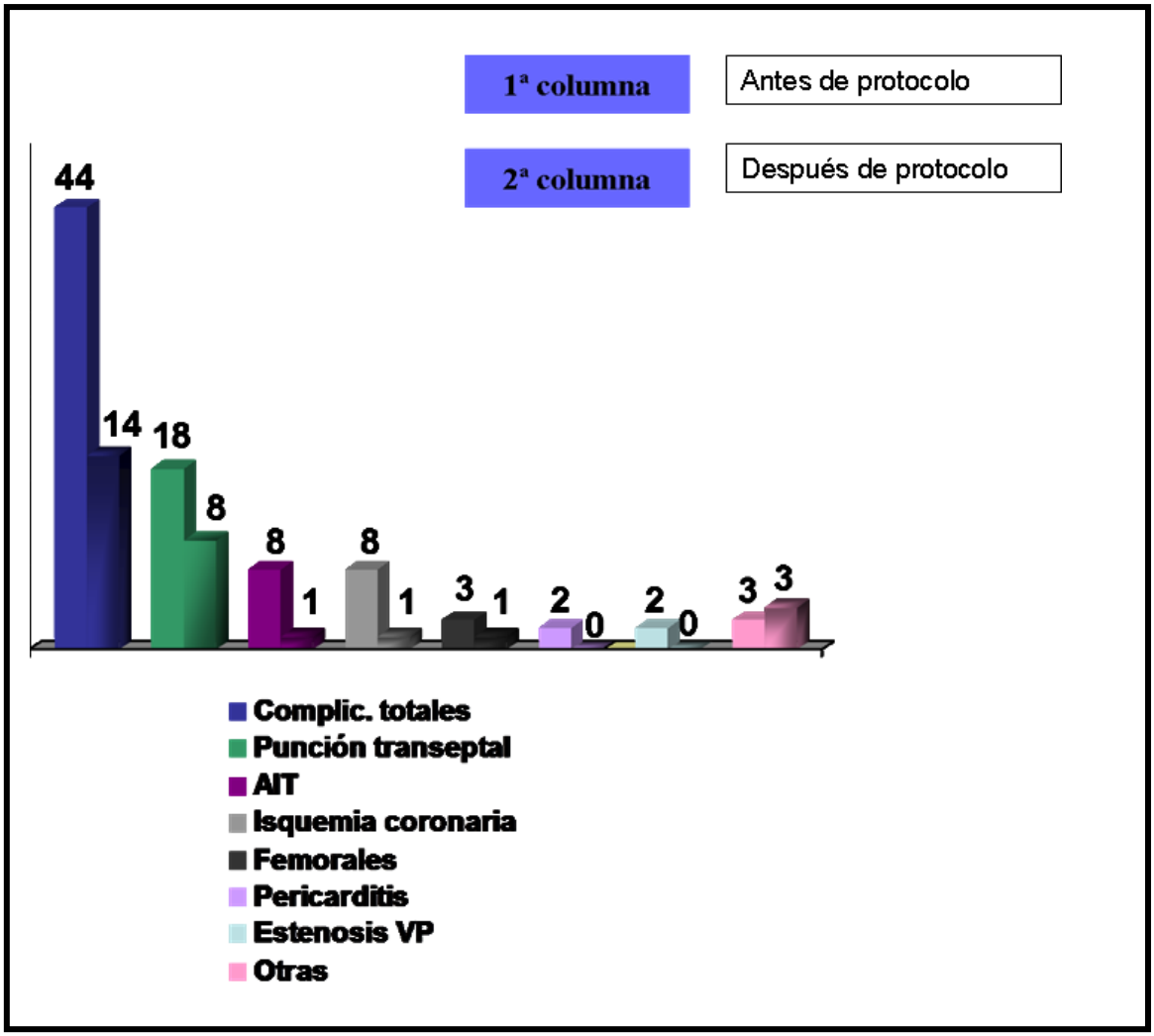


Figura 3. Número de complicaciones antes y después de la instauración de un protocolo de anticoagulación y sedación consciente intraprocedimiento.

Con respecto a los resultados de la AC de la FA, es bien conocida su eficacia en pacientes con FA y factores de riesgo clásicos. Sin embargo, existe un grupo de pacientes, los deportistas de alta intensidad, en los que se ha demostrado un aumento en la incidencia de FA a pesar de no presentar ninguno de los factores de riesgo clásicamente descritos. La eficacia de la ablación en este grupo de pacientes, en los que el mecanismo fisiopatológico de la arritmia podría diferir respecto a la población general con FA, es desconocida. Por este motivo, planteamos un estudio que incluyó a pacientes deportistas con FA y a pacientes con FA y factores de riesgo clásicos sometidos a ablación de FA con el fin de conocer y comparar su evolución.

Se definió al paciente deportista como aquél con una práctica deportiva intensa de más de 3h a la semana durante más de 10 años. Esta definición se basó en estudios previos de nuestro centro, en los que se identificó que una práctica deportiva acumulada >1500h se asocia con un incremento del riesgo de FA (109). Para la evaluación de la práctica deportiva, se empleó el cuestionario reflejado en la tabla 2.

	Actividad	Edad inicio	Edad Final	Frecuencia práctica			Tiempo diario (horas)	Intensidad (2-4)
				Día	Semana	Mes		
1								
2								
3								
4								
5								
6								

Intensidad:

2) Esta actividad requería poco esfuerzo físico. No sudaba y no notaba que su pulso (frecuencia cardíaca) se acelerara.

3) Esta actividad requería un esfuerzo físico moderado: Durante su práctica sudaba un poco y se notaba un ligero aumento de las pulsaciones..

4) Esta actividad requería un esfuerzo físico importante: Durante su práctica sudaba mucho y se notaba un importante aumento de las pulsaciones.

Tabla 2. Cuestionario para evaluar la práctica de actividad física.

Una de los principales hallazgos de nuestro estudio fue el alto porcentaje de deportistas entre los pacientes referidos para AC de FA (35%). Este volumen de deportistas supera significativamente el porcentaje de deportistas en la población general, según datos del

estudio REGICOR (110). Estos resultados están en consonancia con estudios previos en los que se ha demostrado una asociación entre la práctica deportiva de alta intensidad y el desarrollo de FA (109,111-116).

Se desconoce el mecanismo fisiopatológico para el desarrollo de FA en pacientes deportistas, aunque estudios experimentales recientes (117) han demostrado que la práctica deportiva promueve el desarrollo de fibrosis en el miocardio auricular, lo que podría ser responsable del sustrato para dicha arritmia. Por otra parte, en los deportistas se produce un incremento del tono vagal, que acorta el periodo refractario auricular, favoreciendo así el desarrollo de FA.

Hasta el momento del estudio, no existían datos en la literatura acerca del éxito de la ablación en deportistas con FA aislada en comparación con un grupo control. Dado que los deportistas con FA aislada no tienen factores de riesgo de FA cabía suponer que el éxito del procedimiento iba a ser mayor en este grupo. Sin embargo, un posible mecanismo fisiopatológico diferente en deportistas frente a la población general pudiera conllevar un fracaso de la terapia destinada al aislamiento de las VVPP.

Por ello, se compararon los resultados de la AC entre un grupo de pacientes deportistas con FA aislada y la población control.

Nuestro estudio demostró que no existen diferencias en cuanto a la probabilidad libre de arritmias entre ambos grupos y, de manera similar a los hallazgos de otros estudios, únicamente el tamaño de la AI y la presencia de HTA fueron factores predictores de éxito de la ablación, independientemente de la práctica deportiva.

2. Eficacia y complicaciones de la ablación percutánea de la FA en comparación con la ablación quirúrgica.

La ablación quirúrgica de la FA fue desarrollada por Cox y col. en 1987 como tratamiento de la FA refractaria a tratamiento médico. El procedimiento se basaba en la creación de incisiones quirúrgicas en ambas aurículas para así interrumpir los circuitos de macrorreentrada responsables de la FA. A pesar del éxito inicial superior al 95%, la complejidad y carácter invasivo de la técnica quirúrgica hizo que este procedimiento quedara relegado a pacientes muy seleccionados con FA refractaria a tratamiento médico, y en un número limitado de centros.

La descripción del papel de las venas pulmonares en el origen y mantenimiento de la FA por Haissaguerre (30) junto con la necesidad de un abordaje menos invasivo ha conducido a la búsqueda de procedimientos quirúrgicos mínimamente invasivos.

La ablación quirúrgica de FA mediante video-toracoscopia fue descrita por Wolff y col. en 2006. Mediante una minitoracotomía bilateral guiada por vídeo, el aislamiento de las VVPP se realizaba mediante una pinza de radiofrecuencia bipolar junto con la excisión de la orejuela izquierda.

Desde entonces, la técnica ha evolucionado sucesivamente hacia procedimientos menos invasivos, como un abordaje completamente toracoscópico bilateral. Actualmente, las guías clínicas establecen una indicación de clase IIb para la ablación quirúrgica en pacientes con FA sintomática y refractaria a tratamiento médico con un intento previo fallido de ablación percutánea.

Una revisión de Khargi y col. (118) comparó la eficacia y seguridad del tratamiento de la FA mediante un abordaje percutáneo o quirúrgico. Se evaluaron un total de 48 artículos con 2279 pacientes sometidos a ablación percutánea frente a 1553 pacientes

sometidos a ablación quirúrgica. El análisis de regresión demostró que el porcentaje de pacientes en RS en el postoperatorio fue mayor entre los pacientes sometidos a ablación quirúrgica (84,9% vs. 78,3%, p = 0,03). Sin embargo, una vez ajustado el análisis por el tipo de FA y por el tipo de cirugía (cirugía aislada de FA o cirugía concomitante), no hubo diferencias significativas en la tasa de RS postoperatoria (p = 0,260). Tampoco hubo diferencias significativas en la tasa de morbilidad y mortalidad entre ambos abordajes.

Una revisión más reciente de Mack (119) analizó una serie de 14 artículos de ablación quirúrgica aislada mínimamente invasiva en 605 pacientes con FA. El éxito global del procedimiento fue del 99,5%, con un porcentaje libre de recurrencias de entre el 59 y 91%, dependiendo del tipo de FA (79-100% en FA paroxística frente a 27-87% en FA persistente), de la fuente de energía usada, y de la duración y método de seguimiento. Las complicaciones incluyeron 2 fallecimientos (0,3%), implante de marcapasos (5%), parálisis del nervio frénico (3%), hemotórax (1%), accidente isquémico transitorio (0,3%) y lesión del plexo braquial (0,3%).

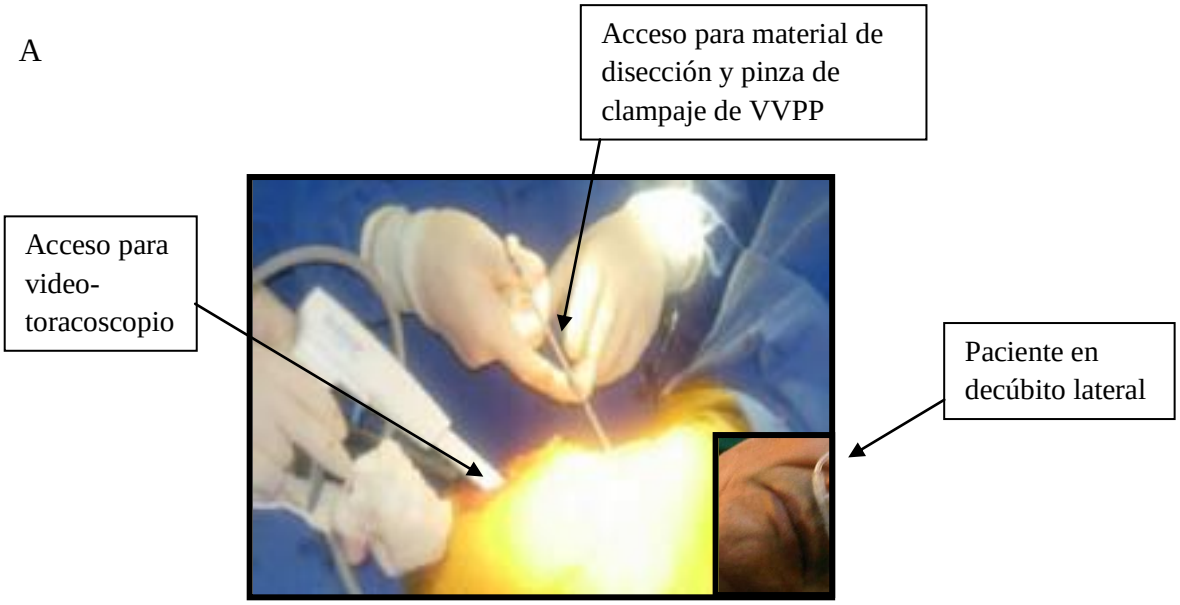
Los resultados publicados hasta la fecha reflejan la experiencia de un número limitado de centros, con una gran heterogeneidad tanto de los pacientes, como de la técnica quirúrgica empleada y del seguimiento (tabla 3) (120). Por otra parte, hasta la fecha sólo existen estudios observacionales no randomizados, por lo que se desconoce la verdadera eficacia y seguridad de la ablación percutánea en comparación con la ablación quirúrgica.

Primer autor (ref.)	Seguimiento (meses)	% ptes libres de recurrencia arrítmica	% ptes en tratamiento antiarrítmico	Complicaciones (%)
Loulmet (121)	8	-	100	0
Salenger (122)	12	67	-	42,8
Wolf (123)	5,7	91,3	9	14
Charohopos (124)	66	100	0	0
Koistinen (125)	11	100	2	22,7
Sagbas (126)	8	72	19	0
Puskas (127)	6	100	-	0
Mc Clelland (128)	17	75	25	10
Wudel (129)	18	91	9	9,1
Edgerton (130)	6	En FA pers.:90 En FA larga evolución: 75	En FA pers.:22 En FA larga evolución: 53	5,4
Sirak (131)	6	87,5	12	3,1
Pruitt (132)	23	42	11	13
Li (133)	6	60	40	0
Bayer (134)	13	87	36	13
Edgerton (135)	6	82	37	-
Han (136)	12	65	9	8,8
Bagge (137)	12	76	32	16,2
Cui (138)	12	79,6	-	7,4
Yilmaz (139)	11	77	35	10
Sirak (140)	6	100	-	4,1
La Meir (141)	27	95,5	11	0
Jansens (142)	3	60	-	14,2
Gerosa (143)	3	100	0	0
Balkhy (144)	-	100	100	0
Poa (145)	-	-	0	0
La Meir (146)	4	100	0	0
Klinkemberg (147)	24	46,6	40	13,3
Bevilacqua (148)	9	85,7	-	0
Nasso (149)	17	89	47	2,8
Moten SC (150)	12	87	-	0
Cheema FH (151)	6,5	100	0	0
Lee (152)	12	100	19	0

Tabla 3. Resultados y complicaciones de la cirugía mínimamente invasiva para el tratamiento aislado de la FA. Pers: persistente; FA larga evolución: FA persistente de larga evolución. Adaptado de Gelsomino S y col. (120).

Nuestro estudio permitió comparar por primera vez la eficacia y seguridad de la ablación quirúrgica respecto a la ablación percutánea (figura 4) en pacientes con un intento fallido de ablación percutánea o pacientes con HTA y AI dilatada.

A



B

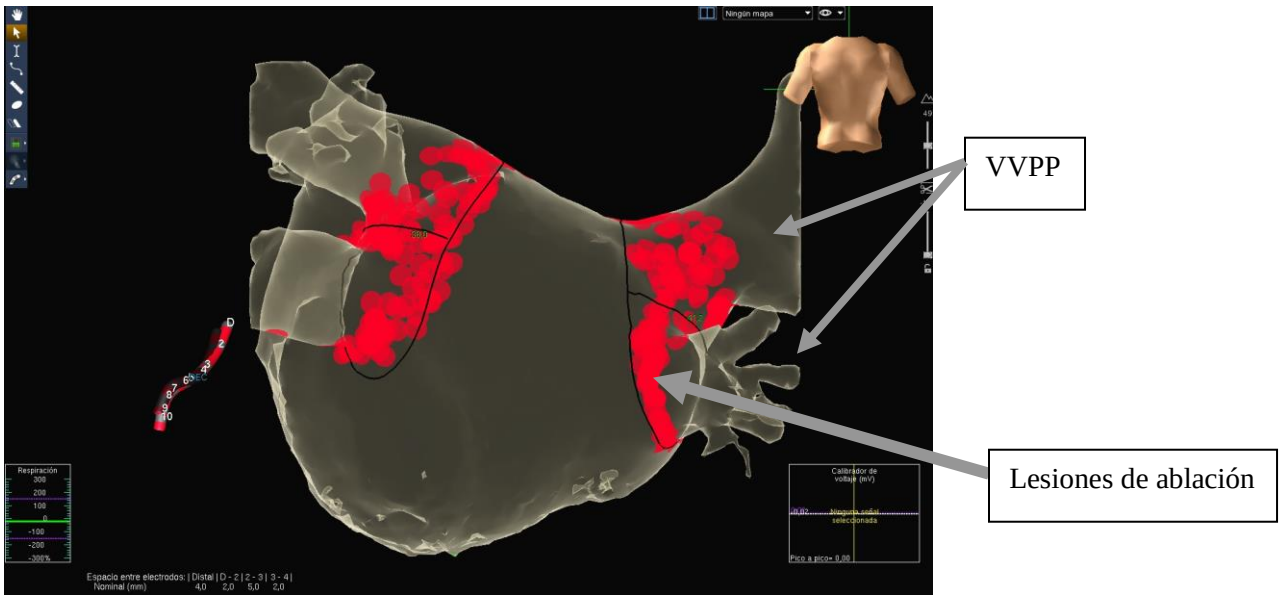


Figura 4. A) Procedimiento de ablación quirúrgica asistida mediante video-toracoscopia. Obsérvese la posición inicial del paciente en decúbito lateral izquierdo para el abordaje, a través del 4º y 7º espacio intercostal, de las VVPP derechas. A continuación, se repite el procedimiento en decúbito lateral derecho para acceder a las VVPP izquierdas. B) Ablación percutánea de FA mediante radiofrecuencia y sistema de navegación no fluoroscópica. Los puntos rojos corresponden a las lesiones de radiofrecuencia.

Tras un seguimiento de 12 meses, la eficacia de la ablación quirúrgica fue significativamente mayor en este grupo de pacientes. Aunque se desconoce la razón de la superioridad de la ablación quirúrgica frente a la percutánea, la transmuralidad de las

lesiones quirúrgicas así como una mayor extensión de las lesiones realizadas mediante el abordaje quirúrgico, englobando la ablación ganglionar y la escisión de la orejuela izquierda, podrían ser responsables del mayor éxito de esta técnica. Sin embargo, permanece en entredicho el papel de la transmuralidad de las lesiones como requisito para el mantenimiento del RS. Santiago y col. (153) correlacionaron la temperatura intra-tisular con el grosor tisular y con la histología de las lesiones en 10 pacientes. Se observaron lesiones transmurales en un 20%, un daño miocárdico variable en el 30% y daño endocárdico en el 50%. A los 6 meses, 4 de los 5 pacientes con afectación no transmural estaban en RS así como 2 de los 5 pacientes con afectación exclusivamente endocárdica. Estos hallazgos sugieren que incluso las lesiones no transmurales se asocian con el mantenimiento del RS.

En nuestro trabajo, destaca el mayor porcentaje de complicaciones observadas en el brazo de ablación quirúrgica (23%) frente al brazo de ablación percutánea (3,2%). Las complicaciones de la ablación quirúrgica consistieron principalmente en lesiones mecánicas durante el procedimiento, fundamentalmente neumotórax. No hubo diferencias en las complicaciones entre ambos grupos a los 12 meses de seguimiento. La mejora de la tecnología, una mejor selección de los pacientes, así como la progresiva experiencia del operador podrán en el futuro reducir estas tasas de complicaciones.

Los resultados de nuestro estudio sugieren que la ablación quirúrgica de FA en pacientes con un intento fallido de ablación percutánea o en pacientes hipertensos y con AI dilatada conlleva un menor índice de recurrencias en comparación con la ablación percutánea. Sin embargo, el alto porcentaje de complicaciones en el momento actual hace que la ablación quirúrgica deba limitarse a un grupo selecto de pacientes en los que la ablación percutánea tenga un alto riesgo de recurrencia.

CONCLUSIONES

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Subproyecto 1.

1. La puesta en práctica de un protocolo de actuación conjunta en diferentes niveles asistenciales y un programa educativo para el tratamiento farmacológico de la FA se asocia a una optimización y una mayor adherencia a las guías de práctica clínica, tanto en lo relacionado con el control de la arritmia como en el tratamiento anticoagulante, de los pacientes con FA.

2. A lo largo de los años se ha producido una reducción en la práctica de la CVE como tratamiento para el control del ritmo cardiaco en pacientes con FA. Los pacientes sometidos a CVE en la actualidad presentan una mayor morbilidad cardiovascular. Ello puede ser explicado por un mayor esfuerzo para conseguir el control del ritmo cardíaco, aun en pacientes con enfermedades más avanzadas, así como por un cada vez más habitual control del ritmo cardíaco mediante la ablación percutánea.

3. La incidencia de trombos intracavitarios en pacientes sometidos a ablación percutánea es baja y su aparición se asocia al sexo femenino, la dilatación auricular, la FA persistente y a la presencia de cardiopatía.

4. La instauración de un protocolo de anticoagulación y sedación consciente en los pacientes sometidos a AC de FA parece asociarse a una reducción significativa de las complicaciones totales así como a una mejoría de la eficacia del procedimiento de ablación.

5. Los resultados de la AC en pacientes deportistas con FA aislada no difiere de los resultados en la población general con FA.

Subproyecto 2.

1. La eficacia de la ablación quirúrgica en pacientes con un intento fallido de ablación percutánea o pacientes con HTA y AI dilatada es significativamente mayor que en los pacientes sometidos a AC.

2. La ablación quirúrgica de FA se asocia a un riesgo de complicaciones significativamente superior que la AC.

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ADÉNDUM

ADÉNDUM: OTROS ARTÍCULOS RELACIONADOS PUBLICADOS

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