Ablació amb Catèter de Radiofreqüència de la Fibril·lació Auricular: Tècniques, Complicacions i Resultats

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Ablació amb Catèter de Radiofreqüència de la Fibril·lació Auricular: Tècniques, Complicacions i Resultats.

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Índex

Llistat d'abreviatures utilitzades

FA: fibril·lació auricular.

VP: venes pulmonars.

RF: radiofreqüència.

AE: aurícula esquerra.

AOSS: ablació ostial segmentària i selectiva.

ACVP: ablació circumferencial de venes pulmonars.

FE: fracció d'ejecció.

PP: paret posterior.

CMC: catèter de mapeig circular

INTRODUCCIÓ GENERAL

La fibril·lació auricular (FA) no només és l'arítmia més freqüent en la pràctica clínica, sinó que també és una de les més complexes. La morbi-mortalitat associada i el deteriorament en la qualitat de vida, així com el seu impacte en els recursos del sistema sanitari, fa que el tractament de la FA sigui un dels grans objectius de l'electrofisiologia actual[1-3].

Fins fa uns anys, en cas d'una mala resposta al tractament convencional (fàrmacs i/o cardioversió elèctrica), l'alternativa disponible era la cirurgia del laberint o *Maze*[4], una intervenció habitualment realitzada de forma secundària a una altra cirurgia cardíaca. En la cirurgia del laberint es creen una sèrie d'incisions a les aurícules per reduir la quantitat de teixit contigu amb viabilitat elèctrica. L'objectiu d'aquest procediment és evitar tenir la massa auricular mínima que, segons la teoria dels múltiples fronts d'ona, se suposa necessària per sostenir la FA[5].

La teoria dels múltiples fronts d'ona era la més acceptada per explicar el mecanisme de la FA fins que, fa una dècada, Haissaguerre i col·laboradors van descriure paroxismes de l'arítmia desencadenats per activitat ectòpica ràpida originada en les venes pulmonars (VP)[6;7]. Aquest descobriment va obrir noves vies per tractar la FA amb tècniques d'ablació per catèter de radiofreqüència (RF), i va redirigir noves investigacions sobre els mecanismes responsables de l'arítmia.

En les primeres ablacions de FA, la RF s'aplicava directament sobre els focus d'ectòpia de VP que s'observaven durant el procediment[8]. Aquests focus poden tenir una localització distal dins la vena, on l'aplicació de RF té un alt risc d'estenosar-la[9].

Per aquest motiu, l'aproximació va evolucionar a deixar el focus elèctricament exclòs enlloc d'eliminar-lo directament. Això s'aconseguia aïllant la VP ectòpica aplicant RF en la inserció veno-atrial o *óstium* de VP[10]. Aquesta tècnica es coneix com aïllament ostial i segmentari, degut a que la connexió elèctrica entre vena i aurícula esquerra (AE) no es troba present en tot el *óstium*, sinó només en determinats segments del seu perímetre on les fibres miocàrdiques s'insereixen en la regió venosa en forma d'espiral[11]. La identificació d'aquests segments, així com la confirmació de la seva desconnexió, es va descriure amb la guia d'un catèter circular multipolar específic per aquest propòsit.

Per la seva banda, Pappone i col·laboradors van descriure l'ablació circumferencial de VP[12], una altra aproximació per excloure elèctricament les VP de l'AE. En aquest procediment, totes les VP són encerclades creant lesions contigües que envolten cada conjunt ipsilateral. En l'ablació circumferencial de VP, la RF s'aplica en la regió més proximal de la inserció venosa, reduint encara més la probabilitat d'estenosis de VP respecte l'aïllament ostial. Una altra novetat descrita en la tècnica va ser la utilització d'un sistema de navegació que permetia reconstruir tridimensionalment les cambres cardíaques i localitzar la posició del catèter de RF en temps real. Això permetia guiar la creació i validació de les lesions de manera que es simplificava considerablement el procés. En els darrers anys, el ús dels sistemes de navegació s'ha estès en els laboratoris d'electrofisiologia, i han aparegut eines més sofisticades amb noves aplicacions i millors tècniques d'imatge.

Tot i els nous estudis sobre els mecanismes de la FA i els grans avenços fets durant la darrera dècada en les tècniques d'ablació, encara avui existeixen moltes questions sobre aquesta prometedora teràpia pel tractament de l'arítmia. L'ablació percutània de FA amb catèter de RF es realitza a la Unitat d'Electrofisiologia de l'Hospital Clínic de Barcelona des del 2001, desenvolupant-se de forma paral·lela una línia d'investigació sobre el tema. Els estudis que formen part d'aquesta tesi doctoral pertanyen a diferents treballs sobre ablació de FA que han aportat informació rellevant en aquest camp i que han estat recollits en articles originals publicats en revistes de difusió internacional. En la present memòria es descriuen aquests treballs segons l'ordre cronològic en el que aquests es van desenvolupar.

ANTECEDENTS i HIPÒTESIS de TREBALL

Els mecanismes de la FA, tot i no estar clarament definits, són diversos i no actuen de la mateixa manera en cada cas. Per això, realitzar el mateix procediment d'ablació en tots els pacients podria no ser l'aproximació òptima. Recentment s'han proposat estratègies d'ablació de FA per passos, on la quantitat de lesions realitzades s'adapta en funció de determinats esdeveniments observats durant el propi procediment, però el criteri adequat per guiar aquest tipus d'aproximació encara no està clar[13;14]. Identificar aquells casos en els que la responsabilitat de la FA és eminentment focal, enfront a perfils de l'arítmia dependents de mecanismes més difusos, simplificaria el procediment d'ablació i reduiria la quantitat de lesions creades. En pacients amb FA i una aurícula estructuralment normal, la presència d'ectòpia d'AE freqüent i sostinguda indicaria molta activitat focal de VP i poca presència de substrat auricular. En aquests casos, l'aïllament selectiu de les VP ectòpiques podria ser suficient per tractar la FA, sense necessitat de realitzar lesions més extenses. Tanmateix, en el cas de l'ablació ostial, el risc potencial d'estenosis de VP augmenta al aplicar-se la RF en la inserció veno-atrial[9], i també s'ha de valorar al plantejar el procediment.

L'eficàcia de l'ablació de FA, amb les diferents variacions tècniques plantejades, és encara sub-òptima i varia en funció, entre d'altres, de les característiques dels pacients de cada sèrie, i les complicacions associades a aquests procediments no són despreciables[15]. Identificar factors que condicionin el resultat de l'ablació permetria conèixer la relació risc/benefici del procediment i seleccionar els millors candidats a la teràpia.

A més, el resultat de l'ablació es pot valorar no només en funció del seu efecte en la funció elèctrica auricular, és a dir, del restabliment del ritme sinusal, sinó que també resulta d'interès el seu efecte sobre la funció mecànica. Les dades d'estudis previs sobre remodelat auricular post ablació de FA són contradictòries. Això pot ser degut a diverses raons: primer, les diferents tècniques d'imatge que es van fer servir: ecocardiografia[16-19], ressonància magnètica[20] o tomografia axial computada[21]. Segon, quina mida auricular es va utilitzar: els tres diàmetres ortogonals[16;18;20], només el diàmetre antero-posterior[17;19], o la mesura del volum auricular [21]. Tercer, excepte en un sol estudi[19], les mesures es van realitzar només durant la diàstole auricular. Finalment, en la majoria d'aquests estudis, no es va donar importància al fet de que el pacient estigués o no en FA en el moment de l'adquisició de la imatge[17;19-21]. Aquestes limitacions tècniques aportaven resultats limitats en l'estudi de la funció auricular post-ablació.

La quantitat de lesions creades condiciona el resultat de l'ablació: aproximacions més agressives tracten una major quantitat de mecanismes potencialment responsables de l'arítmia, però també augmenten els riscos associats al procediment i el possible dany sobre la funció contràctil. La quasi totalitat dels procediments d'ablació de FA descrits en la literatura incorporen com a objectiu l'aïllament de les VP. L'adició de línies d'ablació en l'AE han demostrat millorar la eficàcia del procediment[22-25], però el nombre i la localització idonis d'aquestes lesions no està establert. En aquest sentit, el paper de la paret posterior de l'AE com a disparador i substrat de la FA s'ha suggerit en diversos estudis, però no existeix confirmació sobre el benefici d'aïllar aquesta regió[26-34]. Per altra banda, la millor aproximació per confirmar l'aïllament de les VP també és tema de debat, especialment en procediments on les lesions es creen de forma extra-ostial. Actualment, alguns laboratoris utilitzen un sol catèter en l'AE tan per mapejar com per ablacionar[24;35;36], però altres defensen la necessitat d'afegir un o més catèters de mapeig circular per demostrar l'aïllament de la zona encerclada[37-39].

Donats aquests antecedents, les hipòtesis en les que es van basar els treballs de recerca descrits en la present memòria van ser les següents:

- L'ablació limitada sense modificació de substrat arritmogènic és suficient en aquells casos de FA amb mecanismes eminentment focals.
- El risc d'estenosis de VP en ablació ostial no és despreciable.
- Existeixen característiques clíniques que permeten predir la probabilitat d'èxit de l'ablació de FA.
- L'ablació de FA millora la funció mecànica auricular tot i la creació de lesions extenses.
- L'aïllament de la paret posterior de l'AE augmenta l'eficàcia de l'ablació de FA.
- La utilització d'un catèter circular per comprovar l'aïllament de la regió de les VP encerclades millora l'eficàcia del procediment.

OBJECTIUS

Els objectius plantejats en cadascun dels treballs que formen part de la present tesi van ser, segons l'ordre cronològic en que es van elaborar, els següents:

I. Avaluar els resultats d'una estratègia en la que la tècnica d'ablació de FA s'individualitza en funció de les característiques de cada pacient.

II. Comparar la incidència d'estenosis de VP després d'un procediments d'ablació ostial segmentària i d'ablació circumferencial de VP.

III. Identificar predictors de fracàs de l'ablació circumferencial de VP.

IV. Valorar l'efecte de l'ablació circumferencial de VP sobre els volums auriculars i la seva funció mecànica.

V. Comprovar si l'aïllament de la paret posterior de l'AE incrementa l'eficàcia de l'ablació circumferencial de VP.

VI. Comprovar si utilitzar un catèter circular per assegurar l'aïllament de les zones antrals encerclades millora els resultats de l'ablació circumferencial de VP.

Els resultats obtinguts en l'elaboració de cada objectiu anterior van donar lloc a les publicacions següents:

- Selective segmental ostial ablation versus electroanatomical encircling for atrial fibrillation: an individualizad approach based on patient characteristics.

  ***Tamborero D**, Mont Ll, Molina I, Matiello M, Vidal B, , Berruezo A, Bartholomay E, Scalise A, Nava S, de Caralt TM, , Sitges M and Brugada J.*

  Journal of Interventional Cardiac Electrophysiology 2007; 19:19-27.

- Incidence of pulmonary vein stenosis in patients submitted to atrial fibrillation ablation: a comparison of the segmental ostial ablation vs the electroanatomical encircling.

  Tamborero D*, Mont Ll, Nava S , Caralt TM de, Molina I, Scalise A, Perea R J, Bartholomay E, Berruezo A, Matiello M and Brugada J.*

  Journal of Interventional Cardiac Electrophysiology 2006;14: 21-5.

- Pre-procedural predictors of atrial fibrillation recurrence after circumferential pulmonary vein ablation.

  Berruezo A,* ***Tamborero D****, Mont L, Benito B, Tolosana JM, Sitges M, Vidal B, Arriagada G, Mendez F, Matiello M, Molina I and Brugada J.*

  *(*first two authors contributed equally to this work).*

  European Heart Journal 2007; 28:836-841.

- Left atrial contractility is preserved after successful circumferential pulmonary vein ablation in patients with atrial fibrillation.

  Perea RJ,* ***Tamborero D****, Mont L, De Caralt TM, Ortiz JT, Berruezo A, Matiello M, Sitges M, Vidal B, Sanchez M and Brugada J.*

  *(*first two authors contributed equally to this work).*

  Journal of Cardiovascular Electrophysiology 2008; 19:374-379,

- Left atrial posterior wall isolation does not improve the outcome of circumferential pulmonary vein ablation for atrial fibrillation: a prospective randomized study.

  Tamborero D*, Mont L, Berruezo A, Matiello M, Benito B, Sitges M, Vidal B, de Caralt TM, Perea RJ, Vatasescu R and Brugada J.*

  Circulation: Arrhythmia and Electrophysiology 2008 (in press).

- Circumferential pulmonary vein ablation: does the use of a circular mapping catheter improve results?

  Tamborero D*, Mont L, Berruezo A, Guasch E, Rios J, Nadal M, Matiello M, Andreu D, Sitges M and Brugada J.*

  Journal of the American College of Cardiology 2009 (submitted).

A continuació es descriuran breument els mètodes i resultats de cadascun d’aquests treballs que formen part d’aquesta tesi. Els detalls d’aquests es poden trobar en els corresponents articles que s’adjunten en l’annex de la present memòria.

MÈTODES I RESULTATS

I. Individualitzar el mètode d'ablació.

En les primeres sèries publicades, l'ablació limitada a aïllar les VP ectòpiques reportava una eficàcia limitada en FA no paroxística[40], però procediments on es creava una major quantitat de lesions en AE reportaven una eficàcia similar en les diferents presentacions de l'arítmia[17;41]. Fins al moment de l'elaboració d'aquest treball, els estudis sobre ablació de FA descrivien els resultats obtinguts amb un determinat procediment, o comparaven dos mètodes en una sèrie aleatoritzada independentment del perfil del pacient. Per això, l'objectiu del present estudi va ser avaluar una estratègia en la que el mètode d'ablació es va triar segons les característiques de cada pacient.

Per fer aquesta selecció, es va realitzar un ecocardiograma transtoràcic i un registre Holter de 24 hores abans del procediment. En aquells pacients amb una AE estructuralment normal i amb un registre d'ectòpia auricular esquerra freqüent i sostinguda durant un mínim de 10 batecs consecutius es va assumir una FA eminentment depenent d'activitat focal; en aquests pacients es va realitzar una ablació ostial segmentària i selectiva (AOSS). En la resta dels casos, es va suposar una major presència de substrat arritmogènic que requeriria de lesions més extenses; en aquests pacients es va realitzar una ablació circumferencial de VP (ACVP).

Els detalls d'aquest treball es poden trobar en l'article adjuntat en la present memòria[42]. Breument, en l'AOSS es van aïllar les VP amb activitat elèctrica amb la guia d'un catèter multipolar circular, tal i com va descriure inicialment el grup de Haissaguerre[10]. En l'ACVP es van envoltar les VP ipsilaterals i es van crear lesions lineals per la paret posterior i l'istme mitral utilitzant la guia d'un sistema de navegació, tal i com va descriure inicialment el grup de Pappone[17]. Es van incloure un total de 131 pacients consecutius, 50 dels quals van ser seleccionats per una AOSS i els 83 restants es van seleccionar per una ACVP segons els criteris definits. El diàmetre mig de l'AE en el grup d'AOSS va ser de 37±4 mm, i en el Holter previ al procediment es van registrar 2727±3387 extrasístoles aïllades, 654±794 extrasístoles en parelles i 658±746 ratxes de taquicàrdia auricular d'una duració màxima de fins a 136±193 batecs.

El temps del procediment va ser menor en l'AOSS que en l'ACVP, encara que el temps de radioescòpia va ser superior. El nombre de complicacions peri-procediment va ser comparable entre els dos grups. Globalment, considerant també aquells casos en els es va repetir el procediment d'ablació, un 70.0% i un 71.6% dels pacients d'AOSS i ACVP es trobaven lliures d'arítmies, respectivament, durant un seguiment mig de 22±16 mesos. Tanmateix, separant els resultats segons la presentació de l'arítmia, l'eficàcia obtinguda en FA paroxística va resultar similar entre els dos grups (77.3% *versus* 74.5% respectivament; log rank test p=0.9), però l'AOSS van obtenir una eficàcia molt limitada i inferior a la de l'ACVP en FA persistent (16.7% vs. 64.3%; log rank test p=0.02) tot i la estricta pre-selecció de pacients realitzada.

Aquest treball va concloure que una ablació limitada com l'AOSS era efectiva en pacients amb aurícula estructuralment normal i ectòpia esquerra freqüent i sostinguda en el cas de la FA paroxística, però lesions més extenses com les realitzades en l'ACVP semblaven necessàries en tots els casos de FA persistent.

II. Risc d'estenosis de venes pulmonars

L'ablació de FA és un procediment complex i no exempt de complicacions, entre les quals hi ha l'estenosis de VP per danys en la musculatura venosa durant l'aplicació de RF. Les estenosis de VP, associades a complicacions respiratòries severes [43-46], es van descriure inicialment en els primers procediments d'ablació de FA, on la RF s'aplicava directament sobre els focus ectòpics originats en l'interior d'una VP. Per aquest motiu, es va desenvolupar la tècnica d'aïllament de VP ostial. En aquesta regió, on es localitza la connexió elèctrica veno-atrial, l'aplicació de RF presenta un risc menor de provocar estenosis de VP que quan la RF s'aplica en el seu interior. Tot i això, en les sèries on es realitzava l'aïllament ostial de VP es continuarien reportant d'un 5 a un 30% d'incidència d'aquesta complicació[9].

Donat que l'ACVP crea les lesions de RF en un aspecte més proximal de la inserció veno-atrial que l'aïllament ostial, el risc d'estenosis de VP hauria de ser també menor. L'objectiu d'aquest treball va ser avaluar la incidència d'aquesta complicació després de realitzar una AOSS i una ACVP. Els detalls de l'estudi es troben en l'article adjuntat en la present memòria[47].

Breument, es va incloure una sèrie consecutiva de 73 pacients sotmesos a ablació de FA, 32 dels quals van ser seleccionats per una AOSS i els 41 restants per una ACVP. En tots ells, es va realitzar una angio-ressonància magnètica als 4 mesos post-ablació, donat que la progressió de les estenosis de VP és rara passat aquest temps[9;44]. Durant un seguiment mig de 15±12 mesos, cap pacient de la sèrie va desenvolupar símptomes compatibles amb estenosis de VP. Tanmateix, es van detectar estenosis severes en 6 pacients gràcies al control rutinari, tots ells en el grup d'AOSS i cap en el grup d'ACVP (18.8% vs. 0%; p=0.005). L'estenosis es va trobar en la VP superior esquerra en 4 pacients, en la VP inferior esquerra en 1 pacient, i en ambdues VP esquerres en un altre pacient. Tenint en compte que en l'AOSS només s'aïllen aquelles VP que mostren activitat elèctrica, el percentatge entre vena estenosada i vena tractada en aquesta sèrie va ser del 15.2% per la VP superior esquerra i de 33.3% per la VP inferior esquerra.

Aquest estudi també es va utilitzar per reportar la presència de variants anatòmiques de VP, un aspecte important en procediments d'ablació de FA. Es van trobar 16 pacients (22% del total) amb una distribució diferent a les 4 VP independents; la més comuna d'aquesta sèrie va ser l'existència d'un tronc comú esquerre i d'una VP dreta intermèdia (en un 15% i un 5% dels pacients, respectivament).

El treball va concloure que l'AOSS presenta un risc d'estenosis de VP que pot estar infravalorat si no s'avalua de forma rutinària, un risc que no s'observa en el cas d'ablacions extra-ostials com l'ACVP, i va confirmar que la angio-ressonància magnètica resulta útil per detectar aquesta complicació així com per avaluar l'anatomia de les VP.

III. Predictors d'èxit de l'ablació circumferencial de VP

La difusió i estandardització de les tècniques d'ablació de FA han fet que aquesta teràpia sigui més utilitzada durant els darrers anys. De la mateixa manera, els criteris de selecció dels candidats a ablació de FA són actualment menys restrictius que en les primeres sèries descrites[15]. El fet de tractar formes de l'arítmia més cròniques i aurícules més deteriorades requereix de procediments més agressius, amb ablacions més extenses que les realitzades en procediments on només s'actua sobre mecanismes focals. Per aquest motiu, i degut als resultats dels treballs descrits en els apartats anteriors, l'ACVP és actualment el procediment d'ablació de FA més utilitzat en el nostre centre.

L'eficàcia de l'ACPV i les complicacions associades al procediment són encara sub-òptimes, per lo que seleccionar pacients amb una alta probabilitat de beneficiar-se de la teràpia resulta d'especial interès. Fins al moment de l'elaboració d'aquest treball, s'havien descrit marcadors d'èxit de l'ablació de FA relacionats amb events observats en el seguiment o durant el propi procediment[17;48-53], però no s'havien descrit variables prèvies a l'ablació que condicionessin el seu resultat. L'objectiu d'aquest treball va ser identificar predictors de recurrència de FA després d'una ACVP.

Els detalls d'aquest estudi es troben en el corresponent article adjuntat en la present memòria[54]. Breument, es van incloure un total de 148 pacients consecutius sotmesos a ACVP en el nostre centre, sent una mostra representativa dels pacients habitualment seleccionats per ablació de FA: eren majoritàriament homes, amb una edat mitja de 52±11 anys, un 60% d'ells tenien FA paroxística, presentaven una incidència limitada (20%) de cardiopatia estructural i tenien un diàmetre mig d'AE lleugerament dilatat. Considerant aquells 22 (15%) pacients en els que es va realitzar un segon procediment d'ablació, un 74% de la sèrie estava lliure de recurrències de FA durant un seguiment mig de 13±8 mesos.

Entre totes les variables basals avaluades, l'edat, la presència d'hipertensió, una presentació de FA permanent, i el diàmetre d'AE i de VE es van relacionar significativament amb les recurrències de FA post-ablació. El corresponent anàlisis multivariat va mostrar que la hipertensió i el diàmetre antero-posterior de l'AE eren els predictors independents de que l'ACVP no fos eficaç. Les diferents validacions estadístiques que es van realitzar amb els resultats van demostrar un valor predictiu robust, possibilitant la creació d'un model per estimar la probabilitat d'èxit de l'ACVP en funció d'aquests dues variables. Així per exemple, els pacients no hipertensos amb una AE ≤ 45mm tenen una probabilitat superior al 85% de mantenir el ritme sinusal després de l'ACVP; en canvi, pacients hipertensos amb una AE >45mm tenen més del 50% de probabilitats de continuar amb episodis de FA tot i haver-se sotmès al procediment.

La principal conclusió d'aquest treball va ser, doncs, que la hipertensió i el diàmetre d'AE eren predictors independents de recurrències de FA post ACVP, amb l'ajuda que aqueta informació representa per ajudar a triar els millors candidats a aquesta teràpia.

IV. Contractilitat auricular post-ablació circumferencial de VP.

Els resultats de l'ablació de la FA es valoren en funció del restabliment del ritme sinusal, però també resulta d'interès conèixer la funció mecànica auricular post-ablació, especialment en aquells procediments en que, com és el cas de l'ACVP, es creen lesions extenses en l'AE.

Fins al moment de l'elaboració del present treball, les dades disponibles sobre l'evolució dels volums d'AE després d'una ablació de FA eren contradictoris[16-21], i només existia una publicació sobre la contractilitat auricular post-procediment[55]. L'objectiu d'aquest estudi va ser avaluar l'efecte de l'ACVP sobre els volums i contractilitat d'AE, així com valorar la seva relació amb l'eficàcia del procediment.

Els detalls d'aquest treball es troben en l'article corresponent, adjuntat en la present memòria[56]. Breument, es va realitzar una ressonància magnètica a tots els pacients en els que es va realitzar una ACVP abans del procediment i de 4 a 6 mesos després d'aquest, mesurant en cada cas el volum d'AE sistòlic i diastòlic (excloent l'orelleta). La contractilitat auricular es va determinar calculant la fracció d'ejecció (FE) d'AE a partir de la mesura d'aquests volums. En aquest estudi només es van incloure als pacients que es trobaven en ritme sinusal en el moment de la realització d'ambdues ressonàncies, per tal de no avaluar la progressió dels volums auriculars en el cas de que alguna de les mesures estigués feta durant l'arítmia. Addicionalment, les mateixes mesures es van realitzar independentment per l'orelleta esquerra. Es van incloure un total de 55 pacients en els que es va realitzar una ACVP (41 homes, 52±11 anys, 74%

FA paroxística). Durant un seguiment de 12±7 mesos, 38 (69%) dels pacients de la sèrie van estar lliures de recurrències.

El volum auricular basal era més gran en els pacients amb recurrències post ACVP (diastòlic: 128±33 vs. 98±20 ml; sistòlic: 78.4±22.2 vs. 58.6±16.1 ml; $p<0.05$ en ambdós casos). En tots els pacients de la sèrie, independentment de l'eficàcia del procediment, es va observar que el volum auricular diastòlic es reduïa després de l'ablació; a més, el percentatge de reducció del volum diastòlic va ser equivalent entre els pacients amb i sense recurrències durant el seguiment (17±14% vs. 13±12%, respectivament; $p=0.22$). En canvi, el volum auricular sistòlic només es va reduir en el grup de pacients lliures d'arítmies durant el seguiment (de 59±16 ml a 52±12 ml; $p=0.004$). En quan a l'efecte de l'ACVP en la contractilitat auricular, es va observar que la FE d'AE es preservava després de l'ablació en el grup de pacients sense recurrències (de 40±11% a 38±10%; $p=0.3$), però empitjorava en els pacients en els que l'ACVP no va ser exitosa (de 37±10% a 27±10%; $p<0.001$). Per altra banda, l'orelleta va mostrar uns canvis de volum després de l'ablació similars als observats en la resta de l'AE però en un menor grau, de manera que la seva FE no va canviar ni en els pacients lliures d'arítmies (41±20% *versus* 40±20%; $p=0.8$) ni en els pacients amb recurrències (31±20% *versus* 32±16%; $p=0.9$) durant el seguiment.

Les conclusions d'aquest treball van ser que el volum diastòlic d'AE es reduïa després de l'ACVP independentment de l'eficàcia clínica del procediment, però el volum sistòlic només remodelava en aquells pacients que recuperaven el ritme sinusal durant el seguiment. La contractil·litat auricular es conservava o millorava en la majoria de pacients en els que l' ablació va resultar eficaç, però empitjorava en la resta.

V. Paper de l'aïllament de la paret posterior d'AE en l'eficàcia de l'ablació circumferencial de VP

Tot i que s'han desenvolupat diverses aproximacions a l'ablació de FA, l'aïllament de les VP segueix sent una part imprescindible en la majoria d'aquestes[10;17;57]. En aquest sentit, l'adició de lesions lineals a l'AE ha demostrat millorar la eficàcia de l'aïllament de VP[22-24]. Les més utilitzades són l'ablació de l'istme mitral, creant una línea de RF entre la VP inferior esquerra i la vàlvula mitral, i la creació d'una línea de bloqueig unint les VP contralaterals superiors pel sostre de l'AE[25;58]. Altres autors han proposat afegir també una segona línia d'ablació que uneixi les l'aspecte inferior de les VP contralaterals, per tal d'aïllar també la paret posterior de l'AE[24;59-61]. L'eficàcia d'aquests dos esquemes de lesions no havia estat comparada fins al moment de l'elaboració del present treball. Per això, l'objectiu d'aquest estudi va ser avaluar si l'aïllament de la paret posterior (PP) de l'AE redueix el risc de recurrències post ACVP.

Els detalls del treball es troben adjuntats en el corresponent article adjuntat en la present memòria. Breument, es van incloure un total de 120 pacients aleatoritzats a dos grups d'ablació. En el primer, es va realitzar una ACVP envoltant les VP ipsilaterals amb lesions de RF continues i es va ablacionar l'istme mitral (grup ACVP-1). En el segon grup, es va afegir una línea de RF unint l'aspecte inferior de les VP contralaterals aïllant així la PP d'AE (grup ACVP-2).

No es van observar diferències estadísticament significatives entre els dos grups ni en les dades globals del procediment (temps total del procediment, de RF o de radioscòpia) ni en les complicacions degudes a aquest. Els objectius de cada procediment també es van aconseguir en un percentatge similar (90% vs. 92%, respectivament; p=0.75). Durant un seguiment mig de 9.8±4.3 mesos, no es van observar diferències en la probabilitat de recurrències entre els dos grups (log rank test p=0.94): després d'un sol procediment d'ablació, l'eficàcia va ser la mateixa en els dos grups, concretament, un total de 33 (55%) pacients de cada grup estaven lliures d'arítmies. Les recurrències del grup ACVP-1 van ser degudes a episodis de FA en 24 pacients (40%) i a l'aparició de flutter atípic en 3 (5%). En el grup ACVP-2, 23 pacients (38%) van tenir recurrències de FA i en 4 (7%) va aparèixer un flutter atípic. Tampoc no es van observar diferències d'eficàcia entre els dos grups d'ablació analitzant per separat els pacients amb FA paroxística i els pacients amb FA persistent o permanent.

En 25 (21%) pacients es va realitzar un segon procediment, augmentant l'èxit global de la sèrie lliures d'arítmies fins al 68% de pacients lliures d'arítmies. En 4 d'aquests pacients en els que es va repetir l'ablació, es va realitzar l'ablació d'un flutter atípic de nova aparició, que en tots els casos es va mapejar entre discontinuïtats de les corones d'ablació al voltant de les VP. En els 21 pacients restants es va realitzar un segon procediment degut a recurrències de FA, trobant-se re-conducció d'alguna VP en el 84% d'aquests, i re-conducció de la línia d'ablació del sostre o activitat elèctrica en la PP d'AE en el 69% i 67% d'aquests pacients en els grups ACVP-1 i ACVP-2, respectivament.

La principal conclusió d'aquest treball va ser, doncs, que l'aïllament de la paret posterior de l'AE no oferia benefici en l'eficàcia obtinguda per l'ACVP.

VI. Benefici de comprovar l’aïllament de l’antrum de VP amb catèter circular

En l’actualitat, existeixen laboratoris que realitzen l’ACVP amb un sol catèter en l’AE, que es fa servir tan per aplicar la RF com per mapejar l’efecte de les lesions creades al voltant de les VP[24;35;36], però altres investigadors defensen la necessitat d’utilitzar catèters de mapeig circular (CMC) per assegurar l’aïllament de la zona encerclada[37-39] o per poder realitzar un aïllament ostial després de l’encerclament de VP[62]. Afegir catèters en l’AE augmenta la complexitat i el cost del procediment, a més del risc potencial de complicacions. Per això, l’objectiu de l’estudi va ser comprovar el benefici d’utilitzar un CMC en els resultats de l’ACVP, ja que no existeixen dades al respecte.

Els detalls d’aquest treball es troben en el corresponent article adjuntat en la present memòria. Breument, es van incloure un total de 146 pacients aleatoritzats a dos procediments d’ablació. En ambdós es va crear el mateix esquema d’ablació: lesions contínues encerclant cada grup de VP ipsilaterals a nivell del seu antrum a més d’una línia de bloqueig pel sostre d’AE unint les corones d’ablació esquerra i dreta. En el primer grup, es va utilitzar un catèter d’ablació de punta irrigada tan per crear les lesions com per mapejar, de tal manera que la desaparició de l’activitat elèctrica en la regió de les VP encerclada es va comprovar utilitzant el dipol distal del catèter d’ablació (grup ACVP). En el segon grup, es va afegir un CMC, comprovant la desaparició de la senyal de la zona encercada en els seus 10 dipols (grup ACVP-CMC).

El procediment d’ACVP-CMC va durar més (154±59 vs. 175±43 minuts; p=0.021) i va necessitar de més temps de radioescòpia (20±16 vs. 31±10 minuts;

p<0.001) que l'ACVP, tot i que el temps de radiofreqüència va ser similar. El percentatge de complicacions no va presentar diferències estadísticament significatives (1.4% vs. 4.1%; p=0.620), tot i que el segon grup va presentar una complicació exclusiva de la utilització d'un CMC, això és, un pacient en el que aquest catèter va quedar atrapat en la vàlvula mitral requerint de cirurgia per reparar una ruptura de muscle papil·lar deguda als intents d'alliberar-lo manualment.

L'eficàcia del procediment va ser més alta en el grup d'ACVP-CMC: després d'un seguiment mig de 9±3 mesos, 31 (42.5%) pacients del grup ACVP i 47 (64.4%) pacients del grup ACVP-CMC estaven lliures d'arítmies després d'un sol procediment d'ablació i sense tractament antiarítmic (p=0.008). Addicionalment, 6 (8.2%) pacients més de cada grup estaven lliures de recurrències però sota tractament d'un fàrmac antiarítmic que o bé no va ser suspès o bé va ser re-iniciat durant el període de cegament inicial degut a recurrències precoces post procediment. L'anàlisi multivariat van obtenir que la hipertensió i la FA permanent eren els predictors de recurrències post primer procediment d'ablació, a més de la no utilització del CMC en el procediment (HR=1.835 [1.119-3.003]; p=0.016).

La conclusió d'aquest treball va ser doncs que la utilització d'un CMC, tot i augmentar alguns requeriments del procediment, millorava l'eficàcia de l'ACVP enfront d'utilitzar un sol catèter en l'AE tan per ablacionar com per mapejar.

DISCUSSIÓ GENERAL

Realitzar una ablació limitada com l'AOSS en pacients seleccionats segons els criteris descrits en el nostre estudi[42] va obtenir bons resultats en els pacients amb FA paroxística. En canvi, en FA persistent, l'AOSS va tenir una baixa eficàcia tot i la estricta pre-selecció, i una ablació més extensa com l'ACVP semblaria necessària en tots els casos. L'AOSS lesiona una petita quantitat de teixit auricular, perquè només aïlla aquelles VP que mostren activitat elèctrica i ho fa aplicant RF només en certs segments del seu perímetre ostial. Per això, hauria de ser el procediment d'elecció en aquells casos on ha demostrat una bona probabilitat d'èxit. Tanmateix, els resultats del nostre treball també van demostrar que el risc d'estenosis de VP és més alt en l'AOSS que en altres procediments en els que les lesions, tot i ser més extenses, es creen més allunyades de l'ostium de VP. En la nostra sèrie, cap dels pacients en els que es va detectar estenosis de VP va tenir símptomes relacionats durant el seguiment. Així, la incidència d'estenosis de VP després d'una ablació de FA podria estar subestimada quan no es valora de manera sistemàtica; tot i tractar-se de reduccions superiors al 70% del diàmetre d'una o fins i tot dues VP, aquestes es van detectar en la nostra sèrie gràcies al control rutinari. Per altra banda, totes les estenosis es van produir en venes del costat esquerre, coincidint amb els resultats observats en altres estudis[9]. Aquest fet podria ser degut a que el catèter de RF col·locat en AE via accés transseptal té poca estabilitat quan es recolza en l'òstium d'una VP del costat esquerre, augmentant el risc de que el catèter progressi de forma inesperada al interior de la VP durant l'aplicació de RF i el possible dany de les estructures musculars venoses que això comporta.

En els nostres treballs es va observar que l'ACVP aconseguia un percentatge d'eficàcia similar en diferents perfils de pacient sense incidència d'estenosis de VP. Actualment, en el nostre laboratori, en aquells pacients amb FA paroxística, aurícula estructuralment normal i alta activitat ectòpica originada en VP es segueix realitzant un aïllament selectiu de VP. Tanmateix, l'alta ocurrència d'estenosis de VP que varem observar després d'un aïllament de vena ostial ha fet que s'incorporés l'ús d'un sistema de navegació per guiar la reconstrucció de les zones d'interès i monitoritzar-ne la localització del catèter en tot moment, encara que aquest és un procediment on l'extensió de lesions és limitada i originalment estava descrit sense la guia d'aquest tipus d'eina. Actualment, el nostre percentatge d'eficàcia en aquest tipus de pacient és superior al 80% sense observar-se cap estenosis en les VP tractades. Tanmateix, aquest és un perfil de pacient molt determinat que cada cop és menys freqüent entre els candidats a ablació de FA, on els criteris d'inclusió han esdevingut més amplis en els darrers anys per tractar pacients amb un estat més evolucionat de l'arítmia. De fet, en l'actualitat, en el nostre laboratori així com en la majoria d'altres centres, l'ACVP és el procediment realitzat en la gran majoria dels casos. Per aquest motiu, els estudis següents del nostre grup sobre ablació de FA es van centrar en aquesta tècnica.

Després de realitzar un procediment d'ACVP estàndard en una sèrie àmplia de pacients, un anàlisi de les dades recollides prospectivament va demostrar que el diàmetre de l'AE i la presència d'hipertensió eren els factors predictors de recurrències de FA post ablació. En estudis previs ja s'havia descrit la relació entre la grandària auricular i l'èxit de la cardioversió elèctrica o la cirurgia *mini-maze*, respectivament[63;64]. Per altra banda, la hipertensió, que és el factor més prevalent de la FA[65], augmenta les pressions d'ompliment ventricular i crea fibrosis en el teixit cardíac[66-68], contribuint a l'aparició de substrat auricular arritmogènic. Resultaria especulatiu saber si aquest substrat pot quedar fora de les regions tractades amb l'ACVP, i per això la seva eficàcia és més baixa en pacients hipertensos, o el major risc d'aquest grup per seguir tenint FA després de l'ablació pot ser degut a un mal control de la hipertensió durant el seguiment. En aquest sentit, estudis de prevenció primària i secundària de FA han mostrat que la utilització de certs hipertensius i el bon control de la pressió arterial redueixen la ocurrència de FA[69;70].

La identificació de factors previs al procediment que condicionen l'eficàcia del procediment permet estimar la probabilitat d'èxit per cada pacient. D'aquesta manera, és possible establir certs criteris per seleccionar candidats a l'ablació i informar a aquests del risc-benefici estimat per cada cas. Així, es podria realitzar l'ACVP en estadis d'aparició de l'arítmia més primerencs si la probabilitat d'èxit del procediment és alta, però altres alternatives serien recomanables en aquells pacients amb una baixa probabilitat de que l'ablació sigui efectiva.

A més de la capacitat de controlar el ritme cardíac, el nostre treball també va mostrar que la contractilitat auricular es manté o millora en la majoria dels pacients que mantenen el ritme sinusal després de l'ablació, tot i que aquesta empitjora en pacients on l'ACVP fracassa. Això es degut a que el volum auricular diastòlic es redueix en tots els pacients després de l'ablació, però el volum auricular sistòlic només decreix en els pacients lliures d'arítmies. Les dades contradictòries sobre l'evolució dels volums auriculars post ablació que existeixen en la literatura podrien ser explicades per les divergències metodològiques d'aquests treballs. En el nostre estudi es va utilitzar un mètode òptim, mesurant manualment i per separat el volum auricular sistòlic i diastòlic amb la tècnica de *la suma de discs* sobre una seqüència de cine adquirida per ressonància magnètica, que evita errors per assumpcions geomètriques, incorrecta col·locació del pla o mala definició del contorn auricular, i es van excloure aquells pacients que es trobessin en FA durant l'adquisició de la imatge prèvia i/o posterior a l'ablació. Per altra banda, només dos estudis anteriors havien avaluat la FE d'AE post ablació de FA, també obtenint resultats contradictòris[55;71]. En aquests, però, no es van analitzar les dades en funció de l'eficàcia del procediment.

El fet de que el volum auricular diastòlic es redueixi en tots els pacients i ho faci en el mateix ordre de magnitud podria ser degut a una retracció auricular secundària a l'efecte de la RF, i la reducció del volum sistòlic que només es va observar en els pacients lliures de recurrències podria ser degut a un procés de remodelat auricular secundari al manteniment del ritme sinusal. Tanmateix, aquestes explicacions resulten especulatives sense tenir disponibles les mesures dels volums en més moments del seguiment. Addicionalment, també es va comprovar que en l'orelleta esquerra hi havien canvis estructurals similars als de la resta de l'AE però en un grau significativament menor, de manera que la contractilitat d'aquesta estructura no es va veure modificada en cap pacient després de l'ablació, un aspecte important degut a la necessitat d'anticoagulació en cas de mala contracció de l'apèndix. Això podria ser degut a que l'aplicació de RF evita aquesta regió, de manera que els possibles efectes de la retracció del teixit l'afecten de forma marginal.

En aquest sentit, l'ACVP és un procediment on es creen lesions extenses, que no només poden afectar a la funció mecànica sinó també augmentar els riscos associats al procediment. La formació d'una fístula aurículo-esofàgica és una complicació que és poc freqüent però resulta fatal quan es produeix[15]. L'aplicació de RF en la paret posterior de l'AE augmenta el risc de danyar l'esòfag, degut al contacte virtual amb aquesta estructura[72]. En el nostre treball, l'aïllament de la paret posterior no va millorar l'eficàcia de l'ACVP, tot i que existeixen estudis previs on es documentava el paper d'aquesta regió en la ocurrència de FA. Una possible explicació d'aquests resultats seria que, en l'ACVP, les lesions de RF envolten les VP ipsilaterals en la part més proximal de la seva inserció auricular, encerclant més teixit que en altres procediments on l'aïllament de VP es fa amb lesions ostials. Si els substrat de la paret posterior es trobés principalment en aquesta zona, l'aïllament de la resta de la paret posterior no aportaria benefici a aquesta tècnica d'ablació. De fet, un estudi previ va relacionar la grandària de les corones d'ablació al voltant de les VP amb l'eficàcia de l'ACVP[43]. Així, tot i que no es pot descartar que l'aïllament de la paret posterior d'AE sigui necessari en alguns casos concrets, no s'hauria de realitzar de forma rutinària en procediments d'ACVP. En canvi, el que sí va demostrar millorar el resultat del procediment va ser assegurar l'aïllament de l'antrum de VP utilitzant un CMC. L'ACVP va ser inicialment descrita utilitzant un sol catèter, que servia tan per ablacionar com per mapejar l'efecte de les lesions creades; en aquest cas, la desaparició de la senyal es comprova amb el registre del dipol distal del catèter d'ablació[12]. Tanmateix, existeixen diverses publicacions que senyalen que aquest mètode no assegura l'aïllament de les VP[73-75], però també existeixen dos estudis que suggereixen que aconseguir aquest aïllament elèctric de VP no condiciona l'eficàcia de l'ACVP[60;62]. Degut a aquestes dades controvertides, existeixen laboratoris que segueixen fent servir un sol catèter en l'AE per realitzar l'ACVP, però altres grups defensen la necessitat d'afegir un CMC per assegurar l'aïllament de VP. El nostre estudi va ser el primer en comparar l'eficàcia de l'ACVP en funció de si l'aïllament de l'antrum de VP es demostra amb un CMC o no.

L'ablació de FA utilitzant un CMC afegeix algunes avantatges respecte a utilitzar un sol catèter en AE. Primer, la grandària i distribució dels elèctrodes en el

CMC identifica millor els electrogrames residuals comparat amb el registre del dipol distal del catèter de RF[73]. Segon, els canvis en el patró d'activació de la zona encerclada durant l'aplicació de RF pot ser immediatament observada en els registres del CMC, mentres que l'ablació i el procés de mapeig ha de ser realitzat de manera seqüencial quan es fa servir un sol catèter. Finalment, un CMC permet un mapeig multipolar que facilita la localització de discontinuïtats en les línies d'ablació. Per altra banda, la utilització d'un altre catèter en l'AE augmenta la complexitat i el cost del procediment, a més del seu risc potencial de complicacions que, en el cas concret del CMC, presenta a més el risc de quedar atrapat en la vàlvula mitral[76]. Aquests pros i contres han de ser considerats a l'hora de plantejar la utilització d'un CMC.

L'elaboració dels estudis que formen part de la present tesi van seguir les hipòtesi plantejades i plans de treball previstos, complint adequadament amb els objectius plantejats inicialment. A més, no només han estat una aportació remarcable en la investigació sobre ablació de FA de la comunitat científica, amb el resultat de la publicació i difusió d'aquests resultats, sinó que també han contribuït a una millor pràctica clínica en el nostre centre mitjançant un major coneixement sobre la tècnica d'ablació òptima, els mecanismes associats als seus resultats i una millor relació risc/benefici obtinguda. Les principals conclusions finals obtingudes es resumeixen a continuació:

- En la FA paroxística, amb aurícula estructuralment normal i ectòpia auricular esquerra freqüent i sostinguda, l'aïllament segmentari i ostial d'aquelles VP amb activitat elèctrica resulta eficaç sense necessitat de realitzar lesions més extenses.

- Aquesta aproximació té un risc considerable d'estenosis de VP, resultant d'especial interès la utilització d'eines que permetin localitzar el catèter de RF amb precisió i en temps real.

- La hipertensió i el diàmetre auricular són predictors de recurrència de FA després d'una ablació circumferencial de VP, i aquestes dues variables es poden utilitzar per seleccionar els millors candidats a aquesta teràpia.

- El volum auricular diastòlic es redueix després d'una ablació circumferencial independentment del seu resultat, mentre que el volum sistòlic només remodela en pacients que mantenen el ritme sinusal durant el seguiment. La contractilitat auricular es conserva o millora en la majoria de pacients en els que l' ablació resulta eficaç, però empitjora en la resta.

- L'aïllament de la paret posterior de l'AE no millora l'eficàcia de la ablació circumferencial de VP, i no hauria de realitzar-se de forma rutinària en aquest tipus de procediments.

- La utilització d'un CMC per demostrar l'aïllament de l'antrum de VP millora els resultats de l'ACVP, i hauria d'incorporar-se en el procediment tot i augmentar-ne alguns dels seus requeriments.

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ANNEX: PUBLICACIONS RESULTANTS DE LA TESI

A continuació s'adjunten les publicacions resultants dels diferents estudis realitzats en la present tesi. Els articles es presenten segons l'ordre cronològic en que van ser elaborats. També s'adjunta el darrer treball actualment pendent de revisió en la revista *Journal of the American College of Cardiology*..

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Selective segmental ostial ablation and circumferential pulmonary veins ablation. Results of an individualized strategy to cure refractory atrial fibrillation

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Abstract
Aims Previous studies have analyzed the efficacy of atrial fibrillation (AF) ablation in series of consecutive patients or comparing methods in a randomized way, without taking account individual patient characteristics. The purpose of this study was to evaluate the results of a strategy based on selecting the ablation method according to patient clinical features in drug-refractory paroxysmal or persistent AF.
Methods and results Patients with left atrial diameter ≤40 mm and runs of atrial tachycardia of more than ten beats during Holter recording were selected for selective segmental ostial ablation (SSOA) in order to disconnect only those pulmonary veins with electrical potentials. The remaining patients underwent circumferential pulmonary veins ablation (CPVA) to modify left atrial substrate by extensive linear lesions. A group of 131 consecutive patients were included. Mean follow-up was 21.5±15.2 months. In paroxysmal AF, 44 and 55 patients were selected for SSOA and CPVA, respectively, and the efficacy of the procedure was similar in the two groups (77 vs 74%; log-rank test p=NS). In persistent AF, 6 and 26 patients underwent SSOA and CPVA, respectively, and greater efficacy was observed in the second group (17 vs 65%; log-rank test p=0.004).
Conclusions Selecting the ablation method according to patient characteristics achieved good results and reduced the overall amount of ablated atrial tissue in patients with paroxysmal AF. However, in persistent AF the SSOA technique showed very limited efficacy despite the previous patient selection and a CPVA-like procedure may be the appropriate choice in all cases.

Keywords Atrial fibrillation · Catheter ablation · Pulmonary veins

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1 Introduction

The exact mechanisms underlying atrial fibrillation (AF) are not fully understood and are the source of intense investigation. Ectopic beats originating from the pulmonary veins (PVs) can trigger AF [1, 2] and PV electrical isolation from the left atrium (LA) can cure it [3, 4]. However, selective segmental ostial ablation (SSOA) has limitations, such as the risk of PV stenosis and the low efficacy in certain patients [5, 6]. For this reason, at present, the segmental technique has evolved from a limited ablation applied to those arrhythmogenic PVs to the treatment of all PVs.

On the other hand, several studies have described the role of the LA posterior wall as well as the PVs in AF [7–10] and advocate a circumferential pulmonary veins ablation (CPVA) based on PV isolation plus extended LA linear lesions [11]. This method reported better efficacy rates than SSOA in treatment of drug-refractory paroxysmal AF and mainly in persistent and permanent AF [12, 13]. CPVA is probably a more aggressive procedure than SSOA, due to the extensive ablation involved. The ultimate goal should be to optimize AF cure rates with the minimum amount of ablated tissue. Additionally, due to diverse mechanisms implied in the genesis of AF, it seems unlikely that a single valid scheme will be the most appropriate for all patients.

Most of the published data report the results of AF ablation using a single method (PV electrical isolation and/or LA substrate modification) in series of consecutive patients, or comparing two methods in a randomized way independently of patient profile. The aim of this study was to evaluate the results of an individualized approach using SSOA or CPVA according to patient characteristics.

2 Materials and methods

2.1 Patients

Consecutive patients submitted to radiofrequency (RF) catheter ablation for symptomatic, paroxysmal or persistent AF refractory to greater or equal to two antiarrhythmic drugs were included. Paroxysmal AF was defined as AF that terminates spontaneously. Persistent AF was defined as AF lasting more than 7 days or requiring electrical cardioversion to be terminated. Patients with continuous AF in whom cardioversion has either failed or not been attempted were classified as having permanent AF, and they were excluded from the study.

Previous echocardiography and 24-h Holter study were systematically performed. Transesophageal echocardiography was performed to discard intracavitary thrombus and anteroposterior LA diameter was measured by transthoracic echocardiography (M mode in long axis paresternal view). Patients with LA diameter ≤40 mm and frequent runs of atrial tachycardia (AT) of greater than ten beats at the Holter recording were assumed to have a focal mechanism and minor presence of atrial arrhythmogenic substrate. They were selected for SSOA in order to electrically disconnect dominant AF triggers raised in PVs (SSOA group). The remaining patients were selected for CPVA in order not only to isolate PV triggers but mainly to modify the atrial substrate with the creation of linear lesions along the left atrium (CPVA group). At least one previous Holter recording in sinus rhythm was obtained in every patient with normal LA in order to apply the described selection criteria.

2.2 Procedure details

Patients were included after written informed consent was obtained. The protocol study was approved by the Hospital's Ethics Committee.

Antiarrhythmic drug therapy was stopped at least five half-lives before the ablation except in patients receiving amiodarone. 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.

Catheters were introduced percutaneously through the femoral vein and a transseptal puncture was performed after verifying the absence of a patent foramen ovale to access the LA. After transseptal access, a bolus of 5,000 IU of heparin was administered with an additional bolus to maintain an ACT between 200 and 250 s. The ablation was performed under deep sedation with propofol IV and fentanyl IV. Oxygen saturation and invasive atrial blood pressure were monitored throughout the procedure.

2.3 Selective segmental ostial ablation method. SSOA group

Pulmonary veins were disconnected using SSOA as initially described by Haissaguerre et al. [3, 4]. Procedure was performed in sinus rhythm or coronary sinus pacing, using electrical cardioversion when necessary. Those PVs with PV potentials were targeted for isolation, whether or not ectopy was present during the procedure [14]. A decapolar Lasso catheter (Biosense-Webster) was used to map the PV potentials. PV ostium was identified using fluoroscopy information, the impedance of the ablation catheter tip and venography under operator judgment. RF energy was delivered at ostial sites where the earliest PV activity was recorded regarding to the atrial potential by a thermocouple-equipped 4-mm tip catheter (Celsius, Biosense-Webster) at a target temperature of 50°C and a maximum output from 40 to 50 W. The end point of SSOA was the elimination or dissociation of PV potentials.

2.4 Circumferential pulmonary veins ablation. CPVA group

CPVA was performed encircling ipsilateral PVs as described by Pappone et al [12, 13]. A three-dimensional map was constructed using a Carto electroanatomical system (Biosense-Webster) to support the creation and validation of RF lesions performed by a thermocouple-equipped 8-mm tip catheter (Celsius, Biosense-Webster) at a target temperature of 55°C and a maximum output from 50 to 60 W.

In the first 23 CPVA patients the ablation scheme consisted in lesions that encircled both left and right-sided PVs, in order to achieve a local electrogram below 0.15 mV within the encircled area. However, a high incidence of left atrial flutter was observed in these patients, and a second ablation procedure was often needed. Thus, the ablation scheme included supplementary radiofrequency lines along posterior wall and mitral isthmus in addition to the PV encirclement in the remaining CPVA procedures of the series. These ablations lines were created anatomically and

Table 1 Patient characteristics

	SSOA group	CPVA group	*P* value
Patients	50	81	
Paroxysmal AF (%)	44 (88%)	55 (68%)	
Persistent AF (%)	6 (12%)	26 (32%)	
Age (years)	47.4±12.5	52.2±11.1	0.02
Male sex (%)	38 (76%)	68 (84%)	NS
Duration of AF (months)	61.3±68.0	81.4±83.1	NS
Ineffective antiarrhythmic drugs	2.5±0.8	2.9±0.7	NS
LA diameter (mm)	37±4	43±5	<0.001
LV end-diastolic diameter (mm)	52±6	52±5	NS
LV end-systolic diameter (mm)	34±6	33±5	NS
LV ejection fraction (%)	59±11	60±10	NS
Hypertension (%)	11 (22%)	29 (36%)	0.04
Structural heart disease (%)	9 (18%)	15 (18%)	NS

Data are expressed as mean±SD when appropriate.
SSOA Selective segmental ostial ablation; *CPVA* circumferential pulmonary vein ablation; *AF* atrial fibrillation; *LA* left atrial; *LV* left ventricular

conduction block was not assessed. Position of the esophagus or esophageal temperature was not monitored in this study.

2.5 Post-ablation care and follow-up

After ablation, patients were anticoagulated for at least 24 h with a subcutaneous weight-adjusted dose of heparin and acenocumanol was restarted on the same evening. All patients were discharged under oral anticoagulation for at least 6–8 weeks following the ablation. Previous antiarrhythmic therapy was maintained for at least 1 month in order to manage early recurrences.

Follow-up consisted of outpatient visits and routine 24-h Holter monitoring at 1, 4 and 7 months, and every 6 months thereafter if the patient remained asymptomatic. Patients were also asked to report any symptoms of arrhythmia between scheduled visits and encouraged to document recurrences by an ECG obtained in their emergency service. A transthoracic echocardiogram and a magnetic resonance angiography were also routinely performed at fourth month after ablation.

Antiarrhythmic drugs were discontinued if there were no recurrences within 1–3 months after ablation. Minimum follow-up in this series was 7 months. Ablation was considered successful if no episodes of AF or atrial flutter were recorded during follow-up, without antiarrhythmic drugs or with the use of one previously ineffective antiarrhythmic drug. Arrhythmic episodes within the first month after the procedure 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 [15–18].

2.6 Statistical analysis

Continuous variables were expressed as mean±SD. Comparisons were made using Student's *t* test or Mann–Whitney test when appropriated. Categorical variables were compared by Chi-square analysis. Freedom from AF was compared using the Kaplan–Meier survival curves with log-rank test. A value of $p \leq 0.05$ was considered statistically significant.

3 Results

We analyzed a series of 131 consecutive patients. Baseline characteristics are depicted in Table 1. Fifty patients were selected to SSOA and the remaining 81 were submitted to CPVA. Details of patients' selection are presented in Fig. 1. Table 2 depicts data of the Holter prior to procedure of those patients with normal LA in whom the ablation method was selected regarding to the Holter evaluation.

Overall, no differences in efficacy were found between SSOA and CPVA groups during a mean follow-up of 21.5±15.2 months (70.0 vs 71.6% arrhythmia-free; log-rank test p=NS; Fig. 2). Among patients with successful ablation: there were 29 (58%) and 48 (59%) patients arrhythmia-free without antiarrhythmic drugs in SSOA and CPVA groups, respectively, seven patients (two and five in each group) received flecainide to manage symptomatic premature atrial contractions, and nine patients (four in SSOA and five in CPVA groups) had sinus rhythm with either flecainide or amiodarone treatment during the follow-up.

Mean duration of procedure (including transseptal puncture) was lower in the SSOA group but their fluoroscopy time was higher (see Table 3 for procedural data). In SSOA procedures a mean of 1.8±0.7 PVs per

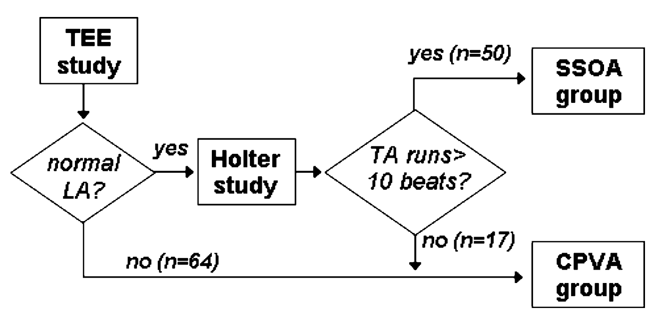

Fig. 1 This scheme shows the results of the criteria applied to assign patients either to segmental ostial ablation (*SSOA*) or to circumferential pulmonary veins ablation (*CPVA*) groups. Patients with structurally normal left atria were selected according to 24-h Holter study and SSOA was performed in those patients with high ectopic activity

Table 2 Pre-ablation Holter data in patients with normal left atria

	SSOA procedure	CPVA procedure	*P* value
Patients	50	17	
Total AT runs	658±746	13±14	0.005
Total AT beats	3973±748	55±84	0.005
Beats in the largest AT	136±193	5±4	0.02
Beats in the fastest AT	10±12	5±3	0.08
Single PACs	2727±3387	236±279	0.005
Pairs of PACs	654±794	2±2	0.001

SSOA Selective segmental ostial ablation; *CPVA* circumferential pulmonary vein ablation; *AT* atrial tachycardia; *PAC* premature atrial contraction

patient were disconnected. Pulmonary vein potentials were found in 90% of the left superior, 64% of the right superior, 22% of the left inferior and 14% of the right inferior PVs.

3.1 Complications

In the SSOA group, two patients showed transient inferior myocardial ischemia probably related to catheter manipulation during transseptal catheterization due to air embolism; the ischemia was resolved with sublingual NTG within few minutes without consequences. One patient presented a post-procedural pericarditis that required anti-inflammatory treatment. One patient had a femoral arteriovenous fistula that required surgical correction.

In the CPVA group, one patient suffered a transient cerebrovascular ischemia with dyplopia during the ablation which resolved a few hours later, there were no neurological consequences and the computed tomography scan was normal. A total of six patients presented a post-procedural pericarditis that was treated with anti-inflammatory medication; two of these patients developed a full Dressler syndrome, one of them with constriction that required steroid therapy.

Cardiac tamponade occurred in three patients in relation to transseptal puncture, all them resolved by percutaneous pericardiocentesis.

A magnetic resonance angiography (MRA) was routinely performed in the last 74 patients of the series in order to evaluate the prevalence of significant PV stenosis (>70% of lumen reduction) 4 months after the ablation procedure [19]. There were five patients with stenosis of a single PV and one patient with stenosis of two PVs, all in the SSOA group (18.2% of the evaluated patients; Fig. 3). All them remained free of symptoms during the follow-up.

3.2 Repeat ablation procedures

A second SSOA procedure was performed in 4 of the 50 patients (8%) due to AF recurrences. Recovery of conduction in ≥1 previously treated PV was seen in all cases. Three of these four patients (75%) subsequently remained arrhythmia-free during follow-up. In the CPVA group a second procedure was performed in 13 of the 81 patients (16%) due to AF persistence or appearance of left atrial flutter (see next paragraph). Eight of these 13 patients (61%) were subsequently free of arrhythmia recurrences during follow-up. In the remaining SSOA or CPVA unsuccessful procedures a second ablation procedure was not performed because the number of AF episodes was reduced and patients reported a significant clinical improvement. Overall, 3 of the 131 patients of the series (2.3%) with arrhythmia recurrences required a pacemaker plus atrioventricular node ablation.

3.3 Left atrial flutter

Overall, 12 of the 81 CPVA patients (15%) presented new-onset left atrial flutter after the ablation procedure, none was observed in the SSOA group (p=0.003). As described earlier, in the first 23 CPVA patients the ablation scheme was performed by encircling ipsilateral PVs with RF lesions (initial CPVA scheme group). In the next 58 CPVA patients, two ablation lines were created along left atrial posterior wall and another in the mitral isthmus (complete CPVA scheme group). Left atrial flutter was more often observed in the initial CPVA scheme group than in complete CPVA scheme group (30.4 vs 8.6% of the patients; p=0.003).

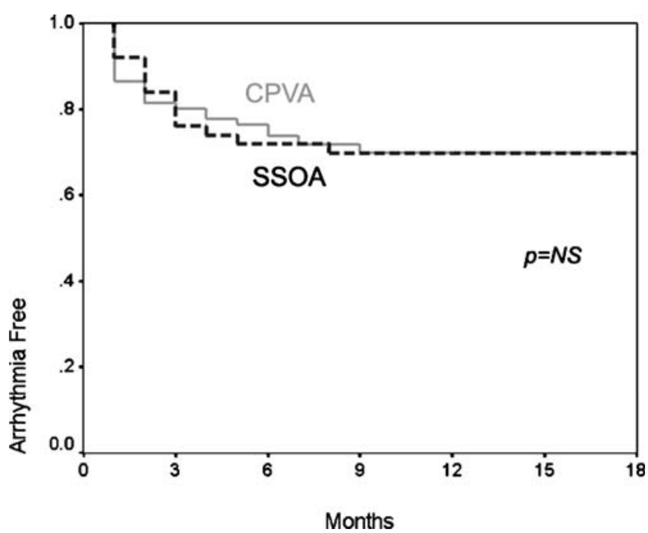

Fig. 2 Kaplan–Meier arrhythmia-free survival curves showing the global outcome of segmental ostial ablation (*SSOA*) and circumferential pulmonary vein ablation (*CPVA*) methods. Recurrences occurring within the first month were blanked out. At a mean follow-up of 21.5± 15.2 months, 70.0% of the SSOA patients were arrhythmia-free compared to 71.6% in the CPVA group. Log-rank test did not show statistical differences between both groups

Table 3 Procedural details

	SSOA procedure	CPVA procedure	*P* value
Patients	50	81	
Repeat procedures (%)	4 (8%)	13 (16%)	NS
Procedural time (min)	106±32	130±35	<0.01
Fluoroscopic time (min)	51±19	29±10	<0.01
Radiofrequency time (min)	10.3±0.8	39.1±15.5	<0.01
Asymptomatic PV stenosis (%)[a]	6 (18%)	0 (0%)	<0.01
Left atrial flutter appearance (%)	0 (0%)	12 (15%)	<0.01
Procedural complications (%)	5 (10%)	9 (11%)	NS
Coronary embolism	2	0	
Transient cerebral ischemia	0	1	
Pericarditis	1	6	
Cardiac tamponade[b]	1	2	
Arteriovenous fistula	1	0	

SSOA Selective segmental ostial ablation; *CPVA* circumferential pulmonary veins ablation; *PV* pulmonary vein

[a] >70% lumen reduction. Ratio was referred to the last 74 patients of the series that were routinely evaluated by magnetic resonance angiography.

[b] Cardiac tamponades were all related to transseptal puncture performance.

Two of the 12 patients who presented left atrial flutter were managed with electrical cardioversion and were not submitted to RF ablation; the remaining ten patients required a second procedure to map and ablate incessant left atrial flutter (Fig. 4). In initial CPVA scheme group, a posterior wall macroreentry in five patients and a reentry between right encircling lesions gaps in one patient were mapped. In complete CPVA scheme group, a reentry using right or left encircling lesions gaps in three patients and a reentry between multiple gaps in one patient were mapped, respectively.

3.4 Efficacy in paroxysmal and persistent AF

Ninety-nine paroxysmal AF patients were treated, 44 being selected to SSOA and the remaining 55 to CPVA. There were no differences in efficacy between both groups (77.3 vs 74.5% arrhythmia-free; log-rank test p=NS; see Fig. 5) during a mean follow-up of 22.2±15.8 months.

In persistent AF, six patients were submitted to SSOA and 26 patients were submitted to CPVA. Despite the previous patient selection, the efficacy of SSOA was lower (16.7 vs 64.3% arrhythmia-free; log-rank test $p=0.02$; see Fig. 5) during a mean follow-up of 19.3± 13.3 months.

4 Discussion

AF is a complex arrhythmia and its underlying pathophysiology is still under debate. Although it could be a simplification, the entity is thought to be mainly focally induced and/or substrate dependent. In the first case, PVs are an important source of spontaneous electrical activity that not only initiates AF but also can maintain reentry circuits within PV–LA region due to heterogeneous electrophysiologic properties [1, 2, 21]. However, the precise relationship between the two mechanisms (PV arrhythmogenity and LA substrate) has not been fully clarified, and the importance of establishing which mech-

Fig. 3 Magnetic resonance imaging obtained 4 months after a segmental ostial ablation showing significant stenosis of the left superior pulmonary vein

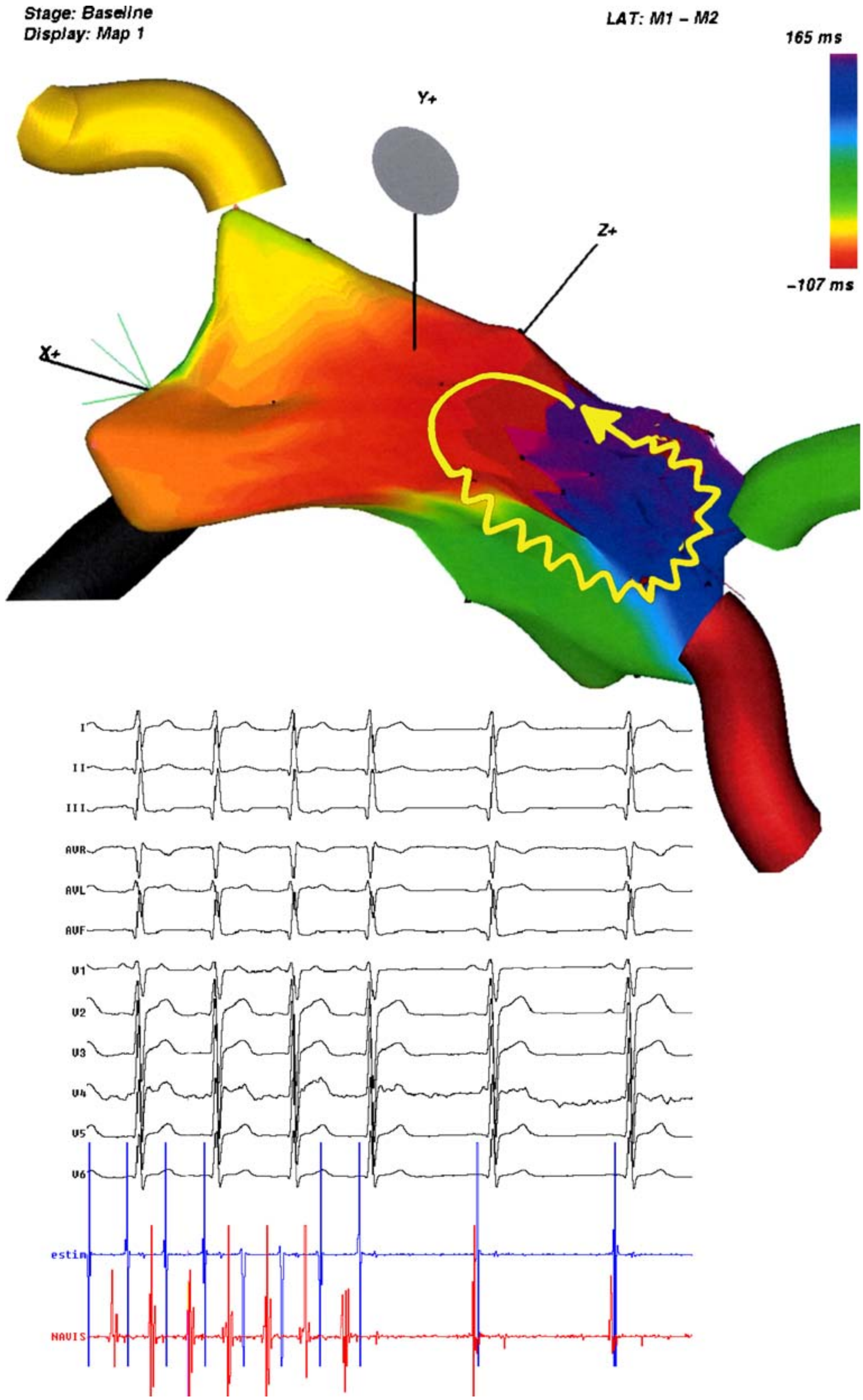

Fig. 4 Electroanatomical activation map of persistent left atrial flutter with a cycle length of 220 ms subsequent to a circumferential pulmonary veins ablation. In a second procedure, a reentry was mapped between gaps of the right encircling lesions that was eliminated completing this radiofrequency line. In polygraph screen, surface electrocardiogram, intracardiac right atrial signal (*blue line*) and ablation catheter signal (*red line*) show the atrial flutter being abolished during the radiofrequency delivery

anism is at work in a particular AF patient would have to be taken into account. The latest data for CPVA reported very high success rates [17]. However, comparative studies have shown contradictory results for preventing paroxysmal and persistent AF recurrences [20, 22, 23]. In spite of these efficacy rates, CPVA involves a greater amount of ablated atrial tissue and longer procedural times that may increase procedural risks (in our series, CPVA is related to a major

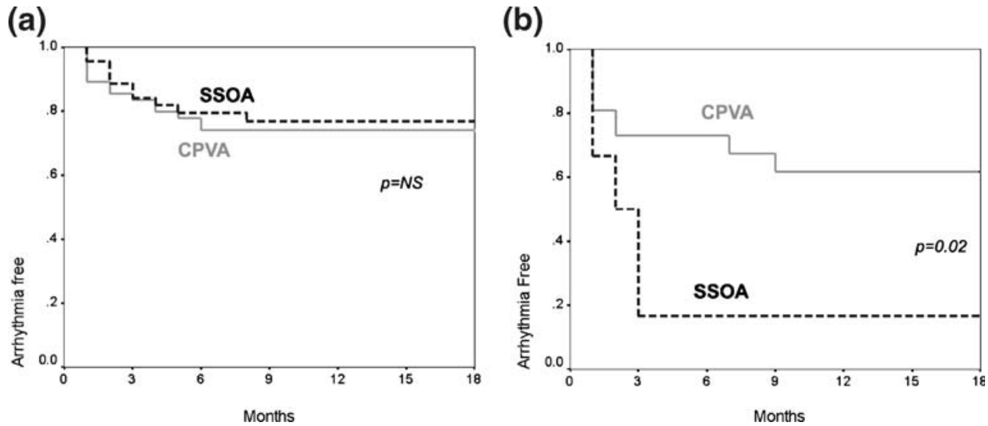

Fig. 5 Kaplan–Meier arrhythmia-free survival curves comparing segmental ostial ablation (*SSOA*) and circumferential pulmonary vein ablation (*CPVA*) by log-rank test. Early recurrences during the first month were not considered. (**a**) In paroxysmal atrial fibrillation (AF), the results of SSOA and CPVA groups were similar. (**b**) In persistent AF, despite previous patient selection, CPVA obtained better outcome

incidence of pericardial complications). Furthermore, in certain patients the extensive lesions may be too aggressive and not necessary. As a consequence, the ultimate goal of our study was to find a criterion for selecting patients who will benefit from a very limited ablation as the selective PV electrical disconnection.

In structurally normal left atria, frequent atrial premature beats reflect ectopic activity arising in the sleeves of left atrial myocardium and extending into the PVs in most cases [1, 2, 24]; furthermore, long runs of atrial tachycardia that do not induce AF may suggest a low presence of arrhythmogenic substrate. In this situation SSOA could be enough to avoid AF occurrence, since it acts by electrically disconnecting the PVs or producing considerable electrical impairment in LA–PV region [25]. In the remaining patients, in whom the focal mechanism is not so clearly manifested, the modification of larger areas of atrial substrate may be needed. CPVA is based not on disconnecting PVs [26] but on modifying the arrhythmogenic substrate of the posterior wall and, perhaps, on preventing rotor occurrence [27] or even on modifying the autonomic nerve function by LA vagal denervation [17]. Moreover, when a double block line along the posterior wall is included, CPVA creates a compartmental scheme similar to the Cox–Maze III surgical procedure [28] which could be as effective as the cut and saw technique if endocardial lesions achieve transmurality.

Using the described criteria to select the ablation method for each patient of our series, SSOA and CPVA presented equivalent efficacy in paroxysmal AF. However, in persistent AF, efficacy was lower in patients submitted to SSOA, in agreement with published data [6, 22]. It is thought that the electroanatomical remodelling that occurs during persistent AF often creates a substrate capable of creating arrhythmia independently of the PV arrhythmogenicity.

Therefore, our data suggest that a limited ablation procedure as SSOA might be enough in paroxysmal AF patients with normal left atria and frequent and large atrial tachycardia runs to achieve a high percentage of success, minimizing the amount of ablated tissue. Moreover, in SSOA procedures of this series, an average of less than two PVs were treated. Differences regarding to other series in which electrical activity were found in a major number of PVs could be due to the strict selection of the patients submitted to SSOA in this study. On the other hand, patients with dilated left atria (measured through antero-posterior diameter) and/or lack of ectopic activity or those patients with persistent AF probably need CPVA-like approach with larger ablation.

The apparition of left atrial flutter after CPVA was high in this series. The addition of ablation lines along posterior LA wall and mitral isthmus reduced the incidence of new-onset LA flutter although they were created anatomically and electrical block was not assessed, in accordance with other published data [29]. Assessment of conduction block across PV encircling lesions and across additional ablation lines could further improve the arrhythmia-free results, but this issue is currently under debate and would increase radiofrequency deployment time and procedural duration that could have result in higher risk of complications. Therefore, the end point of the CPVA procedure performed in our lab at present was the voltage abatement inside encircled areas [11].

The incidence of asymptomatic PV stenosis in SSOA patients of this series was high. This may be due to the output power used in RF deployment: 45 W, as compared to 25–40 W used in other series with lower occurrence of PV stenosis. Although no patient reported symptoms compatible with PV stenosis and all cases were detected in routine magnetic resonance angiography, the potential risk of PV stenosis should be balanced with the risks associated with SSOA. Moreover, the use of new techniques (as the use of electroanatomical mapping together with the integration of imaging techniques) may be considered to perform SSOA in order to minimize the PV stenosis risk and better define the PV potentials during the ostial PV ablation.

Two recent papers have also advocated for the use of an individually tailored approach for paroxysmal AF ablation using the noninducibility of AF as end-point [30, 31]. In both studies, ablation finished after PVs treatment with no further lesions in approximately half of the patients. This would be in accordance with the proportion of paroxysmal AF patients who were selected for SSOA in our study. Nowadays, it seems clear that AF occurrence responds to several mechanisms and therefore, careful patient selection would allow an individualized ablation strategy. The present study describes the results of a simple criteria to pre-select patients who would benefit from a very limited ablation, with a good outcome in paroxysmal AF, whereas persistent AF seems to require more extensive lesions.

5 Study limitations

The number of persistent AF patients submitted to SSOA in this series is low due to the strict selection criteria itself. Therefore, results of the study in this group have to be taken with some reservations. However, the poor results of SSOA observed in persistent AF in our study, even when the proposed selection criteria were applied, corroborate the results of previous studies that argue against the use of a SSOA-like limited ablation in this population [32].

Antiarrhythmic drug treatment was not modified when the Holter recording prior to the ablation was performed. However, only four patients in whom the ablation method was selected depending on the Holter data were under amiodarone. Furthermore, these four patients were all selected to SSOA because they had high atrial ectopy and large AT runs in the Holter recording despite amiodarone. Therefore, we believe that the previous antiarrhythmic drug treatment has not modified the selection results.

6 Conclusions

Selecting the ablation method on the basis of left atrial size and the presence and characteristics of atrial ectopy in Holter register allows an individualized approach in refractory AF treatment. In paroxysmal AF, this strategy achieves good efficacy rates and reduces the overall amount of ablated atrial tissue in many patients, although PV stenosis risk may be balanced when PV ostial ablation is performed. However, in persistent AF, SSOA presents very limited efficacy despite the previous patient selection and a CPVA-like approach is probably the appropriate choice in all cases.

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Incidence of Pulmonary Vein Stenosis in Patients Submitted to Atrial Fibrillation Ablation: A Comparison of the Selective Segmental Ostial Ablation vs the Circumferential Pulmonary Veins Ablation

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Abstract. ***Introduction:*** **Pulmonary vein (PV) stenosis is an important complication of the AF ablation and could be underestimated if their assessment is not systematically done. Selective Segmental Ostial Ablation (SSOA) and Circumferential Pulmonary Veins Ablation (CPVA) have demonstrated efficacy in atrial fibrillation (AF) treatment. In this study the real incidence of PV stenosis in patients (pts) submitted to both SSOA and CPVA was compared.**

Methods: **Those pts with focal activity and normal left atrial size were submitted to SSOA, remaining pts were submitted to CPVA to treat refractory, symptomatic AF. Contrast enhanced magnetic resonance angiography (MRA) was routinely performed in all patients 4 months after the procedure.**

Results: **A series of 73 consecutive patients (mean age of 51 $\pm$ 11 years; 75% male) were included. SSOA was performed in 32 patients, and the remaining 41 patients underwent to CPVA, obtaining similar efficacy rates (72% vs 76% arrythmia free probability at 12 months; log rank test $p =$ NS). Six patients had a significant PV stenosis, all in SSOA group none in CPVA group (18.8% vs 0%; $p = 0.005$). All patients were asymptomatic and the stenosis was detected in routine MRA. No predictors of stenosis has been identified analysing patient procedure characteristics.**

Conclusion: **PV stenosis is a potential complication of SSOA not seen in CPVA. The study confirms than MRA is useful for identifying patients with asymptomatic PV stenosis.**

Key Words. **atrial fibrillation, pulmonary veins stenosis, catheter ablation**

Introduction

Pulmonary vein (PV) radiofrequency (RF) ablation is a curative procedure for patients with atrial fibrillation (AF). Several strategies have been developed to achieve the PV isolation with good clinical results [1–3]. PV stenosis has been recognized as one potential complication of the ablation procedure that can be associated with severe respiratory symptoms that cause significant morbidity [4–7]. Its incidence is unclear, mainly in asymptomatic patients. Several methods have been evaluated for the proper detection of this complication [8] and Magnetic Resonance Angiography (MRA) has become a useful method for the diagnosis [9,10].

The aim of this study was to analyse the incidence of PV stenosis in patients treated with selective segmental ostial ablation (SSOA) or with circumferential pulmonary veins ablation (CPVA) methods.

Methods

Patients

A series of 73 consecutive patients underwent to AF ablation for treatment of drug-refractory, symptomatic AF. All patients were previously studied with 24-hours Holter monitoring and

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Table 1. Demographic characteristics

	SSOA group	CPVA group	P
Patients	32	41	
Paroxysmal AF	27 (85%)	27 (66%)	0.09
Duration of AF (months)	62 ± 71	72 ± 80	NS
Number of failed AAD	2.5 ± 0.9	2.6 ± 0.7	NS
Age (years)	50 ± 12	52 ± 10	NS
Male Sex	23 (75%)	33 (80%)	NS
Left Atrium (mm)	37 ± 4	42 ± 5	0.02
LVEF (%)	58 ± 11	53 ± 17	NS
Structural Heart Disease	8 (25%)	11 (27%)	NS
Arterial Hypertension	9 (28%)	12 (29%)	NS

SSOA: Selective Segmental ostial ablation. CPVA: Circumferential pulmonary veins ablation. AAD: Antiarrhythmic drugs. LVEF: Left ventricular ejection fraction.

transthoracic echocardiography. Informed consent was obtained in all patients before the procedure. Patients with suspected focal origin AF (identified by structurally normal left atria and >10 runs of atrial tachycardia/24 hours) were submitted to SSOA in order to isolate pulmonary veins (PV) from left atria. The remaining patients underwent to CPVA to modify atrial substrate with extended lesions. Demographic characteristics are presented in Table 1.

Ablation Procedure

Selective Segmental Ostial Ablation. After transseptal access, PV disconnection was performed as described by Haissaguerre et al. [1]. A decapolar Lasso catheter (Biosense-Webster) was used to map the PV potentials and RF energy was applied by a thermocouple-equipped 4 mm tip catheter (Biosense-Webster). Ostial lesions were created where the PV earliest activity was recorded until PV potentials were eliminated or dissociated at a target temperature of 50°C and a maximum output from 40 to 50 W. Only those PVs with electrical activity were treated. No attempts to induce premature beats were done. Details of the approach used have been previously reported [13].

Circumferential Pulmonary Veins Ablation. Non-fluoroscopic navigation system (CARTO; Biosense Webster) was used to delineate the left atria and PVs and guide the RF lesions after transseptal access. Ablation lines were created as described by Pappone et al. [11,12] surrounding ipsilateral PVs at a minimum distance of 5 mm from their ostium by a thermocouple-equipped 8 mm tip catheter (Navistar, Biosense-Webster) at a target temperature of 55°C and a maximum output from 50 to 60 W. The end point was to reduce the amplitude of the endocardial potentials inside the encircled area below 0.15 mV.

Follow-up

Patients were followed in the outpatient clinic at 1, 4, 7 months and every 6 months thereafter if they remained asymptomatic. Routine 24-hours Holter monitoring was performed before each control and patients were also asked to communicate any symptom suggestive of recurrence between scheduled visits in order to document it. A transthoracic echocardiogram was also performed 4 months after ablation procedure. Acenocumarol was maintained at least for 3 months after the ablation. All patients received antiarrhythmic drugs (flecainide if no structural heart disease was diagnosed or amiodarone if there was evidence of structural heart disease) during the first month to control early recurrences. Drugs were withdrawn afterwards if patients remained free of recurrences.

A contrast enhanced MRA (1.5 T. Signa Horizon. GE Medical Systems) was routinely performed in all the patients submitted to an ablation procedure. A single radiologist blinded to the type and result of the procedure and clinical characteristics of patients evaluated the test. MRA was obtained 4 months after the ablation since progression of the stenosis is rare after this period of time [7,14]. A significant stenosis was considered with a diameter lumen reduction of >70%.

Statistical Analysis

Continuous variables are expressed as mean ± SD. Comparisons were made using the Student's T-test and Chi-square analysis. Recurrence-free was compared using the Kaplan-Meier survival curves with log rank test. Multivariate logistic regression analysis was performed to determine independent predictors of an event. Results with $p < 0.05$ were considered statistically significant.

Results

MRA was performed in 73 of 78 consecutive patients submitted to an AF ablation procedure. The MRA could not be done in 3 patients with claustrophobia, in a patient with a pacemaker and in another with an implantable automatic defibrillator. In 32 patients, the ablation was done with a SSOA approach; in 41 patients the ablation was done with the CPVA method. During a mean follow-up of 14.7 ± 12.1 months, 23 and 31 patients of SSOA and CPVA groups respectively were free from recurrences (72% vs 76% arrythmia free; long rank test $p =$ NS).

None of the patients developed symptoms suggestive of PV stenosis. However, in 6 patients a significant PV stenosis was detected in the routine MRA, all them in the SSOA group, none in the CPVA group (18.8% vs 0% of the evaluated patients; $p = 0.005$). In 4 patients, the stenosis was

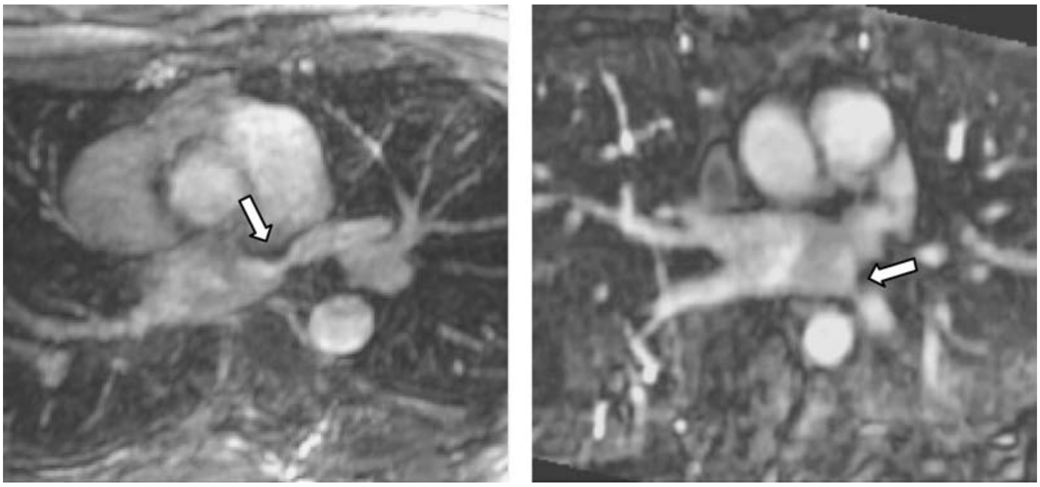

Fig. 1. *Two patients with pulmonary vein (PV) stenosis. Left and right images show left superior and left inferior PV stenosis respectively (arrows).*

located in the left superior PV (LSPV), in 1 patient at the left inferior PV (LIPV) and in 1 patient both the LSPV and the LIPV had a significant stenosis.

In the CPVA group, ablation lines encircled all PV's in all cases. In SSOA group a mean of 1.8 ± 0.7 PVs per patient were treated with a mean of 10.3 ± 0.8 minutes of radiofrequency application. Ostial segments where RF was applied to achieve the PV electrical disconnection were classified by anatomic and fluoroscopic guidance among 4 ostial divisions: anterior, posterior, superior and inferior segments. In our series, the earliest electrical activity was recorded on the inferior segment in the 57 and 58% of the treated LSPV and RSPV respectively (see Table 2). LSPV was isolated in the 93.8% of patients, LIPV in 18.8%, right superior PV (RSPV) in 59.4% and right inferior PV (RIPV) in 6.3%. A second procedure was necessary in 3 patients of the SSOA group due to AF recurrence, therefore the total number of PVs isolated were 33 LSPVs, 6 LIPVs, 21 RSPVs and 2 RIPVs. Overall, 15.2% of the LSPVs and 33.3% of the LIPVs treated by SSOA developed stenosis.

Table 2. *PV ostial segments in which RF energy was deployed in SSOA group*

	Inferior (%)	Posterior (%)	Superior (%)	Anterior (%)
LSPV ($n = 30$)	56.6	26.6	23.3	26.6
RSPV ($n = 19$)	57.9	26.3	21.0	21.0
LIPV ($n = 6$)	16.7	33.3	50.0	16.7
RIPV ($n = 2$)	0	0	100	100

PV: pulmonary vein. RF: radiofrequency. SSOA: selective segmental ostial ablation. LSPV: left superior PV. RSPV: right superior PV. LIPV: left inferior PV. RIPV: right inferior PV.

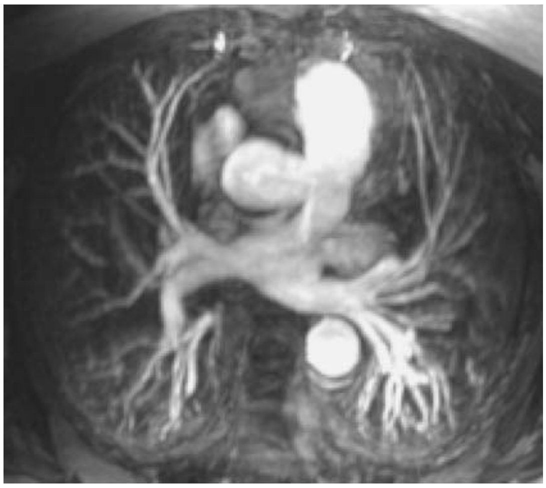

Fig. 2. *Example of anatomical variant of the pulmonary veins where a single ostium of both left and right sided was observed.*

No differences in patient characteristics or procedural details were found between patients with and without PV stenosis in SSOA group, and no predictors of stenosis could be identified.

In our series 16 patients (22% of the total) had some anatomical variant of the PVs, being the most common variant the presence of single ostium of the left PVs (15% of the patients) and the presence of 3 right PVs (5% of the patients; see Fig. 2).

Discussion

PV stenosis is a potential complication of AF ablation. Correlation between the technique employed for the ablation and the incidence of PV stenosis has been studied by Saad et al. [7]. The authors suggest that the most important point is the accuracy of the technique for differentiating the real ostium of the PV. Therefore, different methods like venography, intracardiac ultrasonography and electroanatomic mapping are used to define more accurately the junction between the atrial wall and the PV [5–8]. Even with these techniques, in large series, stenosis persists as a complication ranging between 5 to 30% [14]. Some authors do not look systematically for PV stenosis in all patients and only if the patient becomes symptomatic, a diagnostic procedure is performed [15]; our results show that this method may underestimate the real incidence of this complication.

In our series, AF ablation was performed using two different approaches and the incidence of PV stenosis was compared. The absence of stenosis in the CPVA group correlates with the findings of the series published by Pappone et al. [3,12,13,16], and although there are reports of PV occlusion using this technique [17], the risk seems lower because of a better definition of the catheter position in respect of the PV ostium. Furthermore, in CPVA procedures RF is delivered at least 5 mm away from the defined ostium.

In our experience, all PV stenosis were found in the SSOA group and this is in part, due to the more difficult differentiation of the PV ostium and because of the need to apply energy close to the ostium, making it easier to produce a lesion inside the vein. Moreover, although the total amount of RF energy was higher in CPVA than in SSOA, a major concentration of RF lesions was required in SSOA technique in order to achieve the PV isolation, delivering the RF energy in a more limited region of the PV ostium. It is of interest that in the SSOA group the left sided PVs were more stenosed, and this correlates with previous reports in the literature [14]. A possible explanation may be that the ablation catheter moves easily inside the left sided veins with each breathing movement, thus delivering the energy inside the PV. In our approach, SSOA was performed treating only those PVs showing electrical activity, being the most commonly treated the LSPV and the RSPV. These results were in accordance with other studies where only arrythmogenic PVs were treated an could be explained because the muscular sleeves insertion into PVs was more developed in upper than in lower veins [1,2].

Recently, a study comparing the efficacy and safety of both ablation strategies in a series of 100 randomized patients has been published [18]. Multislice CT was routinely performed 3 months after the ablation procedure, and stenosis of at least 1 PV was found in 12 and 6% of the SSOA and CPVA patients respectively. This PV stenosis incidence is similar to our results in the SSOA group, however we had not observe any stenosis in the CPVA group. This discrepancy maybe due to the higher power limit output used in this study, up to 70 W in 8 mm tip or 50 W in cooled 4 mm tip catheter respectively.

All patients with PV stenosis in our series were asymptomatic, and were identified because MRA was sistematically performed. The development of clinical symptoms is associated with the number of PVs affected and the degree of narrowing [14]. Lung perfusion defects were seen in PV narrowing greater than 70% in the left PV [7]. When right PV are affected lung scan perfusion defects appear with somewhat lower degrees of stenosis ranging between 50 to 65%; this might be explained because of the lower pressure in the right PV that may increase the pressure gradient [19]. In our series there were no total occlusions, all but one patient had only one vein affected, and right sided veins were not involved, contributing to the absence of respiratory symptoms associated with found PV stenosis.

In this series, a single MRA was performed 4 months after the ablation procedure, so later PV stenosis progression could have been missed. However, although PV narrowing have not been exactly quantified because a previous MRA was not performed, all PV stenosis images we obtained showed a focalised and high degree narrowing that must be catalogued as severe (>70%) in all cases. In the remaining patients, PVs ostium did not show appreciable alterations, and normal or mild narrowed (<50%) PVs rarely progress beyond the third month [7,14]. Therefore, we decided not repeat MRA beyond the 4th month since the ablation procedure because of the low probability to observe new findings.

Conclusions

Pulmonary vein stenosis is a potential complication of the selective segmental ostial ablation of atrial fibrillation. The PV stenosis is seldom observed in circumferential pulmonary veins ablation approach. The study confirms that magnetic resonance angiography is useful for identifying patients with asymptomatic pulmonary vein stenosis and anatomical variants of the left atria.

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Clinical research

Pre-procedural predictors of atrial fibrillation recurrence after circumferential pulmonary vein ablation

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KEYWORDS
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Ablation;
Predictors

Aims The success rate of circumferential pulmonary vein ablation (CPVA) to treat atrial fibrillation (AF) ranges from 60 to 90%, depending on the series. The objective of the study was to identify predictors of AF recurrence after a standardized CPVA procedure.

Methods and results A series of 148 consecutive patients undergoing CPVA for symptomatic paroxysmal (60.8%), persistent (23.6%), or permanent (15.5%) AF refractory to antiarrhythmic drugs were included in the study. CPVA with the creation of supplementary block lines along the posterior wall and mitral isthmus was performed and a minimum of 6 months follow-up completed in all patients. Structural heart disease was present in 19.6% and hypertension in 33.8% of patients. After 13.1 ± 8.4 months follow-up, 73.6% of patients were free of AF recurrences after a mean of 1.18 ± 0.45 procedures/patient (one procedure in 85.2%, two procedures in 14.8%, and three procedures in 2.7%). Univariable analysis showed that the risk of AF recurrence increases with age (HR 1.03; 95% CI 1.00–1.06, $P = 0.031$), with the presence of previous hypertension (HR 2.7; 95% CI 1.43–5.07, $P = 0.002$), and if AF is permanent (HR 2.23; 95% CI 1.08–4.59, $P = 0.042$). In addition, larger anteroposterior left atrial diameter (LAD) (HR 1.11; 95% CI 1.05–1.18, $P = 0.001$) and larger left ventricular end-systolic diameter (HR 1.07; 95% CI 1.00–1.15, $P = 0.029$) prior to the procedure were associated with AF recurrence after CPVA. Cox regression analysis showed that hypertension (OR = 2.8; 95% CI 1.5–5.4; $P = 0.002$) and LAD (OR = 1.1; 95% CI 1.05–1.19, $P < 0.001$) were independent predictors of AF recurrence. The mean predicted proportion of patients with AF recurrence after CPVA of the multivariable model showed a linear relationship with the increase in LAD prior to the procedure. The presence of hypertension further increased the mean predicted proportion of patients with AF recurrence at each LAD.

Conclusion Hypertension and LAD are independent pre-procedural predictors of AF recurrence after CPVA to treat AF. These data may help in patient selection for AF ablation.

Introduction

Unlike electrical cardioversion or antiarrhythmic drugs, pulmonary vein ablation offers the possibility of curing AF. Initially, there was a great variety of different technical approaches, with a low success rate and a relatively high rate of complications. Therefore, the procedure was cautiously reserved for highly symptomatic patients as a 'last resort' therapy.[1] However, the ablation procedure has become more standardized in recent years and many centres have reported high success rates and a reduction in complications. In this regard, the patient selection criteria for performing the procedure are less restrictive and the procedure is now indicated for diseased atria. Circumferential pulmonary vein ablation (CPVA), with the creation of additional lines to prevent macro-re-entrant atrial tachycardia, is a widely used technique for AF ablation.[2] However, the success rate falls short of 100% (~80% in the most recent series of selected patients) and the risk of severe complications remains a matter of concern: severe vascular events in 1%, tamponade/perforation in 0.5%, severe-to-moderate pulmonary vein stenosis in 1.5%, and atrial macro-re-entrant tachycardia in 29%.[1,3] Thus, not all patients may be suitable candidates for AF ablation and it seems desirable to identify pre-procedural predictors of recurrence that would be useful for defining selection criteria.

To date, investigators have identified some intraprocedural predictors of recurrences for AF ablation, namely, pre-existent left atrial scarring during catheter mapping,[4] voltage abatement,[5] the percentage of left atrium ablated

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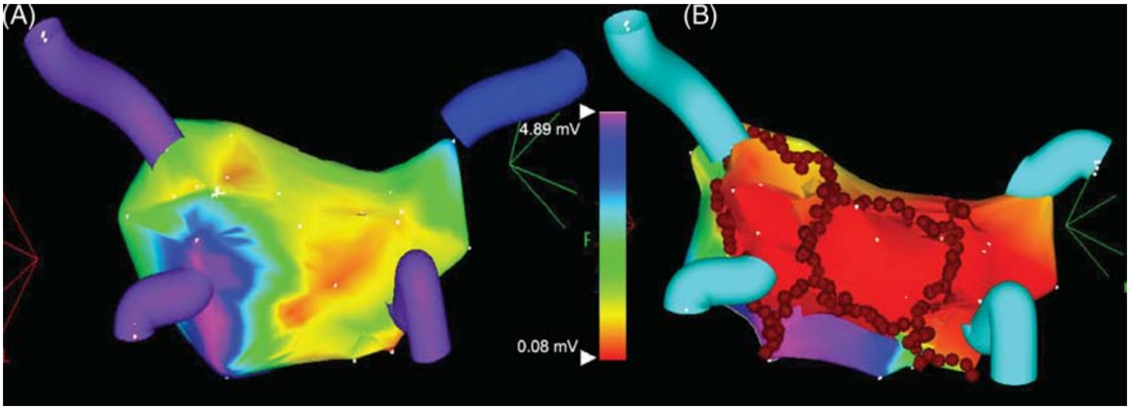

Figure 1 (*A*) The ablation scheme performed in all patients and (*B*) checking of low voltage inside the encircled area after the procedure.

or vagal denervation of the pulmonary veins,[6] conduction slowing or block across the ablation lines,[7,8] AF inducibility after left atrial circumferential ablation,[9] and after-segmental ostial ablation.[10] Also, some independent pre-procedural predictors of AF recurrence have been described for segmental ostial ablation, i.e. age >50 years, paroxysmal vs. non-paroxysmal AF.[11] Finally, early AF recurrence has been identified as an independent post-procedural predictor of late AF recurrence in paroxysmal AF.[12] However, pre-procedural independent predictors of AF recurrence have not been described for CPVA. The objective of this study was to identify the clinical and echocardiographic parameters obtained prior to the procedure, which may help to predict AF recurrences after CPVA in a consecutive series of patients.

Methods

Study population

All patients referred to our institution for AF ablation between January 2003 and November 2005 were included in the study. Exclusion criteria were age <18 or >75 years, anteroposterior LAD at transthoracic echocardiography >55 mm, presence of LA thrombus on transoesophageal echocardiography, and the presence of a mechanical prosthetic heart valve. No patient was excluded on the basis of their AF duration. Patients were included after written informed consent was obtained. No patient refused to give their consent and no patient was lost to the follow-up. The study protocol was approved by the hospital's Ethics Committee.

Procedure

Antiarrhythmic drug therapy was stopped at least five half-lives before the ablation, except in patients receiving amiodarone. Patients on oral anticoagulation stopped medication 3 days prior to the procedure and low-molecular-weight heparin was administered until the day before ablation. Patients underwent transoesophageal echocardiography prior to the ablation.

Catheters were introduced percutaneously through the femoral vein and a transseptal puncture was performed after verifying the absence of a patent foramen ovale to access the LA. After transseptal access, a bolus of intravenous heparin (5000 IU) was administered, with an additional bolus to maintain an activated clotting time of more than 200 s. The ablation procedure was performed under deep sedation.

All the patients underwent CPVA in order to achieve voltage abatement of the electrograms of the encircled areas, as previously described.[5] A three-dimensional map was constructed using an electroanatomical mapping system (CARTO, Biosense-Webster) to support the creation and validation of RF lesions. A thermocouple-equipped 8 mm or irrigated tip catheter (Navistar, Biosense-Webster) was used. Target temperature was 55°C at a maximum output of 60 W for the 8 mm tip catheter and 45°C at a maximum output of 40 W for the irrigated tip catheter.

The ablation scheme consisted of lesions that encircled both left- and right-sided PVs in order to achieve a local electrogram <0.15 mV within this area. Supplementary lineal lesions along the LA posterior wall and roof and along mitral isthmus were deployed. Finally, electrical disappearance/reduction was checked by mapping the encircled area (*Figure 1*).

Long-term follow-up

All included patients were followed up for at least 6 months. Follow-up consisted of outpatient visits and 24 h Holter monitoring at 1, 4, and 7 months, and every 6 months thereafter if the patient remained asymptomatic. Patients were also asked to report any symptoms of arrhythmia between scheduled visits. A transthoracic echocardiogram and a magnetic resonance angiography were routinely performed 4 months after ablation. All patients continued oral anticoagulation to maintain an international normalized ratio of between 2.0 and 3.0 for a minimum of 2 months. Previous antiarrhythmic therapy was maintained for at least 1 month and then discontinued if there were no recurrences 1–3 months after ablation.

Symptomatic or asymptomatic AF episodes presenting after the first month were considered as a recurrence.

Statistical analysis

The relationship between baseline clinical and echocardiographic characteristics and the time to recurrence during follow-up was evaluated using survival analysis methodology (Cox regression models). Variables were included in the multivariable analysis using a forward stepwise procedure with a criteria of $P < 0.05$ for inclusion and $P > 0.10$ for removal from the model.

Validation of the proportional hazard assumption for the final multivariable model was made through a graphical examination of log minus log plots of the Kaplan–Meier survival curves vs. the log of time.

The multivariable model was validated by bootstrap bagging with 1000 samples. In the bootstrap procedure, repeated samples of the same number of observations as the original database were randomly selected with replacement from the original set observations. For each sample, stepwise regression analysis was performed. The stability of the final stepwise model can be assessed by identifying the variables that enter most frequently in the repeated bootstrap models and comparing those variables with the variables in the final stepwise model. If the final stepwise model variables occur in >50%

of the bootstrap models, the original final stepwise regression model was judged as stable.

A two-sided P-value $\leqslant 0.05$ was considered statistically significant. The analyses were performed using the SPSS 11.0 (SPSS, Chicago, IL, USA) and Stata 9 (Stata Corp., College Station, TX, USA) statistical packages.

Results

Patient characteristics and results

A group of 148 consecutive patients were included in the study. A second procedure was performed in 22 (14.8%) patients because of recurrent AF (8 patients, 5.4%) or left atrial flutter (14 patients, 9.5%), and a third procedure was necessary in four of those patients (2.7%). Structural heart disease was present in 19.6% of patients and hypertension in 33.8%, and AF was persistent or permanent in 39.2% of the study population. Baseline clinical and echocardiographic pre-procedural characteristics are depicted in *Table 1*.

After a mean follow-up of 13.1 $\pm$ 8.4 months, 73.6% of patients in the whole group were free of AF recurrences.

Complications

Two (1.3%) patients suffered a transient cerebrovascular ischaemia. Six (4%) patients had post-procedural pericarditis, and two of them (1.3%) developed a Dressler syndrome. Cardiac tamponade occurred in three (2%) patients, two during transseptal puncture (resolved by pericardiocentesis) and one during ablation (resolved by surgery). Magnetic resonance angiography was performed in all patients prior to and 4 months after CPVA and did not reveal any stenosis of the pulmonary veins.

After the first procedure, 16 patients presented LA flutter, 14 underwent a second procedure, and 2 patients were treated with electrical cardioversion. After a second procedure, only three (2%) patients presented recurrent LA flutter (one post-CPVA relapse and two post-electrical cardioversion); one was resolved through a third procedure and the other with antiarrhythmics and cardioversion.

Table 1 Characteristics of patients included in the study

Characteristics of patients	
Patients	148
Age (years)	52 $\pm$ 11
Male gender	122 (82.4)
Hypertension	50 (33.8)
Type of AF	
Paroxysmal	90 (60.8)
Persistent	35 (23.6)
Permanent	23 (15.5)
Structural heart disease	29 (19.6)
AF duration (months)	74.6 $\pm$ 68.4
Echocardiography	
LAD (mm)	41.4 $\pm$ 5.6
LVEDD (mm)	51.3 $\pm$ 5.3
LVESD (mm)	32.7 $\pm$ 5.1
IVS (mm)	10.6 $\pm$ 1.5
LVPW (mm)	10.1 $\pm$ 1.1
LVEF (%)	60 $\pm$ 10.9

Data are expressed as mean $\pm$ SD or number (%) of patients. AF, atrial fibrillation; LAD, anteroposterior left atrial diameter; LVEDD, left ventricular end-diastolic diameter; IVS, interventricular septum; LVPW, left ventricular posterior wall; LVEF, left ventricular ejection fraction.

Univariable analysis

Table 2 shows the univariable analysis of pre-procedural variables and the risk of AF recurrence. It should be noted that the risk of AF recurrence increases with age (HR 1.03; 95% CI 1.00–1.06, $P = 0.031$), with the presence of previous hypertension (HR 2.7; 95% CI 1.43–5.07, $P = 0.002$), and when AF is permanent (HR 2.23; 95% CI 1.08–4.59, $P = 0.042$). Furthermore, larger LAD (HR 1.11; 95% CI 1.05–1.18, $P = 0.001$) and larger left ventricular end-systolic diameter (LVESD) (HR 1.07; 95% CI 1.00–1.15, $P = 0.029$) prior to the procedure were associated with AF recurrence after CPVA.

Multivariable analysis

Cox regression analysis showed that the presence of previous hypertension (OR = 2.8; 95% CI 1.5–5.4, $P = 0.002$) and of an enlarged LAD (OR = 1.1; 95% CI 1.06–1.2, $P = 0.001$) was an independent predictor of AF recurrence after CPVA (*Table 3*).

The log minus log plots of the Kaplan–Meier survival curves vs. the log of time showed approximately parallel straight lines, indicating that the proportional hazard assumption was reasonable.

Table 2 Univariable analysis of pre-procedural variables and the risk of AF recurrence

	HR (95% CI)	*P*-value
Age (years)	1.03 (1.00–1.06)	0.031*
Male gender	1.02 (0.45–2.32)	0.942
Hypertension	2.70 (1.43–5.07)	0.002*
Permanent AF	2.23 (1.08–4.59)	0.042*
Structural heart disease	1.28 (0.61–2.69)	0.331
AF duration (months)	1.00 (1.00–1.00)	0.989
LAD (mm)	1.11 (1.05–1.18)	0.001*
LVEDD (mm)	1.05 (0.98–1.12)	0.175
LVESD (mm)	1.07 (1.00–1.15)	0.029*
LVEF (%)	0.98 (0.95–1.01)	0.128
IVS (mm)	0.99 (0.78–1.27)	0.843
LVPW (mm)	1.05 (0.74–1.48)	0.927

LVESD, left ventricular end-systolic diameter.
*$P < 0.05$.

Table 3 Multivariable analysis

	HR (95% CI)	*P*-value
LAD	1.1 (1.06–1.2)	0.001
Hypertension	2.8 (1.5–5.4)	0.002

Independent pre-procedural predictors of AF recurrence after ablation procedure.

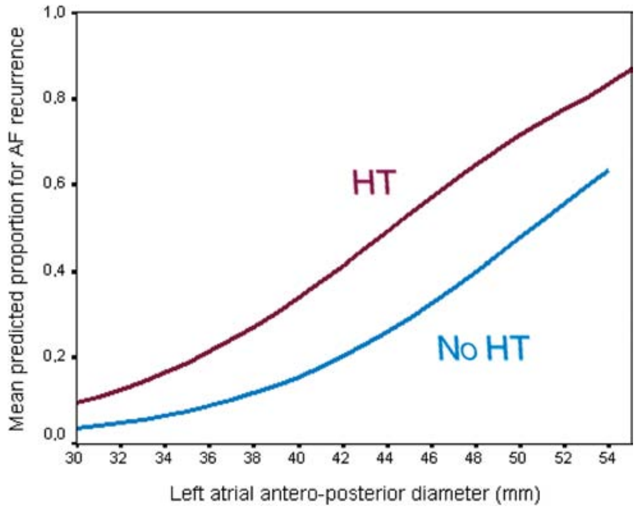

Figure 2 The mean predicted proportion of patients with atrial fibrillation (AF) recurrence after ablation procedure, related to anteroposterior left atrial diameter (expressed in millimetres) and to the presence of hypertension. HT, hypertension.

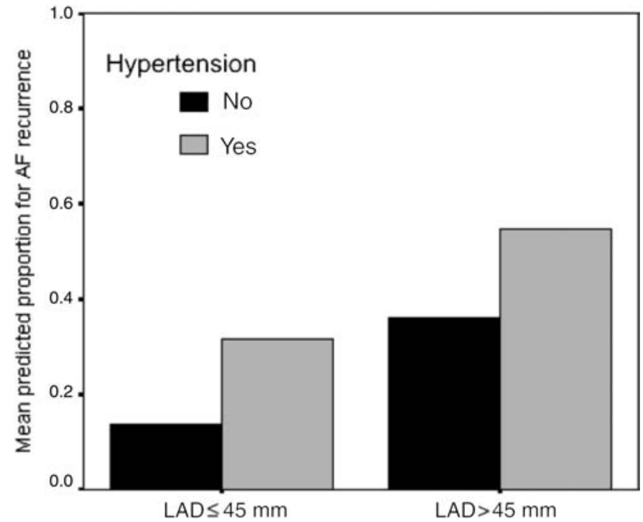

Figure 3 Mean predicted proportion of patients with AF recurrence after ablation procedure in the four groups created by the combination of the presence of hypertension and left atrial diameter (LAD).

Bootstrap validation of the multivariable model showed that hypertension and LAD variables entered in 90 and 80% of the analyses, respectively. Moreover, estimated model (only hypertension and LAD as independent predictors) was observed in 54% of the bootstrapped samples; additionally, in 19% of the models, these two variables appeared with another variable and only in 3% of them, they did not appear simultaneously.

Predicted model for atrial fibrillation recurrence

The mean predicted proportion of patients with AF recurrences after CPVA of the multivariable model showed a linear relationship with the increase in LAD prior to the procedure. In addition, the presence of hypertension further increased the mean predicted proportion of patients with AF recurrences at each LAD (*Figure 2*).

Given these data, it is possible to identify four subgroups of patients with different probabilities of AF recurrence (*Figure 3*). The subgroup of patients with an LAD $\leqslant$45 mm and without hypertension has a probability of >85% of maintaining long-term sinus rhythm after CPVA. In contrast, the subgroup of patients with hypertension and an LAD >45 mm have a probability of maintaining sinus rhythm after CPVA of ~50%.

Discussion

Previous reports have demonstrated that LAD is a predictor of recurrences after cardioversion or mini-maze procedure.[13,14] Thus, it is not surprising that LAD prior to CPVA was shown to be a stronger independent predictor of AF recurrences. The major contribution of this study is the demonstration of a linear relationship between the increase of LAD and the mean predicted proportion of patients with AF recurrence after CPVA, and the additional increase of this proportion in the presence of hypertension. Up to now, pre-procedural independent predictors of AF recurrence have not been described for CPVA, probably because most reports included a relatively small number of patients or multivariable analyses either were not performed or may not have had sufficient power to identify them.[15]

As far as we have known, only the age >50 years and the presence of persistent vs. paroxysmal AF have been identified as independent pre-procedural predictors of AF recurrences after AF ablation, but only for segmental ostial ablation.[11] In the present study, the univariable analysis shows that the risk for AF recurrence increases with age, with the presence of previous hypertension, when AF is permanent, and with the increase of LAD and LVESD (significant statistical association). However, the multivariable analysis shows that the only independent predictors of AF recurrence are LAD and the presence of previous hypertension, thus suggesting that permanent AF is associated with more powerful predictors of recurrences, i.e. enlarged LAD.

The results of the present study are consistent with the published data as regards the efficacy of CPVA. It has recently been reported that CPVA may achieve restoration of sinus rhythm in chronic AF[16] and even in prosthetic heart valve patients.[17] The success rate achieved in these circumstances (74 and 73%, respectively) was lower than that for paroxysmal AF (85%) reported by the same investigators.[6] It is noteworthy that the mean LAD in a case of chronic AF or a prosthetic heart valve patient (45 $\pm$ 6 and 55 $\pm$ 5 mm, respectively) was larger than in paroxysmal AF patients (<40 mm), thus illustrating that the more dilated the atria the lower the success rate.

The finding that hypertension is a risk factor for AF recurrence after CPVA is consistent with the literature. Hypertension is the most prevalent risk factor for AF, with a relative risk of ~1.2 in the general population.[18] However, it is also a modifiable cause of left atrial enlargement and fibrosis, which both contribute to the development of AF. The fact that a history of hypertension acts as an independent predictor of AF after CPVA, with a relative risk of 2.8, suggests two explanations for its negative effect: hypertensive patients might have more diseased atria for the same LAD or, alternatively, there is poor control of hypertension after the procedure. We could assume that LAD enlargement is a surrogate measure of chronic elevation of left ventricular filling pressures as a consequence of poor diastolic function in hypertensive patients.[19–21]

Although patients with AF recurrences were more likely to suffer from hypertension, there were no differences between patients with or without AF recurrences, with respect to the thickness of the septum and the posterior wall of the left ventricle (*Table 2*). However, the lack of difference in wall thickness suggests that more subtle changes, probably at the atrial level, occur in patients with hypertension, even before changes in the thickness of the left ventricular wall develop.

Clinical implications

The identification of strong predictors of AF recurrences (i.e. hypertension) and the linear relationship between LAD and the mean predicted proportion of patients maintaining sinus rhythm after CPVA makes it possible to identify patients with different long-term success probabilities. This stratification may help to select patients to undergo the procedure and to inform them about the risk–benefit ratio. Given the present results, it may be acceptable to start performing CPVA for ablation of symptomatic recurrent AF as an intervention of choice in the subgroup with a greater probability of success.

The results also highlight the need for aggressive treatment of hypertension to prevent AF, because the probability of restoring long-term sinus rhythm after AF ablation is smaller in these patients. In addition, it is not known whether certain antihypertensive drugs or well-controlled arterial pressure after CPVA may reduce AF recurrences, as has been demonstrated in primary and secondary prevention trials of AF.[22,23] Further studies are needed to clarify these points.

Study limitations

It is not possible for us to know the number of patients initially assessed for inclusion into the study because our institution is a reference centre and we ignore the number of screened patients. Thus, we do not know the proportion of ineligible AF patients for AF ablation, although the inclusion criteria are not highly restrictive.

Although variables like structural heart disease vs. normal heart did not show any predictive value for recurrence, it is possible that these conditions are underrepresented in this study population. Therefore, it is likely that they are also important factors to be taken into account. However, we have analysed only the most well-known clinical and echocardiographic predictors of new onset AF[4,18] or recurrent episodes after conversion to sinus rhythm.[13] Although other clinical variables may predict AF recurrence, the present results suggest that it would be appropriate to stratify the probability of success by means of these two simple variables.

Conclusions

Hypertension and LAD are strong predictors of AF recurrence after CPVA and may be useful in selecting the best candidates in whom to perform the procedure.

Acknowledgement

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Conflict of interest: none declared.

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Left Atrial Contractility is Preserved After Successful Circumferential Pulmonary Vein Ablation in Patients with Atrial Fibrillation

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Left Atrial Contractility. ***Introduction:*** **Circumferential pulmonary vein ablation (CPVA) for atrial fibrillation (AF) consists of creating extensive lesions in the left atrium (LA). The aim of the study was to evaluate changes in LA contractility after ablation and their relationship with procedure outcome.**

Methods and Results: **A series of 90 consecutive patients underwent cardiac magnetic resonance imaging (MRI) before and 4–6 months after CPVA. Only patients in sinus rhythm during both imaging acquisitions were included in the study to measure LA end-diastolic (LAmax) and LA end-systolic (LAmin) volumes. Fifty-five patients were finally analyzed (41 men, 52 ± 11 years, 74% paroxysmal AF). During a mean follow-up of 12 ± 7 months and after 1.2 ± 0.3 ablation procedures, 38 patients (69%) were arrhythmia-free (group I), and the remaining 17 patients had recurrences (group II). There was a significant decrease in mean LAmax volume in both groups, whereas mean LAmin volume only decreased in group I. Mean LA ejection fraction (EF) was preserved after CPVA in group I (40 ± 11% vs 38 ± 10%; $P = 0.27$) but decreased in patients with arrhythmia recurrences (37 ± 10% vs 27 ± 10%; $P < 0.001$). In fact, LA EF remained stable or increased in 68% of patients without arrhythmia recurrences.**

Conclusions: **LAmax volume reduction following CPVA occurs regardless of the clinical efficacy of the procedure, whereas mean LAmin volume only decreased in patients without recurrences. LA EF was preserved or even increased in most patients with successful CPVA.** *(J Cardiovasc Electrophysiol, Vol. pp. 1-6)*

atrial fibrillation, catheter ablation, atrial contractility

Although several studies have shown a decrease in left atrial (LA) size following atrial fibrillation (AF) ablation,[1-6] data on the response of atrial contractility are limited. A recent study in a small series found an impaired LA ejection fraction (LA EF) after paroxysmal AF catheter ablation.[7] LA EF reflects the relationship between atrial end-diastolic and end-systolic volumes, and has been proposed as a good method for evaluating global atrial contractility.[7-10] With regard to changes in LA volume after AF ablation, the data are contradictory. While some authors have reported that LA size decreases only after successful ablation,[1,3,6] others have suggested that LA size is reduced regardless of the clinical outcome of the procedure.[2,4,5] However, in the majority of these studies, LA end-diastolic (LAmax) and LA end-systolic (LAmin) volumes were not measured separately, and imaging acquisitions were performed regardless of whether the patients were in sinus rhythm or arrhythmia.

Current cardiac cine magnetic resonance imaging (MRI) techniques are accurate for depicting the anatomical structures of LA, allowing calculation of LA volumes with unusual precision.[11-15] The purpose of this study was to assess the effect of circumferential pulmonary vein ablation (CPVA) on LA volumes and LA EF, as well as their relationship with procedure outcome using cardiac MRI.

Methods

Patients

Cardiac MRI was performed before and 4–6 months after CPVA in a series of 90 consecutive patients with symptomatic, ≥2 drugs-refractory AF. No electrical cardioversion was performed for at least 2 weeks prior to the MRI study. A total of 55 patients were in sinus rhythm at the time of both imaging acquisitions and were included in this study. LAmax and LAmin volumes were measured and LA EF was calculated.

Paroxysmal AF was defined as AF that terminates spontaneously. Persistent AF was defined as AF lasting more than 7 days or requiring electrical cardioversion to be terminated. Patients with continuous AF in whom cardioversion had either failed or had not been attempted were classified as having permanent AF and were excluded from the study.

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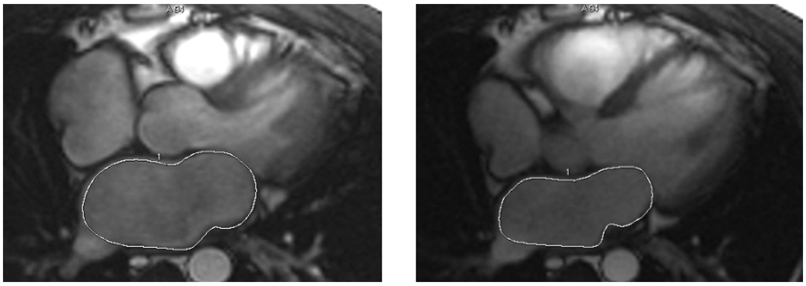

Figure 1. *In a gradient-echo sequence the boundaries of the left atrium at maximum dilation (left panel) and at maximum contraction (right panel) are manually drawn for each slice. Left atrial maximal and minimal volumes were both calculated by the disc-summation technique (Simpson's rule).*

The study population was divided into two groups: those arrhythmia-free after the ablation procedure (group I) and those with recurrences during follow-up (group II) beyond a one-month blanking period (see follow-up section). Patients were included after written informed consent was obtained. The protocol study was approved by the hospital's Ethics Committee.

Magnetic Resonance Imaging

Image acquisition

Cardiac MRI was performed using a 1.5 Tesla scanner (Signa Horizon CV, GE Medical Systems, Milwaukee WI, USA) using a dedicated cardiac phase-array coil. Image acquisition was gated by surface electrocardiogram during breath-hold at end-exhalation. Fast spoiled gradient-echo localizer scans were performed in sagittal and axial views. A segmented gradient-echo cine sequence (FIESTA) was then carried out in the axial plane to cover the entire heart. Sequence parameters were as follows: TE 1.6 ms, TR 3.7 ms, 45° flip angle, matrix size 256×256, field of view 360–440 mm, slice thickness 10 mm without gap, and 125 kHz receiver bandwidth. The time of acquisition varied according to the heart rate. A 3D magnetic resonance angiography in the axial plane was acquired following intravenous administration of a gadolinium-based contrast bolus at a dose of 0.75 mg/kg. The 3D angiographic and volume rendered data sets were registered with the electroanatomic maps to locate the pulmonary veins (PVs) and their connections to the LA and to assist with the ablation procedure.

Image analysis

LAmax volume was measured on the frame before mitral valve opening was identified and the LAmin volume was quantified on the first frame showing mitral valve closure. The inner contours of the LA were manually traced for all sequential axial cine images with digital markers excluding the PVs at their ostia and the LA appendage (LAA) (Fig. 1). The actual atrial volumes were calculated by disc summation (Simpson's rule). LA EF was then calculated as follows: (LAmax − LAmin/LAmax) ×100. Additionally, the contractility of the LAA was evaluated by calculating the LAA EF. For this purpose, LAA diastolic and systolic volumes were measured independently from the atrial region.

All data sets were analyzed by two independent radiologists blinded to clinical outcomes. A maximal discordance of 5% in the volume estimation was accepted. When a higher discordance was observed, measurements were repeated. Final measurements were recorded as the average of the two observations for all parameters.

Ablation Procedure

Conventional transthoracic echocardiography plus transesophageal echocardiography were performed prior to the ablation procedure in order to discard intracavitary thrombus. Continuous radiofrequency lesions were delivered after transseptal access as described elsewhere[16–18] surrounding each ipsilateral PV. Ablation lines were also deployed along LA roof, LA posterior wall, and mitral isthmus by a thermocouple-equipped 3.5 mm cooled tip catheter at a target temperature of 50°C and a maximum output from 35 to 40 W (Fig. 2). The endpoint of the ablation procedure was to reduce the amplitude of the local electrogram inside the surrounded area to below 0.15 mV. Ablation lines were created anatomically with the aid of a three-dimensional LA reconstruction performed by the CARTO (Biosense Webster) or NaVx (Endocardial Solutions) navigation systems. After circumferential lines were completed, the assessment of the electrogram abatement was performed in sinus rhythm (after cardioversion if needed) at several sites within the encircled antrum and inside each PV by the ablation catheter itself.

Follow-up

Patients were followed up as outpatients at 1, 4, and 7 months following the ablation procedure, and every six months thereafter if they remained asymptomatic. Routine 24- or 48-hour Holter monitoring was performed before each visit and patients were also asked to communicate any symptom suggestive of AF recurrence between scheduled visits.

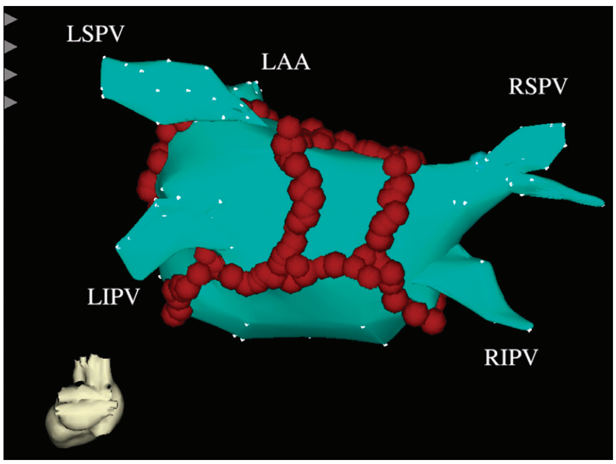

Figure 2. *Three-dimensional anatomical reconstruction of the left atrium (posteroanterior view) showing ablation scheme. Red dots represent radiofrequency delivery sites. LAA = left atrial appendage; PV = pulmonary vein; LSPV = left superior PV; LIPV = left inferior PV; RSPV = right superior PV; RIPV = right inferior PV.*

TABLE 1

Patient Characteristics

Age (years)	52.0 ± 11.3
Male gender	44 (80.0%)
Type of AF	
Paroxysmal	41 (74.5%)
Persistent	14 (25.5%)
Hypertension	12 (21.8%)
Structural heart disease	9 (16.3%)
LV DD (mm)	52.4 ± 4.7
LV SD (mm)	33.1 ± 3.8
LV EF (%)	60.0 ± 8.8
AF evolution time (years)	8.4 ± 8.1

All patients continued oral anticoagulation to maintain an international normalized ratio between 2.0 and 3.0 for a minimum of 2 months after ablation. All patients received antiarrhythmic drugs (flecainide in the absence of structural heart disease or amiodarone otherwise) at least during the first 4 weeks after the procedure in order to manage early recurrences. CPVA was considered successful if no arrhythmias were recorded during the follow-up after a 5-week blanking period without antiarrhythmic treatment or with the use of one previously ineffective drug. Minimum follow-up of this series was 6 months.

Statistical Analysis

Quantitative data are reported as mean ± SD. MRI measures before and after ablation between subjects were compared using a paired Student's *t*-test. The relationship between patient variables and the time to recurrence during follow-up was evaluated using survival analysis methodology (Cox regression models). Variables were included in the multivariate analysis using a forward 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. The analyses were performed using the SPSS 12.0 statistical package (SPSS, Chicago, IL, USA).

Results

From a series of 90 consecutive patients, 35 were excluded because they were not in sinus rhythm at the time of the first and/or second MRI studies. Therefore, a total of 55 patients were finally analyzed. Their baseline characteristics are summarized in Table 1.

Thirty-eight patients (69.1%) were arrhythmia-free (group I), whereas the remaining 17 patients had arrhythmia recurrences (group II) after 1.2 ± 0.3 ablation procedures and a mean follow up of 11.8 ± 7.2 months (15 patients with AF relapses and two patients with new-onset LA flutter). Among patients with successful ablation, 33 (60%) were without antiarrhythmic drug treatment, three patients received flecainide to manage symptomatic premature atrial contractions, and two patients were arrhythmia-free under either flecainide or amiodarone treatment that started during blanking period and was not stopped afterwards by the referring physician.

Table 2 shows the changes in LA measurements after CPVA according to procedure outcome. Figure 3 shows the same data for each patient in the series. Firstly, it can be observed that mean LAmax volume after CPVA decreased in both group I and group II; furthermore, no differences in the mean percentage of LAmax volume reduction were observed between the two groups (13 ± 12% vs 17 ± 14%, respectively, $P = 0.217$). Secondly, mean LAmin volume only decreased significantly in group I. Consequently, there were no significant changes in the mean LA EF after ablation in group I, whereas a decrease in the mean LA EF was seen in group II. In fact, LA EF remained stable or increased in 68% of patients without arrhythmia recurrences after CPVA (Fig. 4).

On the other hand, the contractility of the LAA showed no change after ablation. EF of the LAA before and after CPVA was similar in both group I (41 ± 20% vs 40 ± 20%, $P = 0.8$) and group II (31 ± 20% vs 32 ± 6%, $P = 0.9$). In group I, there was a reduction in LAA diastolic volume (from 8.8 ± 4.4 to 7.6 ± 4.4 mL, $P < 0.001$) and in LAA systolic volume (from 5.2 ± 4.2 to 4.3 ± 3.3 mL, $P < 0.001$) after ablation. In group II, there was a trend to LAA diastolic volume reduction (from 7.1 ± 3.4 to 6.2 ± 3.3 mL, $P = 0.08$), and no significant changes in LAA systolic volume (from 4.5 ± 2.1 to 4.1 ± 2.2 mL, $P = 0.11$) after ablation.

Univariate analysis showed that patients with recurrences after the ablation procedure had a higher proportion of hypertension, larger LA volumes (measured before and after CPVA) and lower postablation LA EF (Table 3). The only variable independently associated with arrhythmia recurrence in the multivariate model was the LAmin volume measured after the ablation procedure, with a hazard ratio of 1.04 (95% confidence interval, 1.02–1.06, $P < 0.001$). The best cut-off obtained by receiver operating characteristic (ROC) analysis for this variable (area under curve = 0.85) was LAmin volume ≥75 mL (sensitivity = 89%, specificity = 35%), which had a hazard ratio for arrhythmia recurrence of 11.5 (95% confidence interval, 3.8–34.5, $P < 0.001$).

Discussion

The main finding of this study is that LA contractility evaluated by means of LA EF is preserved or even increased

TABLE 2

Left Atrial Values Before and 4–6 Months After Ablation Procedure

	No Recurrences (n = 38)				Recurrences (n = 17)			
	Pre CPVA	Post CPVA	Mean Decrease	P-Value	Pre CPVA	Post CPVA	Mean Decrease	P-Value
LAmax (mL)	98.0 ± 19.9	84.9 ± 17.1	13%	<0.001*	126.2 ± 32.8	103.5 ± 28.1	17%	<0.001*
LAmin (mL)	58.6 ± 16.1	52.2 ± 12.1	10%	0.004*	78.4 ± 22.2	75.8 ± 24.3	4%	0.315
LA EF (%)	40.2 ± 11.5	38.1 ± 9.8	2%	0.268	37.4 ± 10.1	26.9 ± 10.2	11%	<0.001*

*Means P< 0.05.

LAmax = left atrial maximal volume; LAmin = left atrial minimal volume; LAEF = left atrial ejection fraction; pre/post CPVA = previous/posterior to circumferential pulmonary vein ablation.

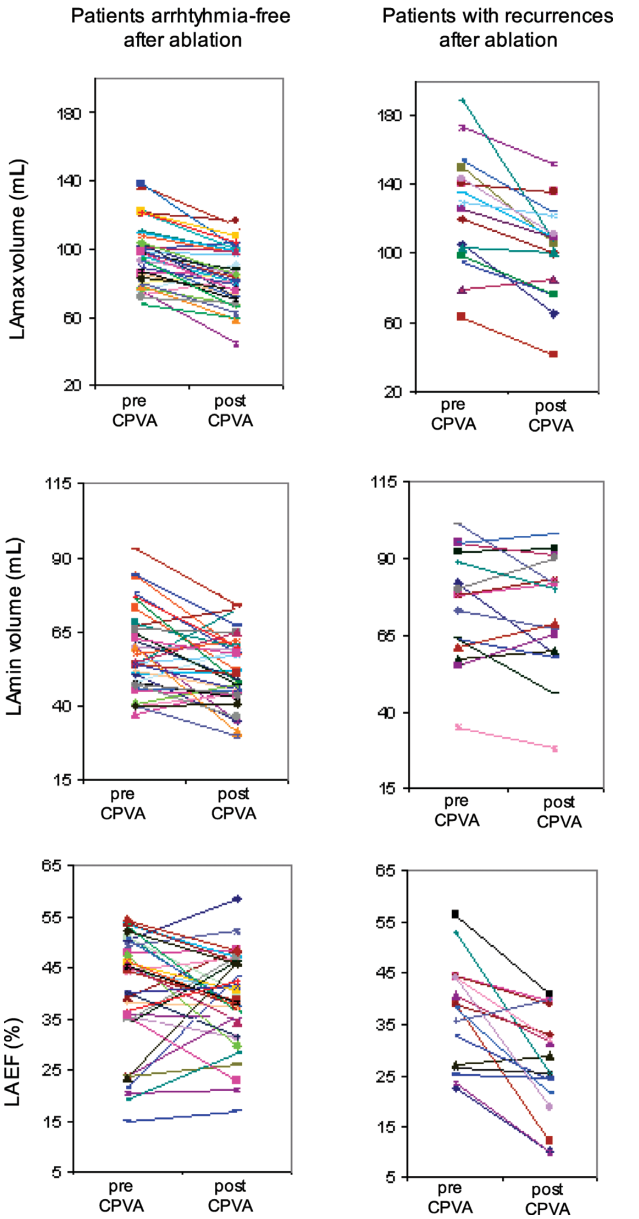

Figure 3. *Evolution of left atrial (LA) end-diastolic (LAmax) volume, LA end-systolic (LAmin) volume and LA ejection fraction (LA EF) 4-6 months after circumferential pulmonary vein ablation (CPVA) in each patient in the series. Data are shown depending on whether patients were arrhythmia-free (left panels) or had arrhythmia recurrences (right panels) during the follow-up.*

after CPVA in the majority of patients who had no arrhythmia recurrences after ablation. In fact, our data showed a similar reduction of LAmax volume in all patients, regardless of the ablation outcome, whereas mean LAmin volume only decreased in those showing a successful outcome of the procedure. Previous data regarding this issue have proven contradictory. Some investigators have reported that LA size after AF ablation decreased significantly only after a successful procedure, whereas LA size remained unchanged or even increased in the remaining patients.[1,3,6] In contrast, other investigators have found that LA size after AF ablation decreased in all patients regardless of the procedure outcome.[2,4,5]

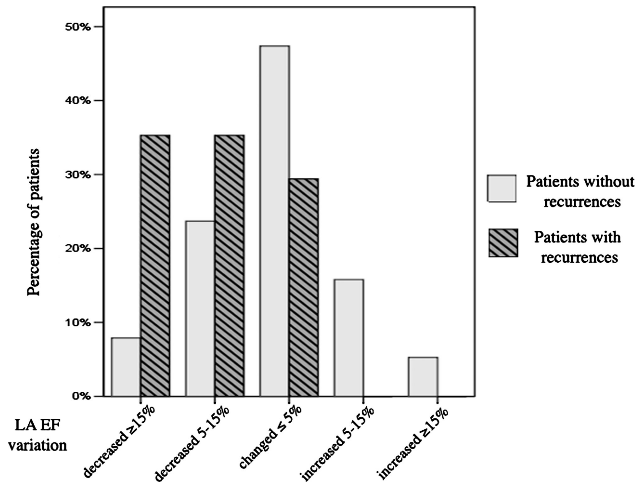

Figure 4. *Variation of left atrial ejection fraction (LA EF) following ablation procedure.*

There could be several reasons for these discrepancies. First, different image techniques were used: echocardiography,[1,4–6] magnetic resonance angiography,[2] or computed tomography.[3] Second, LA size was determined using different measures: LA anteroposterior diameter,[4,6] LA three orthogonal diameters,[1,2,5] or LA volume.[3] Third, with the exception of one reported study,[6] only the maximal atrial dimension was measured. Last, in the majority of these studies, the LA measurements did not take into account whether patients were in AF or not at the time of image acquisition.[2–4,6] This could interfere with a correct measurement of the LA volume variation after ablation. In fact, if one of the LA images was acquired during AF and the other in sinus rhythm, it may overestimate the variation of LAmin. In the present study, in order to calculate LA EF, LAmax, and LAmin volumes were determined separately. Therefore, only patients who were in

TABLE 3

Univariate Analysis Related to the Risk of Arrhythmia Recurrence

	Hazard Ratio (95% CI)	P-Value
Age (years)	1.021 (0.976–1.067)	0.366
Male gender	0.986 (0.281–3.461)	0.983
Paroxysmal AF	1.347 (0.468–3.881)	0.581
Hypertension	3.782 (1.396–10.246)	0.009*
Structural heart disease	2.078 (0.661–6.530)	0.211
Ablation procedures	1.132 (0.322–3.976)	0.847
Radiofrequency time (min)	1.000 (0.994–1.006)	0.955
LV DD (mm)	1.036 (0.876–1.226)	0.679
LV SD (mm)	1.098 (0.908–1.328)	0.336
LV EF (%)	0.972 (0.910–1.038)	0.390
MRI measurements		
Preablation LAmax (mL)	1.026 (1.011–1.042)	0.001*
Preablation LAmin (mL)	1.039 (1.017–1.062)	0.001*
Preablation LA EF (%)	0.978 (0.936–1.021)	0.303
Postablation LAmax (mL)	1.032 (1.009–1.056)	0.006*
Postablation LAmin (mL)	1.044 (1.023–1.065)	<0.001*
Postablation LA EF (%)	0.924 (0.883–0.968)	0.001*

* $P < 0.05$.
LVDD = left ventricular diastolic diameter; LVSD = left ventricular systolic diameter; LV EF = left ventricular ejection fraction. (Measurements performed by echocardiography prior to ablation.)
MRI = magnetic resonance imaging; LAmax = left atrial maximal volume; LAmin = left atrial minimal volume; LA EF = left atrial ejection fraction.

sinus rhythm at both assessments were included to ensure optimal measurements, and no electrical cardioversion was performed during the 2 weeks preceding the MRI in order to avoid "stunning" of the atrial mechanical function.[19] Furthermore, cardiac-gated cine MRI and the disc-summation technique (Simpson's rule) were used to measure both LA volumes to avoid geometric assumptions, image plane positioning errors, and inappropriate sampling of the atrial boundaries.[20-22] It is conceivable that all these methodological limitations could explain the observed discrepancies in the literature.

To our knowledge, two recent studies have analyzed LA EF after AF ablation, showing contradictory data.[7,23] Verma *et al*. reported a improvement in atrial function in a series of 67 patients evaluated by either echocardiography or cine electron beam CT, whereas Lemola *et al*. suggested a deterioration of atrial contractility in a series of 10 paroxysmal AF patients evaluated by 3D CT. However, the authors compared contractility regardless of the success of the procedure. According to our data, LA EF after ablation generally worsened in patients with recurrences. In fact, whereas LAmax volume reduction occurred in almost all patients, mean LAmin volume only decreased in patients without recurrences. Moreover, LAmin volume after CPVA was the only independent variable related to procedure success in the multivariate analysis. Most patients with a successful ablation showed a decrease in both LAmax and LAmin volumes and preserved contractility. Whether the LAmin volume reduction in these cases occurred immediately after ablation due to tissue shrinking as a result of the radiofrequency delivery,[24] or if it was subsequent to a mid-term reverse remodeling secondary to the maintenance of stable sinus rhythm,[25] remains inconclusive in the present study. Another hypothesis that may be taken into account is that the PVs isolation may lead to loss of their contractile capability, and this could cause blood regurgitation from the LA through the PVs during atrial systole. This fact might result in a decrease in atrial systolic volume and an improvement in LA ejection fraction. More data are required to elucidate whether the LAmin decrease was a cause or a consequence of the outcome of the procedure.

Finally, LAA contractility was not compromised after CPVA in any patient of this series. Changes in LAA volumes were in accordance with those observed in the whole LA, although to a lesser extent. This could be due to the fact that RF energy is deployed out of the LAA and the effect of tissue shrinkage may be lower. However, there are methodological limitations in the measurement of volumes in such a small structure. As a consequence, a broader population would be needed to study these subtle differences on detail.

Study Limitations

The impossibility of accurately measuring the AF burden at each time point[25] could partly affect the evaluation of LA contractility. This is a limitation in this type of study, since asymptomatic AF episodes could be misinterpreted unless continuous monitoring of the patient was performed.

In the present study, certain details of the imaging technique should be noted. First, image acquisition was carried out at end-exhalation. Imaging during inspiration may have produced different results related to changes in diastolic relaxation properties and preload conditions. Second, end-systole and end-diastole were defined using direct visualization of mitral valve opening and closure, since electrocardiogram co-registration is not available for MRI image post processing. Finally, PV ostium was defined at the point of inflection between PV and LA wall. This simplification was used to facilitate identification and promote interobserver reproducibility. However, these limitations are unlikely to have had a significant effect on the results of the study since both basal and follow-up measurements were performed in the same manner, and LA variations between subjects may reflect real changes.

On the other hand, the effect of radiofrequency may be more significant in those patients who underwent two ablations, since changes in LA contractility were evaluated in the MRI obtained after the second procedure. However, results in these 10 patients were consistent with those observed in the remaining cases. In fact, LA EF showed no significant changes with respect to the basal measurement in arrhythmia-free patients after the second ablation (from 35 $\pm$ 11% to 32 $\pm$ 7%, $P = 0.50$), whereas LA EF decreased considerably in the remaining patients suffering arrhythmia recurrences in spite of the two procedures (from 28 $\pm$ 9% to 10 $\pm$ 2%, $P = 0.06$). Furthermore, in seven of the 10 second procedures, the amount of radiofrequency delivery was low because only new-onset LA flutter was ablated and no extensive lesions were created.

Finally, it should be considered that the results of this study may vary depending on the ablation approach. However, the effect on LA contractility is unlikely to be greater in other ablation procedures, taking into account the extensive lesions created in CPVA.

Conclusions

LAmax volume reduction after CPVA occurs regardless of the clinical efficacy of the procedure, whereas LAmin volume decreased only in patients free of arrhythmia recurrences. LA EF was preserved or even increased in the majority of patients after successful CPVA.

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AQ: 1

Left Atrial Posterior Wall Isolation Does Not Improve the Outcome of Circumferential Pulmonary Vein Ablation for Atrial Fibrillation

A Prospective Randomized Study

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AQ: 2

P1-foo

Background—Ablation of the pulmonary veins (PVs) for atrial fibrillation treatment is often combined with linear radiofrequency lesions along the left atrium (LA) to improve the success rate. The study was designed to assess the contribution of LA posterior wall isolation to the outcome of circumferential pulmonary vein ablation (CPVA).

Methods and Results—CPVA consisted of continuous radiofrequency lesions encircling both ipsilateral PVs plus an ablation line along the mitral isthmus. Patients were then randomized into 2 groups. In the first group, superior PVs were connected by linear lesions along the LA roof (CPVA-1 group). In the second group, the LA posterior wall was isolated by adding a second line connecting the inferior aspect of the 2 inferior PVs (CPVA-2 group). The study included 120 patients (53±11 years, 77% male, 60% paroxysmal atrial fibrillation, LA of 41.3±5.4 mm, 46% with hypertension, and 22% with structural heart disease). After a single ablation procedure and a mean follow-up of 10±4 months, 24 (40%) patients of the CPVA-1 group had atrial fibrillation recurrences and 3 (5%) had new-onset LA flutter. In the CPVA-2 group, recurrences were due to atrial fibrillation episodes in 23 patients (38%) and LA flutter in 4 (7%). Freedom from arrhythmia recurrences was not statistically different in the CPVA-1 group as compared with the CPVA-2 group (log rank $P=0.943$).

Conclusion—Isolation of the LA posterior wall did not increase the success rate of CPVA. **(*Circ Arrhythmia Electrophysiol*. 2009;2:00-00.)**

Key Words: arrhythmia ■ catheter ablation ■ atrium

AQ: 3

Because the initial description of paroxysmal atrial fibrillation (AF) triggered by pulmonary vein (PV) firing,[1] several approaches to catheter ablation have been developed to treat AF. At present, PV isolation is performed in almost all AF ablation procedures.[2–4] Deployment of linear lesions along the left atrium (LA) in addition to PV ablation has been shown to improve the success rate.[5–7] The most commonly performed procedure involves ablation of the mitral isthmus and connection of the superior contralateral PVs through the LA roof.[8,9] Other authors have suggested a lesion set in which the LA posterior wall is also excluded by connecting superior and inferior contralateral PVs along 2 ablation lines.[6,10–12] However, there are no data comparing the 2 approaches.

Clinical Perspective see p ●●●

The aim of this prospective randomized study was to evaluate whether isolation of the LA posterior wall decreased arrhythmia recurrence risk after circumferential pulmonary vein ablation (CPVA).

Methods

The study included 120 consecutive patients undergoing a first catheter ablation for symptomatic, drug-refractory (≥2 antiarrhythmics) AF, classified as paroxysmal, persistent, or long-standing, according to HRS/EHRA/ECAS consensus.[13] No patient refused to give consent and no patient was lost to follow-up. The study protocol was approved by the hospital's ethics committee. The authors take responsibility for the integrity of the data. All the authors have read and agreed to the manuscript as written. AQ: 4

All patients underwent transesophageal echocardiography 1 to 5 days before ablation to exclude the presence of intracavitary thrombus. A transthoracic echocardiogram and a gadolinium-enhanced magnetic resonance angiogram were also obtained before the procedure.

After trans-septal access, a bolus of intravenous heparin (5000 IU) was administered, with an additional bolus to maintain an activated clotting time of >250 seconds. The procedure was performed under deep sedation. Ablation was assisted by a 3D map of the LA and its adjacent structures, produced with CARTO (Biosense Webster) or NavX (St Jude Medical) systems. Magnetic resonance angiogram images were integrated into the navigation system to support the LA anatomic reconstruction. Radiofrequency was delivered by a

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AQ: 8

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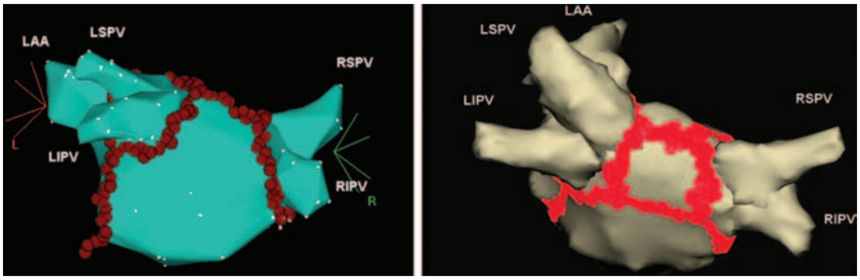

Figure 1. Anatomic reconstruction of the LA showing ablation scheme of CPVA-1 (left panel) and CPVA-2 (right panel) groups. Red dots represent sites of radiofrequency delivery. LAA indicates LA appendage; LSPV, left superior PV; LIPV, left inferior PV; RSPV, right superior PV; RIPV, Right inferior PV.

thermocouple-equipped 3.5-mm cooled-tip catheter at a target temperature of 48°C and a maximum output of 40 W.

Patients were randomized into 2 ablation groups. In both, continuous radiofrequency lesions surrounding each ipsilateral PV antrum were deployed until the local electrogram inside the encircled area disappeared or was dissociated or, when this was not possible, until the bipolar voltage amplitude dropped to <0.15 mV; electric block was confirmed by the inability to conduct to the LA after pacing at several sites within the PV antrum.[2,14] PV antrum was defined as the anatomic transition between LA and PV structures and was mainly identified by 3-dimensional reconstruction. Mitral isthmus ablation was also performed in all patients by creating a radiofrequency line from the inferior-lateral aspect of the left PV lesions to the mitral annulus. Then, in the first group (CPVA-1), a radiofrequency line was created connecting contralateral PV-encircling lesions through the LA roof. In the second group (CPVA-2), the LA posterior wall was excluded by adding a second ablation line connecting the inferior aspect of the 2 inferior PVs. In both groups, separated local double potentials or potential disappearance all along the LA roof ablation line was used as the criterion to define electric block.[6] In the CPVA-2 group, after completion of the roof line, the infero-posterior line was deployed until the absence or dissociation of local electrogram inside the excluded LA posterior region was observed; isolation was confirmed by the inability to conduct to the remaining atria after pacing at several sites within the surrounded LA posterior region with the ablation catheter, observing the local capture in the
F1 proximal bipole of the pacing catheter when possible[10] (Figure 1).

Each end point of the ablation procedure was assessed in sinus rhythm, performing electric cardioversion if necessary.

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 if they remained asymptomatic. Routine 48-hour Holter monitoring was performed before each visit. Patients were also asked to come to the emergency department if any symptom suggestive of recurrence occurred between scheduled visits. All patients continued oral anticoagulation to maintain an international normalized ratio between 2.0 and 3.0 for a minimum of 2 months after ablation. All patients received antiarrhythmic medication for a minimum of 1 month after the procedure to decrease early recurrences (flecainide if no structural heart disease was diagnosed or amiodarone if there was evidence of structural heart disease). Ablation was considered successful in those patients with no AF recurrences or LA flutter after a blanking period of 3 months. Minimum follow-up of this series was 6 months.

Statistical Analysis

The primary end point of the study was freedom from arrhythmia recurrence after a single ablation procedure. On the basis of our own experience, at 6-month follow-up, 55% of patients were expected to be free of arrhythmia after a single CPVA-2 procedure. With a sample size of 60 patients per arm, a log-rank test for equality of survival curves will have 80% power and a 2-sided α value of 0.05 to detect an expected 20% reduction in freedom from arrhythmia in the CPVA-1 group. Subjects were included during the first 18 months of the 24-month study, with no loss to follow-up expected.

Randomization was performed according to a computer-generated algorithm in blocks of 20 patients. The ablation group was blinded to patients and to the physicians evaluating the outcome of the procedure.

Data are reported as mean±SD. Comparisons between groups were performed using Student *t* test or χ^2 analysis. Arrhythmia-free survival curves for each group were presented as Kaplan–Meier plots and compared by log-rank test.

Cox method was used to estimate the effect of LA posterior wall isolation after adjusting for baseline variables. The following potential predictors of recurrence were considered: age, sex, type and duration of AF, LA diameter, left ventricular end-diastolic and end-systolic diameters, left ventricular ejection fraction, hypertension, and structural heart disease. Stepwise method with criteria of $P \leq 0.05$ for inclusion and $P \geq 0.10$ for removal was used to select the covariates and report the estimates from the model that included those covariates and the variable isolation (or not) of the LA posterior wall.

A 2-sided probability value ≤0.05 was considered statistically significant. Analyses were performed using SPSS 12.0 (SPSS Inc) and Stata 9 (Stata Corp) statistical packages.

Results

The study included 120 consecutive patients; baseline characteristics are shown in Table 1. No significant baseline T1, AQ:5
differences were observed between the groups. Procedure details are given in Table 2. End points of the procedure were T2
confirmed using previously described criteria in 54 and 55 patients of the CPVA-1 and CPVA-2 groups, respectively (90% versus 92%; $P=0.75$).

Table 1. Patient Characteristics

	CPVA-1 Group	CPVA-2 Group	*P*
Patients	60	60	
Type of AF			0.75
Paroxysmal	37 (62)	35 (58)	
Persistent	11 (18)	13 (22)	
Long-standing	12 (20)	12 (20)	
Age, years	52.5±10.9	52.9±10.8	0.83
Male sex	44 (73)	48 (80)	0.20
Duration of AF, months	60.8±55.7	67.1±48.2	0.58
LA diameter, mm	41.1±5.0	41.6±5.9	0.65
LV end-diastolic diameter, mm	52.7±4.1	52.5±5.4	0.80
LV end-systolic diameter, mm	32.8±4.8	34.4±7.1	0.25
LV ejection fraction, %	59.8±9.8	59.5±10.1	0.88
Hypertension	26 (43)	29 (48)	0.58
Structural heart disease	13 (22)	13 (22)	1.00

Data are presented as n (%) or mean±SD.

Table 2. Procedural Details

	CPVA-1 Group	CPVA-2 Group	*P*
Patients	60	60	
Procedural time, minutes	14.3±23.4	120.9±37.7	0.10
Fluoroscopic time, minutes	23.2±7.8	22.6±8.3	0.60
Radiofrequency time, minutes	39.2±7.7	42.5±9.2	0.25
Complications	3 (5.0)	2 (3.3)	0.65
Transient cerebrovascular ischemia	2	1	
Transient inferior myocardial ischemia	1	1	

Data are presented as n (%) or mean±SD.

After a mean follow-up of 9.8±4.3 months, 33 patients (55%) in both groups had no arrhythmia recurrences after a single ablation procedure (log-rank test $P=0.943$). The success rate was higher in paroxysmal AF than in persistent/long-standing AF, but no statistical differences were observed in arrhythmia recurrences between those with or without LA
F2 posterior wall isolation (Figure 2). Among patients with no recurrences, 28 CPVA-1 and 27 CPVA-2 patients (47% and 45%, respectively) were not treated with antiarrhythmics (log-rank test $P=0.908$), and 5 CPVA-1 and 6 CPVA-2 patients were taking 1 antiarrhythmic drug: in 3 and 4 patients, respectively, the antiarrhythmic was not withdrawn during the blanking period due to early recurrences, but they had no arrhythmias after the 3-month blanking period, and 2 patients of each group took flecainide due to symptomatic premature atrial beats, but they had no sustained episodes.

In the CPVA-1 group, recurrences were due to AF episodes in 24 patients (40%) and to LA flutter in 3 (5%). In the CPVA-2 group, 23 patients (38%) had AF recurrences, and 4 (7%) had new-onset LA flutter.

Cox regression indicated that the baseline LA diameter was the only covariate significantly associated with arrhythmia recurrence (hazard ratio, 1.078 [95% CI, 1.011 to 1.148]; $P=0.021$). The adjusted hazard ratio obtained for the variable isolation of the LA posterior wall was consistent with the log rank test result (hazard ratio, 0.893 [95% CI, 0.581 to 1.549]; $P=0.722$).

Complications

There were no differences between the groups in the number of procedural complications (Table 2). Two CPVA-1 patients and 1 CPVA-2 patient experienceed a transient cerebrovascular ischemia, which was resolved under heparin with normal computed tomography scanning. One patient in each group showed transient inferior myocardial ischemia, probably related to catheter manipulation during trans-septal catheterization because of air embolism; the ischemia was re-

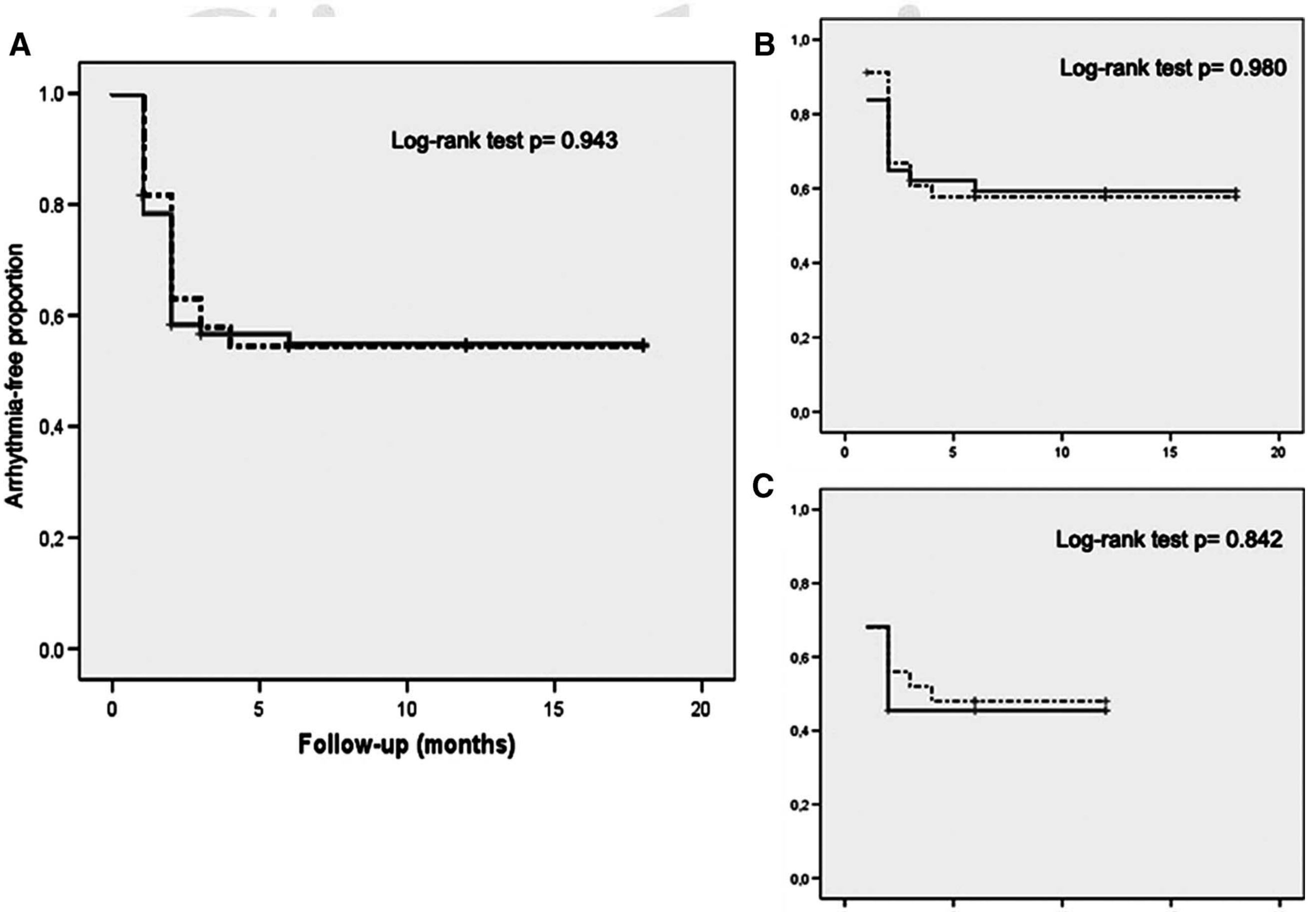

Figure 2. Accumulated arrhythmia recurrence survival after a single ablation procedure in (A) whole series, (B) subgroup of paroxysmal AF patients, and (C) subgroup of persistent or long-standing AF patients. Solid and dotted lines represent CPVA-1 and CPVA-2 groups, respectively.

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solved with sublingual *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine within a few minutes, without consequences.

In addition, 1 CPVA-1 and 2 CPVA-2 patients had post-procedural pericarditis that required nonsteroidal antiinflammatory treatment. Magnetic resonance angiogram performed before and 4 months after ablation in all patients of this series did not reveal any severe (>70%) PV stenosis[15]; one patient of the CPVA-2 group showed a left superior PV narrowing of 55%.

Second Ablation Procedures

The ablation procedure was repeated in 25 (20.8%) patients. Overall, after a mean of 1.2±0.4 ablation procedures; 67.7% of the patients of this series remained arrhythmia-free.

In 4 patients, the ablation was repeated due to new-onset LA flutter. In all 4 cases, an activation map produced by the navigation system plus entrainment maneuvers showed that the reentry was established between gaps of the previous right- or left-sided encircling lesions.

In the remaining 21 patients, the second procedure was performed due to AF recurrences. The previous ablation set was evaluated and radiofrequency was delivered in sites showing conduction gaps. Recurrent electric conduction in a mean of 3.1±0.9 PV per patient was found in 17 of the 21 patients (84%), whereas all PV remained isolated in 4 patients. Conduction across the LA roof line and electric activity within the LA posterior wall was observed in 69% and 67% of the CPVA-1 and CPVA-2 patients, respectively. In 1 CPVA-2 patient, extensive fibrosis was observed along both atria, without electric activity in the previously isolated areas; no further ablation was performed and it was decided to leave the patient in permanent AF.

Discussion

The main finding of this study is that electric isolation of the LA posterior wall did not increase the success of CPVA. Deployment of linear lesions along the LA roof, mitral isthmus or both locations has been shown to improve the outcome of PV ablation.[5,7,9] Moreover, some authors advocate a lesion set in which the LA posterior wall is also excluded by connecting the superior and inferior contralateral PVs through both ablation lines.[6,10–12] However, the number and location of linear lesions that will obtain the best results has not been well established. Several surgical methods were originally used to treat AF with a predefined set of linear
AQ: 6 lesions,[16–20] based on the multiple wavelet hypothesis[21] and the idea that sustained AF requires a critical amount of contiguous atrial tissue. At present, the main mechanism leading to AF is not clearly defined. PV firing has been considered as a main trigger of paroxysmal AF, and larger LA regions may act as the AF substrate in more persistent AF. In this regard, extensive LA ablation has been included in many of the current AF catheter procedures.

The role of the LA posterior wall in triggering and driving fibrillation has been suggested by both human and animal studies.[22–30] However, in the present series, exclusion of the LA posterior wall had no effect on the incidence of AF recurrences after CPVA. It should be noted that a larger area of posterior venous-atrial tissue was excluded when PV encirclement was performed in this study as compared with procedures in which PVs are ablated at their ostia.[31] A recent study suggested that large PV ablation circles increase the success rate of the procedure.[32] It is thus possible that the AF substrate of the LA posterior wall is mainly located within the lesions around the PV antrum and no further ablation is required.

Our results also showed no difference between the CPVA-1 and CPVA-2 groups in terms of the risk of LA flutter. The incidence of new-onset LA flutter has been described after AF ablation procedures, in which gaps along large lesions may create an ideal substrate for reentrant circuits.[33] Pappone et al demonstrated that mitral isthmus ablation plus the addition of 2 posterior linear lesions reduced the risk of developing this arrhythmia after CPVA.[6] In the present study, the deployment of 2 ablation lines connecting left and right sided PVs showed no benefit in preventing LA flutter, compared to creating a single roof line. In all procedures performed to treat LA flutter after the index ablation, a re-entrant circuit through gaps in the prior PV-encircling lesions was observed, in accordance with other series.[34] It is known that the continuity of linear lesions around ipsilateral PVs is difficult to achieve, especially at the PV septal aspect and the region between the LA appendage and the left superior PV.[35]

To our knowledge, this is the first study to demonstrate that the performance of LA posterior wall isolation does not improve the outcome of CPVA. Although the total time of radiofrequency delivery did not increase significantly when the ablation line was added along the LA posterior-inferior wall, there is a major potential risk of lesion to the esophagus, because it is virtually in contact with this region.[36] Moreover, isolation of the posterior LA region could theoretically impair atrial function. Therefore, according to the results of this study, we conclude that the electric exclusion of the LA posterior wall is not necessary when performing CPVA as a predefined lesion set to treat AF.

Study Limitations

The study was planned to detect an absolute reduction of 20% in the proportion of freedom from arrhythmia. However, the same number of patients was arrhythmia free in both groups, and consequently, the result from the formal comparison is far from the 5% significance level and the adjusted hazard ratio for arrhythmia recurrence was close to 1. Therefore, the lack of statistical significance may not be attributable to low statistical power.

The effect of LA posterior wall isolation was evaluated as part of a predefined lesion set performed in all patients. Therefore, the study cannot exclude that the isolation of the LA posterior wall may have some effect in individual AF cases. Recently, individualized approaches for AF ablation have been proposed,[37–39] but the criteria to preselect the ablation method in each patient or the end point for a tailored procedure are still under investigation.

Mitral isthmus ablation was performed anatomically without demonstrating electric block.[7] This may theoretically create a proarrhythmic substrate because of the effect of incomplete linear lesions, although no peri-mitral re-entry was observed in any patient submitted to a second procedure. Additionally, PV isolation was not assessed by circular catheter mapping, as originally described by Haissaguerre et al. In any case, ablation technique was the same in both groups except for the performance of the infero-posterior ablation line, and probably did not affect the conclusions of the study.

Because no additional catheter was placed at the LA, the achievement of local capture during pacing maneuvers was often difficult to demonstrate because it was assessed by the proximal pair recording of the ablation catheter[10] (while pacing through the distal). However, in these cases, the absence of local electrogram or dissociation from the remaining atria should be a reasonable surrogate marker of the LA posterior wall isolation.[6]

Finally, with the available follow-up limited to routine 48 hour-Holter monitoring and ECG recording when symptoms occurred between scheduled visits, arrhythmia recurrences may have escaped detection in asymptomatic patients. However, this was a pragmatic approach that obtained a reasonable follow-up in light of other published studies[5,7,10,12,32,40–42]; moreover, this limitation should have occurred equally in both ablation groups and therefore would not affect the conclusions of the study.

Conclusion

Isolation of the LA posterior wall did not offer additional benefit over a single roof line lesion with respect to the risk of arrhythmia recurrence after CPVA.

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AQ: 7

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Disclosures

None.

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CLINICAL PERSPECTIVE

Since the initial description of extensive atrial lesions performed by surgical procedures, there has been a continuous search for the appropriate amount of ablation to cure atrial fibrillation. In addition to the ablation of pulmonary veins, isolation of the left atrial (LA) posterior wall has been used in several surgical and catheter-based approaches, because it has been suggested that this region may play an important role in triggering and maintaining atrial fibrillation. However, isolation of the LA posterior wall could theoretically impair atrial function and may increase the potential risk of esophageal damage. The present study was designed to analyze whether isolation of the LA posterior wall increased the efficacy of circumferential pulmonary vein ablation as compared with the creation of a single LA roof ablation line. Our results showed that isolation of the LA posterior wall did not decrease the probability of atrial fibrillation nor atrial flutter recurrences. Therefore, atrial fibrillation ablation should not systematically include isolation of the LA posterior wall.

Circumferential Pulmonary Vein Ablation: does the use of a Circular Mapping Catheter improve results? Results from a Prospective Randomized Study

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ABSTRACT

INTRODUCTION

Circumferential pulmonary vein ablation (CPVA) creates continuous lesions surrounding both ipsilateral pulmonary veins (PV) out of their ostia. We hypothesized that assessment of PV antrum isolation using a circular mapping (CM) catheter could improve the outcome of the procedure as compared to use of a single catheter in the left atria (LA) both to ablate and map the electrical signal.

METHODS and RESULTS

A series of 146 consecutive patients (83% males, 53±10 years, 53% paroxysmal AF) were randomized to two ablation strategies. In both, ipsilateral PV encirclement until disappearance or dissociation of the local electrogram within the surrounded area was performed by an irrigated tip catheter. In the first group, only the radiofrequency catheter was used, both to map and ablate (CPVA group, n=73). In the other group, a CM catheter was added to assess the electrical activity of the PV antrum (CPVA-CM group, n=73). In addition, ablation line along the LA roof was created in all patients. Procedure and fluoroscopic times were longer in the CPVA-CM group ($p<0.05$). Severe procedure-related complications occurred in 1 (1.4%) and 3 (4.1%) patients in the CPVA and CPVA-CM groups, respectively ($p=0.317$). Procedural efficacy was lower in the CPVA group as compared to the CPVA-CM: after a mean follow-up of 9±3 months, 31 (42.5%) and 47 (64.4%) patients, respectively, were arrhythmia-free without antiarrhythmic medication ($p=0.008$).

CONCLUSIONS

The use of a CM catheter to ensure the isolation of PV antrum improved the success of the CPVA although it increased some procedural requirements.

Key words: atrial fibrillation, pulmonary veins, radiofrequency catheter ablation

INTRODUCTION

Since the initial description of pulmonary veins (PV) as triggers of atrial fibrillation (AF)[1], PV ablation has become the basis of most AF ablation procedures[2]. Segmental ostial ablation was developed to isolate each individual PV[3]; alternatively, circumferential PV ablation (CPVA) was proposed as an effective AF ablation procedure[4]. Although previous studies comparing these approaches obtained contradictory data[5;6], isolation of large areas around the PV seems to prevent AF recurrences more effectively than ostial ablation[7]. At present, some laboratories perform PV antrum encirclement using one single catheter in the left atria (LA) to both map and ablate [8-10] whereas others advocate for adding one or more circular mapping (CM) catheters either to demonstrate the isolation of the encircled region[7;11;12] or to perform PV ostial ablation after PV encirclement[13]. The addition of catheters in the LA may increase the cost and technical complexity of the procedure as well as the risk of complications. The additional benefit of using a CM catheter to demonstrate the isolation of PV antrum in CPVA had not previously been assessed in a single randomized study.

We hypothesized that using a CM catheter to assess the PV antrum isolation would improve the outcome of the CPVA as compared to use of a single LA catheter.

METHODS

The study included consecutive patients undergoing a first catheter ablation for symptomatic, drug-refractory (≥2 antiarrhythmics) AF classified as paroxysmal, persistent or long-standing, according to HRS/EHRA/ECAS consensus[2]. The study protocol was approved by the hospital's Ethics Committee.

All patients underwent a transoesophageal echocardiography 1 to 5 days before ablation to exclude the presence of intracavitary thrombus. Transthoracic echocardiography and gadolinium-enhanced magnetic resonance angiography (MRA) were also performed before the procedure.

A bolus of intravenous heparin (from 5000 to 6000 IU, according to patient weight) was administered after trans-septal access, followed by additional boluses to maintain an activated clotting time >250 s. The procedure was performed under deep sedation. Ablation was assisted by a three-dimensional map of the LA and its adjacent structures, produced with CARTO (Biosense Webster) or NavX (St Jude Medical) systems. MRA images were integrated into the navigation system to improve the LA anatomical reconstruction. Radiofrequency was delivered by a thermocouple-equipped 3.5 mm or 4 mm cooled tip catheter (NaviStar, Biosense Webster, or Therapy Cool Path, St Jude Medical) at a target temperature of 48ºC and a maximum output of 40 W.

Patients were randomized into two ablation groups. In both, continuous radiofrequency lesions surrounding each ipsilateral PV antrum were deployed. PV antrum was defined as the anatomical transition between LA and PV structures and was mainly identified by three-dimensional imaging. Radiofrequency line was also delivered along the carina between the superior and inferior PV of each side in the case of separate PV ostia[14]. The end-point was the absence (<0.10 mV) or dissociation of local electrogram inside the entire surrounded region.

In the first ablation group (CPVA), a single LA catheter was used for both mapping and ablation. After PV encirclement was completed, disappearance or dissociation of the electrical activity was assessed by mapping several sites within the surrounded region with the distal dipole of the ablation catheter. If electrical activity persisted, the radiofrequency catheter was then carefully moved all along the previously performed encircling lesions to look for conduction gaps and ablate when appropriate [15;16], until disappearance or dissociation of local electrogram inside the surrounded region was achieved, as documented by the ablation catheter recording.

In the second ablation group (CPVA-CM), a CM catheter (Lasso, Biosense Webster, or Inquiry Optima, St Jude Medical) was also advanced into the LA through trans-septal access. The CM catheter was entered into a PV and pulled back as close as possible to the ablation line, adjusting the catheter diameter to the PV antrum if a variable CM catheter was used. Disappearance or dissociation of the electrical activity within the surrounded region subsequent to PV encirclement was assessed by the 10 dipoles of the CM catheter. If electrical activity persisted, conduction gaps of the previously performed encircling lesions were checked with the guidance of the CM catheter: the region of the ablation line closest to the site of the CM catheter with the earliest potential was evaluated and re-ablated when appropriate, until the disappearance or dissociation of local electrogram inside the surrounded area was achieved as documented by the CM catheter (Figure 1).

In addition, a radiofrequency line was created in all patients connecting contra-lateral PV-encircling lesions through the LA roof. The criterion defining electrical block was separated local double potentials and/or potential disappearance all along the LA roof ablation line[10].

Each end-point of the ablation procedure was assessed in sinus rhythm, performing electrical cardioversion if necessary.

Follow-up

Patients were followed up at the outpatient clinic at 1, 3 and 6 months after the ablation procedure and every 6 months thereafter if they remained asymptomatic. Routine 48-h Holter monitoring was performed before each visit. Patients received instructions to regularly assess their cardiac pulse, had detailed information to contact our centre, and were asked to come to the emergency department if any symptom suggestive of recurrence occurred between scheduled visits. All patients continued oral anticoagulation to maintain an international normalized ratio between 2.0 and 3.0 for a minimum of two months after ablation. Patients received antiarrhythmic medication for a minimum of 1 month after the procedure to decrease early recurrences (flecainide if no structural heart disease was diagnosed or amiodarone if there was evidence of structural heart disease). Ablation was considered successful in those patients with no AF recurrences or LA flutter after a blanking period of 3 months. Minimum follow-up of this series was 6 months.

Statistical analysis

The primary end-point of the study was freedom from arrhythmia recurrence beyond the blanking period and after a single ablation procedure without antiarrhythmic treatment. The secondary end-point was freedom from arrhythmia recurrence beyond the blanking period and after a single ablation procedure with the use of ≤1 previously ineffective antiarrhythmic drug.

Based on our own experience, a 45% proportion of arrhythmia freedom without antiarrhythmic medication after one single CPVA procedure was expected at 6 months follow-up. With a sample size of 73 patients per arm, a log-rank test for equality of survival curves will have a 80% power to detect an expected increase of 18% in the proportion of the CPVA-CM patients who were arrhythmia-free with a two-sided alpha value of 0.05[17]. Subjects were included during the first 12 months of the 18-month study, with no loss to follow-up expected.

Once a patient was included in the study and informed consent was obtained, the patient was randomly assigned to one ablation group by a computer-generated randomization scheme in permuted blocks of four, in equal proportions. The patient group was blinded both to physicians enrolling participants and to those performing the follow-up. Data were analysed on an intention-to-treat basis.

Quantitative results are reported as mean±SD or median [Q1-Q3], comparing both study groups using the Student's *t* test or Mann-Whitney *U* test as appropriate. The relationship between a categorical variable and the study group was evaluated using the χ^2 test or the Fisher's exact method. Arrhythmia-free survival curves for each group were presented as Kaplan-Meier plots and compared by log-rank test. Cox regression analysis was used to determine the predictors of arrhythmia recurrence (primary end-point), using backward stepwise selection with criteria of $p \leq 0.05$ for inclusion and $p \geq 0.10$ for removal from the model, including as covariates those baseline and procedural related variables depicted in Table 3. A two-sided p value ≤0.05 was considered statistically significant. Analyses were performed using the SPSS 12.0 statistical package (SPSS Inc., Chicago, Illinois).

RESULTS

Patients

Among 149 patients suitable for inclusion, 146 consented to participate: 73 were assigned to CPVA group and 73 to CPVA-CM.

No patient was lost to follow-up. Baseline characteristics of both groups are listed in Table 1.

Procedural details

In the CPVA-CM group, CM catheter was not used in 5 patients due to trans-septal access difficulties (4 patients) or because it became entrapped in the mitral valve apparatus (1 patient). Overall, end-point of PV encirclement for both left and right-sided PV antrum was achieved in 64 (88.9%) and 54 (75.0%) CPVA and CPVA-CM patients ($p=0.051$), as documented by the ablation or CM catheter recordings, respectively. End-point for the roof ablation line was achieved in 66 (91.6%) and 65 (90.3%) patients of each group ($p=0.77$).

Procedural details are shown in Table 2. CPVA-CM required longer procedural and fluoroscopy durations, although the amount of deployed radiofrequency time did not differ significantly between both groups.

Complications

Procedural related severe complications are listed in Table 2. In the CPVA group, one patient had a cerebrovascular accident during the procedure, with left-side cortico-subcortical ischemic lesions observed in the magnetic resonance imaging; right-hand hypoestesia remained in this patient 6 months after the ablation. In the CPVA-CM group, one patient suffered a periprocedural transient cerebrovascular ischemia, which was resolved under heparin without sequelae and with normal computed tomography scanning; another patient showed periprocedural transient inferior myocardial ischemia attributed to air embolism and resolved with sublingual NTG within a few minutes, with no adverse consequences. Finally, the CM catheter became entrapped in the mitral valve apparatus of one CPVA-CM patient; attempts to free the catheter resulted in rupture of the papillary muscle, requiring open heart surgery repair. Echocardiography performed 5 months after ablation in this patient showed mitral insufficiency of grade I/IV.

MRA performed prior to and 4-6 months after ablation in all patients of this series did not reveal any severe (lumen narrowing >70%) PV stenosis. In addition, 3 and 1 patients of the CPVA and CPVA-CM groups, respectively, had post-procedural pericarditis that required non-steroidal anti-inflammatory treatment.

Follow-up

After a mean follow-up of 9±3 months, 31 (42.5%) patients of the CPVA group and 47 (64.4%) patients of the CPVA-CM group were arrhythmia-free after a single ablation procedure in absence of antiarrhythmic drug therapy ($p=0.008$, Figure 2A). In addition, 6 (8.2%) patients of each group had no arrhythmias during the follow-up taking one antiarrhythmic drug (Figure 2B). In these 12 patients, the antiarrhythmic treatment was not discontinued after ablation or was re-started during the first 3 months following the procedure due to early recurrences, but they had no arrhythmias beyond this blanking period. Characteristics of the patients from both ablation groups who had arrhythmias during the follow-up are reported in Table 3.

Cox multivariable regression indicated that not to have long-standing AF, absence of hypertension and to use a CM catheter in the procedure predicted absence of arrhythmia recurrences without the use of antiarrhythmic drugs and after a single ablation (Table 4).

Repeated ablation procedures

Among patients with AF recurrence after the index procedure, ablation was repeated in 8 (11%) and 4 (5.5%) patients of the CPVA and CPVA-CM groups, respectively. In all of them, the previous ablation set was evaluated using CM catheter: isolation of all PV were still demonstrable in one single patient of each group (12% and 25%, respectively), whereas in the remaining 7 (88%) and 3 (75%) patients a mean of 3.3±0.9 and 1.7±0.6 PV showed electrical reconnection. In addition, gaps on the roof ablation line were observed in a total of 5 (62%) and 3 (75%) of them.

In 2 (2.7%) CPVA and 3 (4.1%) CPVA-CM other patients, a second ablation was performed due to new-onset LA flutter. An activation map produced by the navigation system plus entrainment manoeuvres showed a re-entry established between gaps of the previous right-sided (n=2) or left-sided (n=1) encircling lesions, a re-entry involving both anterior and posterior LA aspect due to re-conduction of the LA roof ablation line (n=1), or a re-entry using the region between the mitral annulus and the left inferior PV as critical isthmus (n=1). In all of them, radiofrequency delivery successfully eliminated the arrhythmia, including the mitral isthmus-related re-entry that required epicardial ablation from the coronary sinus.

DISCUSSION

The main finding of this study was that using a CM catheter to assess PV antrum isolation improved the success of CPVA as compared to use of the radiofrequency catheter to map the voltage disappearance inside the surrounded region.

From the initial identification of PV ectopic impulses triggering AF[1], several AF ablation procedures have been developed[2]. Although additive ablation has been proposed to improve the success of the therapy, there is consensus that PV ablation should be the basis of any procedure[2]. Haissaguerre et al. developed the segmental ostial ablation, in which PV were isolated by using a CM catheter positioned at the ostium of each vein[3]. Alternatively, Pappone et al. developed the CPVA, in which a single catheter in the LA was used both to create continuous radiofrequency extra-ostial lesions and to map the electrical activity within the encircled region[4]. As compared to ostial ablation, CPVA reduced the PV stenosis risk[18] and may act on potentially arrhythmogenic mechanisms located at the PV antrum[19-21].

Two previous randomized studies compared both approaches, but they obtained opposite results[5;6]: Oral et al. reported that CPVA was more effective in paroxysmal AF ablation (88% vs 67%), whereas Karch et al. had better results in the segmental ostial ablation group (42% vs 66%). This divergence could be related to the fact that in CPVA procedure the isolation of the encircled region cannot be ensured simply by documenting abatement of the electrical activity by the ablation catheter recording[7;13;14;16;22;23], since a recent study obtained better efficacy performing CPVA as compared to individual ostial ablation if the electrical block of the encircling line was demonstrated by a CM catheter[7]. In this regard, it has been suggested that the ablation of the PV carina as an adjunct of the CPVA may increase the PV disconnection rate without the use of CM catheter assessement[14]. However, two other studies have reported that the achievement of PV electrical isolation was not related with the success of the CPVA[13;23]. Due to these conflicting data, some laboratories perform PV antrum encirclement with a single LA catheter[8-10]; others add one or two CM catheters to ensure either the PV antrum isolation [7;11;12] or the PV ostial isolation[13]. To our knowledge, this is the first randomized study comparing the outcome of CPVA based on whether PV antrum isolation is demonstrated by a CM catheter or not.

Ablation using a CM catheter adds some benefits compared to using a single catheter in the LA both to map and ablate. Firstly, the size and distribution of the electrodes along the CM catheter better identify the residual electrograms as compared to the distal dipole of the ablation catheter[16]. Note that in the present series the disappearance of electrical activity within the PV antrum was more often achieved in the CPVA group, stressing the fact that the end-point of the procedure may be less restrictive when assessed by the ablation catheter than when using a CM catheter. Secondly, changes in the activation pattern of the encircled region during the radiofrequency delivery can be immediately observed in the CM catheter recordings, whereas ablation and mapping process must be sequentially performed when a single LA catheter is used. Finally, a CM catheter allows multipolar mapping to better guide the location of conduction gaps on the ablation line. On the other hand, the use of another catheter in the LA may increase the potential risk of the procedure; moreover, placing a CM catheter in the LA can result in mitral valve apparatus entrapment, especially when this catheter has a knob on the tip[24]. Finally, the manipulation of a CM catheter added technical complexity to the procedure and required additional procedural and fluoroscopic times, although this increase was minor when a navigation system capable of locating both the ablation and CM catheters was used. These pros and cons should be carefully balanced when an AF ablation approach is considered. As a result of the present study, the use of a CM catheter should be recommended in CPVA procedures.

CONCLUSIONS

The use of a CM catheter to demonstrate the PV antrum isolation improved the success of the CPVA as compared to use of a single LA catheter.

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Table 1
Patient characteristics

	CPVA group	CPVA-CM group	P value
Patients	73	73	--
Type of AF			0.628
Paroxysmal AF	39 (53.4%)	38 (49.4%)	
Persistent AF	25 (34.2%)	22 (30.1%)	
Longstanding AF	9 (12.3%)	13 (17.8%)	
Age (years)	53.2±9.7	51.9±10.2	0.475
Male sex	58 (79.5%)	64 (87.7%)	0.180
Duration of AF (years)	5.5 [2.0-8.5]	4.5 [1.7-7.8]	0.210
LA diameter (mm)	42.6±4.9	43.6±5.3	0.242
LV end-diastolic diameter (mm)	50.9±4.6	52.4±5.0	0.917
LV end-systolic diameter (mm)	33.5±4.8	34.6±5.4	0.959
LV ejection fraction (%)	59.1±8.0	55.6±10.1	0.034
Hypertension	39 (53.4%)	30 (41.1%)	0.136
Structural heart disease	15 (21.1%)	10 (14.3%)	0.288

AF: atrial fibrillation; LA: left atrial; LV: left ventricular.

Continuous data are expressed as mean±SD or median [Q1-Q3] when appropriate.

Table 2
Procedural details

	CPVA group	CPVA-CM group	P value
Patients	73	73	--
Procedural time (min)	154.4±58.6	175.4±42.6	0.021
Fluoroscopic time (min)	19.9±16.0	31.2±9.7	<0.001
RF time (min)	61.1±17.0	59.6±18.7	0.723
Complications			0.620
Pericardial tamponade	0 (0%)	0 (0%)	
Cerebrovascular accident	1 (1.4%)	0 (0%)	
Transient cerebrovascular ischemia	0 (0%)	1 (1.4%)	
Transient inferior myocardial ischemia	0 (0%)	1 (1.4%)	
MV apparatus damage	0 (0%)	1 (1.4%)	
PV stenosis (lumen narrowing> 70%)	0 (0%)	0 (0%)	

RF: radiofrequency; MV: mitral valve; PV: pulmonary vein

Table 3: Characteristics of the patients who had arrhythmia recurrences during the follow-up

	CPVA group	CPVA-CM group	P value
Patients	36	20	--
Type of AF, n (%)			0.143
Paroxysmal AF	17 (47.2%)	10 (50.0%)	
Persistent AF	13 (36.1%)	3 (15.0%)	
Long-standing AF	6 (16.7%)	7 (35.0%)	
Age (years)	55.0±9.7	55.0±7.7	0.992
Male sex, n (%)	30 (83.3%)	17 (85.0%)	0.871
Duration of AF (years)	7.5 [3.0-10.0]	6.7 [3.0-8.0]	0.445
LA diameter (mm)	44.5±4.7	45.1±4.4	0.640
LV end-diastolic diameter (mm)	51.1±5.0	52.7±4.2	0.279
LV end-systolic diameter (mm)	34.2±5.1	34.6±4.6	0.797
LV ejection fraction (%)	57.9±6.6	58.6±7.7	0.750
Hypertension, n (%)	24 (66.7%)	9 (45.0%)	0.114
Structural heart disease, n (%)	10 (27.8%)	3 (15.0%)	0.339
End-point for LARL†, n (%)	32 (88.9%)	18 (90.0%)	1.000
End-point for PVE†, n (%)	31 (86.1%)	15 (75.0%)	0.298
RF time (min)	64.5±16.4	61.7±14.3	0.674
Recurrence			0.142
AF recurrence, n (%)	32 (88.9%)	14 (70.0%)	
LA flutter recurrence, n (%)	4 (11.1%)	6 (30.0%)	

AF: atrial fibrillation; LA: left atrial; LV: left ventricular; RF: radiofrequency delivery during ablation procedure. † Indicates in how many patients the end-point defined in each group for the LA roof line (LARL) creation or for both left and right-sided pulmonary vein encirclement (PVE) was achieved.

Continuous data are expressed as mean±SD or median [Q1-Q3] when appropriate.

Table 4: Final model of Cox regression for arrhythmia recurrence

	HR (95% CI)	P value
Type of AF		
Paroxysmal AF	1 (--)	--
Persistent AF	1.122 (0.646-1.950)	0.683
Long-standing AF	2.397 (1.298-4.426)	0.005
Hypertension	1.863 (1.136-3.054)	0.014
Not to use a CM catheter	1.835 (1.119-3.003)	0.016

AF= atrial fibrillation; CM= circular mapping catheter.

Figure 1. Panel A: Three-dimensional anatomy of the left atria showing the circumferential pulmonary vein lesions (red dots) and the location of both ablation (green tip) and Lasso (yellow) catheters. Panel B: Radiofrequency delivery at the site of the circumferential line closest to the Lasso earliest potential (L4-5) resulted in disappearance of electrical activity in all dipoles of the circular mapping catheter. Panel C: low-amplitude electrogram with multiple components recorded immediately before the radiofrequency delivery by the ablation catheter distal dipole.
RSPV: Right superior PV; RIPV: Right inferior PV; LCT: Left common trunk; LAA: left atrial appendage.

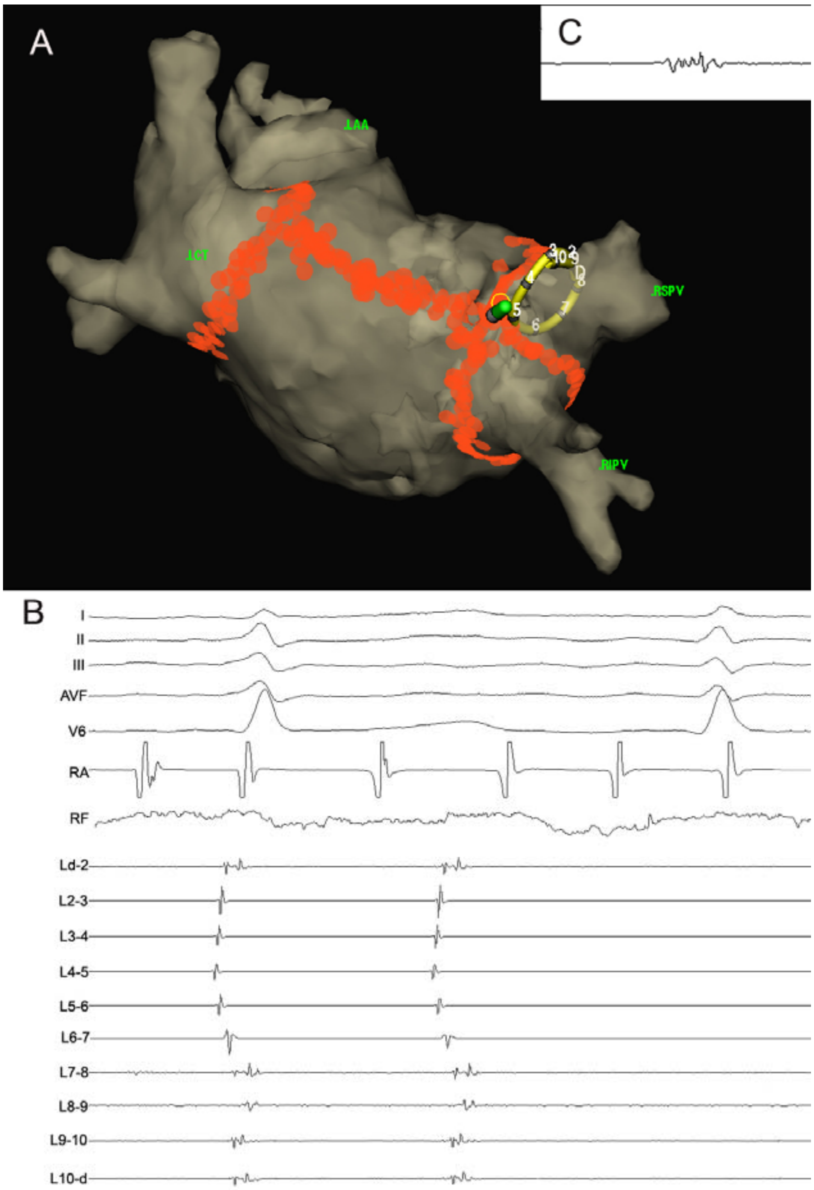

Figure 2. Arrhythmia-free proportion after a single ablation procedure in (A) patients without antiarrhythmic medication, and in (B) patients taking ≤1 antiarrhythmic drug.