AHRQ Comparative Effectiveness Review Surveillance Program

CER # 15:
Effectiveness of Radiofrequency Catheter Ablation for Atrial Fibrillation

Original release date
July 6, 2009

Surveillance Report (1st Assessment/cycle 1)
November, 2011

Surveillance Report (2nd Assessment/cycle 2)
December, 2012

Key Findings (1st assessment/cycle 1)

- KQ1 up to date
- 2 of 5 conclusions for KQ2 possibly out of date
- 1 of 4 conclusions for KQ3 possibly out of date
- KQ4 up to date
- Expert opinion: conclusions for KQ1-4 still valid
- There are no new significant safety concerns

Key Findings – (cumulative: 1st and 2nd assessments/cycle 1-2)

- KQ1 up to date
- 2 of 5 conclusions for KQ2 probably out of date
- 1 of 4 conclusions for KQ3 possibly out of date
- KQ4 up to date
- Expert opinion: conclusions for KQ1-4 still valid
- There are no new significant safety concerns

Source: www.effectivehealthcare.ahrq.gov
Published online: May 16, 2013

Summary Decision:

This CER's priority for updating is **Low** (unchanged from the 1st assessment)

Source: www.effectivehealthcare.ahrq.gov
Published online: May 16, 2013

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Source: www.effectivehealthcare.ahrq.gov
Published online: May 16, 2013

Acknowledgments

The authors gratefully acknowledge clinical content expert Drs Ann Garlitski and her contributions to this project.

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Source: www.effectivehealthcare.ahrq.gov
Published online: May 16, 2013

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1. Introduction

The purpose of this mini-report was to apply the methodologies developed by the Ottawa and RAND EPCs to assess whether or not the CER No. 15 (Comparative effectiveness of radiofrequency catheter ablation for atrial fibrillation),[1] is in need of updating. This CER was originally released in July, 2009. It was therefore due for a surveillance assessment in January, 2010. When the Surveillance program began in the summer of 2011, this CER was selected to be in the first wave of reports to go through the assessment. The first surveillance assessment report of this CER was submitted to AHRQ in November, 2011. This second assessment was completed in December 2012.

This CER included 120 unique studies identified by using searches through December, 2008 and addressed four key questions to evaluate effectiveness and safety of radiofrequency catheter ablation for atrial fibrillation. The key questions of the original CER were as follows:

1. What is the effect of radiofrequency ablation (RFA) on short- (6 to 12 months) and long- (>12 months) term rhythm control, rates of congestive heart failure, left atrial and ventricular size changes, rates of stroke, quality of life, avoiding anticoagulation, and readmissions for persistent, paroxysmal and long-standing persistent (chronic) atrial fibrillation?

2. What are the patient-level and intervention-level characteristics associated with RFA effect on short- and long-term rhythm control?

3. How does the effect of RFA on short- and long-term rhythm control differ among the various techniques or approaches used?

4. What are the short- and long-term complications and harms associated with RFA?

The conclusion(s) for each key question are found in the executive summary of the CER report.[1]

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2. Methods

We followed *a priori* formulated protocol to search and screen literature, extract relevant data, and assess signals for updating. The identification of an updating signal (qualitative or quantitative) would be an indication that the CER might be in need of updating. The Food and Drug Administration (FDA), Health Canada, and Medicines and Healthcare Products Regulatory Agency (MHRA) surveillance alerts received from the Emergency Care Research Institute (ECRI) were examined for any relevant material for the present CER. The clinical expert opinion was also sought. Taken into consideration the totality of evidence (i.e., updating signals, expert opinion, FDA surveillance alerts), a consensus-based conclusion was drawn whether or not any given conclusion warrants any updating (up to date, possibly out of date, or out of date). Based on this assessment, the CER was categorized into one of the three updating priority groups: high priority, medium priority, or low priority. Further details on the Ottawa EPC and RAND methods used for this project are found elsewhere.[2-4]

2.1 Literature Searches

Cycle 2 (2nd assessment)

The same search strategy was used as in the 1st assessment (cycle 1) but using different search dates for MEDLINE (March 20, 2011- June 5, 2012) and the Cochrane Central Register of Controlled Trials (CCRCT; search date June 3, 2012) as per the original search strategies appearing in the CER's Appendix A.[1]

Cycle 1 (1st assessment)

The CER search strategies were reconstructed in MEDLINE (January, 2008-September 23, 2011) and the Cochrane Central Register of Controlled Trials (CCRCT; search date September 23, 2011) as per the original search strategies appearing in the CER's Appendix A.[1] The Cochrane update was run on the Wiley platform as the OVID platform was not available through our institutional subscription. The syntax and vocabulary, which include both controlled subject headings (e.g., MeSH) and keywords, were applied according to the databases indicated in the appendix and in the search strategy section of the CER report. The MEDLINE search was limited to five general medical journals (Annals of Internal Medicine, BMJ, JAMA, Lancet, and New England Journal of Medicine) and several specialty journals (Circulation, Heart Rhythm, American Journal of Cardiology, and the Journal of the American College of Cardiology). Restricting by journal title was not possible in the Cochrane search and pertinent citations were instead selected from the results. Study design filters were not applied to the Cochrane search

since the Cochrane Central Register only contains randomized or controlled clinical trials. Further details on the search strategies are provided in the Appendix A of this mini-report.

2.2 Study Selection

All identified bibliographic records were screened using the same inclusion/exclusion criteria as one described in the original CER.

2.3 Expert Opinion

Cycle 2 (2nd assessment)

We contacted the 2 experts (1 CER-specific and 1 local expert) that had responded to the first assessment.

Cycle 1 (1st assessment)

In total, 4 CER-specific (e.g., lead author, clinical content experts, and technical expert panel members) and 8 additional (local) clinical content experts were requested to provide their opinion/feedback in a pre-specified matrix table (Appendix D) on whether or not the conclusions as outlined in the Executive Summary of the original CER were still valid.

2.4 Check for Qualitative and Quantitative Signals

All relevant reports eligible for inclusion in the CER were examined for the presence of qualitative and quantitative signals using the Ottawa EPC method (see more details in Appendix B). CERs with no meta-analysis were examined for qualitative signals only. For any given CER that included a meta-analysis, the assessment started with the identification of qualitative signal(s), and if no qualitative signal was found, this assessment extended to identify any quantitative signal(s). The identification of an updating signal (qualitative or quantitative) would be an indication that the CER might be in need of updating. The definition and categories of updating signals are presented in Appendix B and publications.[2,3]

2.5 Compilation of Findings and Conclusions

All the information obtained during the updating process (i.e., data on qualitative/quantitative signals, the expert opinions, and safety surveillance alerts) was collated and summarized. Taken into consideration the totality of evidence (i.e., updating signals, expert opinion, and FDA surveillance alerts) presented in a tabular form, a conclusion was drawn whether or not any conclusion(s) of the CER warrant(s) updating.

Conclusions were drawn based on four category scheme:

- Original conclusion is still **up to date** and this portion of CER does not need updating
- Original conclusion is **possibly out of date** and this portion of CER may need updating
- Original conclusion is **probably out of date** and this portion of CER may need updating
- Original conclusion is **out of date** and this portion of CER is in need of updating

In making the decision to classify a CER conclusion into one category or another, we used the following factors when making our assessments:

- If we found no new evidence or only confirmatory evidence and all responding experts assessed the CER conclusion as still valid, we classified the CER conclusion as still up to date.
- If we found some new evidence that might change the CER conclusion, and /or a minority of responding experts assessed the CER conclusion as having new evidence that might change the conclusion, then we classified the CER conclusion as possibly out of date.
- If we found substantial new evidence that might change the CER conclusion, and/or a majority of responding experts assessed the CER conclusion as having new evidence that might change the conclusion, then we classified the CER conclusion as probably out of date.
- If we found new evidence that rendered the CER conclusion out of date or no longer applicable, we classified the CER conclusion as out of date. Recognizing that our literature searches were limited, we reserved this category only for situations where a limited search would produce prima facie evidence that a conclusion was out of date, such as the withdrawal of a drug or surgical device from the market, a black box warning from FDA, etc.

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2.6 Determining Priority for Updating

Determination of priority groups (i.e., Low, Medium, and High) for updating any given CER was based on two criteria:

- How many conclusions of the CER are up to date, possibly out of date, or certainly out of date?
- How out of date are conclusions (e.g., consideration of magnitude/direction of changes in estimates, potential changes in practice or therapy preference, safety issue including withdrawn from the market drugs/black box warning, availability of a new treatment)

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3. Results

3.1 Update Literature Searches and Study Selection

Cycle 2 (2nd assessment)

A total of 97 bibliographic records were identified (MEDLINE=92 and CCRCT =5). After de-duping, 89 records remained (MEDLINE=89 and CCRCT=0), from which 40 potentially eligible records were assessed for full text. Of these, 22 were included in the update.[5-26]

Cycle 1 (1st assessment)

A total of 33 studies (9 randomized trials and 24 non-randomized controlled trials/observational cohort studies) were included and assessed for updating signals.

3.2 Signals for Updating in Newly Identified Studies [Cycle 2]

3.2.1 Study overview

The study, population, treatment characteristics, and results for the 22 included studies[5-26] are presented in Appendix C (Evidence Table).

Two of the 22 included studies were randomized trials[13,14] and the remaining 20 were non-randomized experimental or observational studies. The length of follow-up across majority of studies was between 12[5,11,14] and 60 months.[6] The longest follow-up period was 9 years.[15] The number of participants included in the randomized trials ranged from 80[13] to 124.[14] The sample size of the non-randomized studies ranged from 75[8] to 4,156.[18] Participants included in these studies were diagnosed with atrial fibrillation (AF). None of the included studies compared RFA with anti-arrhythmic drugs (AAD). In two RCTs,[13,14] different techniques of ablation were compared. Specifically, in one trial,[13] duty-cycled bipolar/unipolar ablation with circular catheter was compared with point-by-point antral ablation with 3D mapping system. The other RCT[14] compared catheter ablation and surgical ablation techniques.

Eight studies investigated the value of different patient-level prognostic factors in predicting the risk of AF recurrence (e.g., age, gender, body mass index, hypertension, diabetes, chronic kidney disease, type of AF, temporal regularity index, spacial regularity index, left ventricular diameter, metabolic syndrome, and AF cycle length).[5-12]

The reported efficacy outcome measures for most studies were the recurrence rates of atrial fibrillation (AF), freedom from AF, or termination of AF. Several studies reported rates of complications/adverse events.[5-7,9,10,13-26]

3.2.2 Qualitative signals

See also Table 1 (Summary Table), Appendix B, and Evidence Table (Appendix C)

Key question #1

Comparative effectiveness/safety for reducing recurrence rates of AF (RFA vs. AAD)

No new evidence. **No Signal.**

Key question #2

Predictive power of patient-level characteristics on AF recurrence rates in RFA-treated patients

Type of AF: In agreement with findings from the original CER, one study[6] using a multivariable analysis reported significantly higher rates of AF recurrence in participants with long-standing persistent AF vs. PAF or persistent AF (HR=1.90, 95% CI: 1.00, 3.50). **No Signal.**

Left atrial diameter (LAD): In agreement with the original CER, in two studies,[10,12] multivariable analyses showed larger LAD as a significant predictor of AF recurrence rate (HR range: 1.009-1.45). **No Signal.**

Left ventricular/diastolic diameter (LVEDD): In agreement with the original CER, one trial,[8] showed larger LVEDD as a significant predictor of AF recurrence rate (59% vs. 52%, p=0.005). **No Signal.**

Gender: In conflict with CER findings, 2 non-RCTs[9,10] showed female gender was associated with either a significantly increased[10] or reduced [9] rate of AF recurrence.
1 Signal (other).

Duration of AF: In conflict with CER findings, 1 study,[9] showed a longer duration of AF (> 6 mo) to be a significant predictor of AF recurrence rate (HR=1.64, 95% CI: 1.21, 2.23). **1Signal (other).**

Presence of structural heart disease: as supplementary evidence to the original CER, three studies showed the presence of heart disease as a significant predictor of AF recurrence. **1 signal (other**).

Age: Results agreed with those in the original CER regarding the absence of significant effect of age on AF recurrence. Specifically, the independent effect of age on recurrence of AF was reported in two non-RCTs in both of which the observed effects were statistically non-significant (p=0.14 and p=0.37)[10,12]. **No Signal.**

Other potentially important predictors: The evidence in CER was supplemented by several studies which identified a wide variety of new significant predictors for increased AF recurrence rate. Specifically, increased levels of $CHADS_2$ score[7] temporal regularity/spacial regularity indices[8] monocyte CD36FL (>200),[11] presence of chronic kidney disease,[12] presence of metabolic syndrome[5] were associated with higher AF recurrence. Conversely, increased levels of AF cycle length[9] and monocyte CD36FL[11] were associated with significantly reduced AF recurrence. **1 Signal (other).**

Predictive power of intervention-level characteristics on AF recurrence rates in RFA-treated patients

No new evidence. **No Signal.**

Key question #3

Reduction in recurrence rates of AF (PVI vs. C-PVI)

No new evidence. **No Signal.**

Reduction in recurrence rates of AF (RFA vs. RFA with additional left-sided ablation)

No new evidence. **No Signal.**

Reduction in recurrence rates of AF (PVI vs. PVI with right-sided lines)

No new evidence. **No Signal.**

Reduction in recurrence rates of AF (Different approached of ablation compared)

Rhythm control: 2 RCTs [13,14] reported on the comparison between the following RFA techniques. In the first trial,[13] there was no significant difference in AF termination rates between the duty-cycled bipolar/unipolar and the 3D point-by-point. In the other trial,[14] comparing catheter ablation to surgical ablation, there was a greater AF termination rate in favor of surgical ablation. **No Signal.**

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Published online: May 16, 2013

Key question #4

Rates of adverse events/complications after receiving RFA

Overall, the rates of specific complications and harms in participants receiving RFA were similar to those reported in the original CER. The overall rates of complications/major adverse events were under 7%.[9,10,15,18-20,25]. **No Signal.**

PV stenosis: < 1%[6,7,10,13,15,23]

Tamponade: ≤ 5% [6,7,9,14,15,18,21,22]

Transient ischemic attack: 1 (0.23%),[10] 1 (0.25%),[9] 6 (1.06%)[20]

Pulmonary embolism: 2 (0.35%),[20] 11 (0.7%)[19]

Death: <2%[6,10,14,18-20,22,25]

Pericardial effusion: 5 (1.5%),[17] 2 (0.43%),[23] 11 (0.73%),[5] and 3 (3%)[6]

Pulmonary hypertension: 19 (1.4%)[23]

Esophageal injury: 22/219 (10%)[16]

Excessive transmural injury: 10 (9.6%)[24]

3.2.3 Quantitative signals

No meta-analysis could be performed for any of the key questions

3.3 Safety surveillance alerts [Cycle 2]

None of the received safety surveillance alerts was relevant to the key questions of the given CER.

3.4 Expert opinion [Cycle 2]

Only one (CER-specific) of the contacted clinical experts has provided response/feedback in the matrix table (Appendix D). The responses from the expert were consistent in agreement that all four conclusions outlined in the executive summary of the CER were still valid. The expert was not aware of evidence that would invalidate the four CER conclusions.

4. Conclusion

Summary results and conclusions according to the information collated from different sources (updating signals from studies identified through the update search, FDA surveillance alerts, and expert opinion) are provided in Table 1 (Summary Table). Based on the two assessments (cycles 1-2), this CER is categorized in **Low** (unchanged from the 1st assessment) priority group for updating.

Key Question # 1

Signals from studies identified through update search (Cycle 2)

No new evidence. **No Signal.**

Experts (Cycle 2): One expert stated that conclusions in the key question # 1 are still valid.

Safety surveillance alerts (Cycle 2): No relevant safety alerts.

1st assessment conclusion (Cycle 1): **Up to date**

Total (cumulative) conclusion (Cycles 1-2): **Up to date**

Key Question # 2

Signals from studies identified through update search (Cycle 2)

In disagreement with the original CER conclusions supporting no effect of gender, the duration of AF, and the presence of heart disease on AF recurrence rates, three studies showed that gender was either a significant predictor or protective factor of AF recurrence (**1 signal**), one study showed the duration of AF to be a predictor of AF recurrence (**1 signal**). Three studies showed the presence of heart disease as a significant predictor of AF recurrence (**1 signal**). As supplementary evidence, seven studies revealed other subject-level factors as having independent effects on the rate of AF recurrence (**1 signal**). **4 Signals (Other).**

Experts (Cycle 2): One expert stated that conclusions in the key question # 2 are still valid.

Safety surveillance alerts (Cycle 2): No relevant safety alerts.

1st assessment conclusion (Cycle 1): **2 of 5 conclusions possibly out of date**

Total (cumulative) conclusion (Cycles 1-2): **2 of 5 conclusions probably out of date**

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Key Question # 3

Signals from studies identified through update search (Cycle 2)

No new evidence. **No Signal.**

Experts (Cycle 2): One expert stated that conclusions in the key question # 3 are still valid.

Safety surveillance alerts (Cycle 2): No relevant safety alerts.

1st assessment conclusion (Cycle 1): **1 of 4 conclusions possibly out of date**

Total (cumulative) conclusion (Cycles 1-2): **1 of 4 conclusions possibly out of date**

Key Question # 4

Signals from studies identified through update search (Cycle 2): Overall, rates of complications reported in the original CER were similar to those reported in newly identified studies. **No Signal.**

Experts (Cycle 2): One expert stated that conclusions in the key question # 4 are still valid.

Safety surveillance alerts (Cycle 2): No relevant safety alerts.

1st assessment conclusion (Cycle 1): **Up to date**

Total (cumulative) conclusion (Cycles 1-2): **Up to date**

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Published online: May 16, 2013

Table 1. Summary Table

Conclusions from CER's Executive Summary	Update literature search results	Signals for updating		Safety surveillance alerts	Expert opinion	Validity of CER conclusions	
		Qualitative	Quantitative			Cycle 1 assessment	Cycles 1-2 (total cumulative) assessment
Key Question 1: What is the effect of RFA on short-term (6 to 12 months) and long-term (>12 months) rhythm control, rates of congestive heart failure, left atrial and ventricular size changes, rates of stroke, quality of life, avoiding anticoagulation, and readmissions for persistent, paroxysmal, and long-standing persistent (chronic) atrial fibrillation?							
Rhythm control (RFA as a second-line therapy) There is a moderate level of evidence to show that patients who received RFA as a second-line therapy (i.e., patients who did not respond to medical therapy) had a higher chance of maintaining sinus rhythm than those treated with medical therapy alone (relative risk (RR) 3.46, 95-percent confidence interval (CI) 1.97-6.09) at 12 months postprocedure. The summary estimate was derived from meta-analysis of three RCTs that assessed the rhythm control of patients exclusively after a single procedure.	**Cycle 2 (July 2012)**					Up to date	Up to date
	No new evidence	**No signal**	NA	None	Still valid; one expert mentioned an ongoing RCT (CABANA)		
	Cycle 1 (November 2011)						
	1 RCT[27]	**No signal** Findings in one RCT identified in update search are in agreement with those in the pooled analysis of original CER, indicating higher risk of being free from recurrent AF in RFA vs. AAD (i.e., lower recurrent AF rates in RFA vs. AAD)	**No signal** The MA for the risk of being free from AF recurrence in the original CER was updated by pooling results from 1 RCT[27] Original pooled **RFA vs. AAD** RR=3.46 95% CI: 1.97, 6.09 Updated pooled **RFA vs. AAD** RR=3.72 95% CI: 2.48, 5.58 There was no	None	All 3 experts stated that this conclusion is still valid; two experts mentioned an RCT (CABANA) which is in recruitment phase only		

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			change in statistical significance; % increase in RR<50%				
Rhythm control (RFA as a first-line therapy) There is insufficient evidence to compare freedom from AF recurrence in patients who had RFA as first-line therapy vs. medically treated patients. One fair quality RCT of 67 patients (96 percent PAF) reported an increased freedom from AF recurrence at 12 months for RFA as first-line therapy compared with medical treatment (88 percent vs. 37 percent, P<0.001).	**Cycle 2 (July 2012)**					Up to date	Up to date
	No new evidence	**No signal**	NA	None	Still valid		
	Cycle 1 (November 2011)						
	No new evidence	**No signal**	NA	None	Still valid		
Rates of congestive heart failure There is insufficient evidence to compare the rates of congestive heart failure between RFA and medical treatment. There was only one observational study with data. This study reported that patients who underwent RFA had a lower risk of developing congestive heart failure than those treated with medical therapy (5 percent vs. 10 percent, P value not reported) at a mean follow-up of 30 months.	**Cycle 2 (July 2012)**					Up to date	Up to date
	No new evidence	**No signal**	NA	None	Still valid		
	Cycle 1 (November 2011)						
	1 RCT[27]	**No signal** This trial[27] reported one case of heart failure in RFA arm, i.e., insufficient evidence to compare incidence rates in RFA vs. AAD	No MA in the original CER	None	Still valid		
Left atrial and ventricular size changes There is a low level of evidence showing no statistically significant difference in the improvement of left atrial diameter (LAD), left ventricular end diastolic diameter (LVED), or ejection fraction (EF) at 12 months in patients who underwent RFA compared to those treated with medical therapy.	**Cycle 2 (July 2012)**					Up to date	Up to date
	No new evidence	**No signal**	NA	None	Still valid		
	Cycle 1 (November 2011)						
	No new evidence	**No signal**	No MA in the original CER	None	Still valid		
Rates of stroke There is a low level of evidence showing no statistically significant difference in the risk of cerebrovascular events at 12 months in patients who underwent RFA compared to those treated with	**Cycle 2 (July 2012)**					Up to date	Up to date
	No new evidence	**No signal**	NA	None	Still valid		
	Cycle 1 (November 2011)						

medical therapy (risk difference 0.6 percent, 95-percent CI -1.1 to 2.3 percent favoring AAD). The summary estimate was derived from meta-analysis of six RCTs.	1 RCT[27]	**No signal** This trial[27] reported one case of vascular complication in RFA arm, i.e., insufficient evidence to compare incidence rates in RFA vs. AAD	Cannot update the MA in the original CER due to insufficient new data	None	Still valid		
Quality of life There is a low level of evidence to suggest that RFA improves quality of life more than medical treatment. Three RCTs and one observational study reported more improvement in the general or physical functioning score of the SF-36 health survey in patients who underwent RFA than in patients who had medical treatment alone (net difference between the two treatments, +1 to +25 favoring RFA). However, these studies assessed the results at nonuniform time points and therefore the findings may be difficult to interpret.	**Cycle 2 (July 2012)**					Up to date	Up to date
	No new evidence	**No signal**	NA	None	Still valid		
	Cycle 1 (November 2011)						
	1 RCT[27]	**No signal** Findings in this RCT [27] identified in update search are in agreement with those in the original CER that RFA improved QOL compared to AAD	No MA in the original CER	None	See above		
Avoiding anticoagulation There is a low level of evidence suggesting that patients treated with RFA have a better chance of avoiding anticoagulation than those treated with AADs. There was only one RCT. It found a higher proportion of patients treated with RFA than patients treated with medical therapy reporting freedom from anticoagulation at 12 months (60 percent vs. 34 percent, P=0.02).	**Cycle 2 (July 2012)**					Up to date	Up to date
	No new evidence	**No signal**	NA	None	Still valid		
	Cycle 1 (November 2011)						
	No new evidence	**No signal**	No MA in the original CER	None	Still valid		
Readmissions There is a low level of evidence on differences in readmission rates between patients treated with RFA and those treated with AADs. Two RCTs compared the rates or number of readmissions	**Cycle 2 (July 2012)**					Up to date	Up to date
	No new evidence	**No signal**	NA	None	Still valid		
	Cycle 1 (November 2011)						

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between RFA and medical treatment. One RCT reported a lower readmission rate in patients treated with RFA than medical treatment (9 percent vs. 54 percent, P<0.001), while the other RCT reported no statistically significant difference in the median number of readmissions between RFA and medical treatment (1 readmission vs. 2 readmissions, P=0.34). The findings on the rates of readmissions are inconsistent. This may be because readmission rates depend on many other factors besides the recurrence of disease (e.g., the particular health care system, bed availability, severity of illness)	No new evidence	**No signal**	No MA in the original CER	None	Still valid		
Key question 2: What are the patient-level and intervention-level characteristics associated with RFA effect on short- and long-term rhythm control?							
There is a low level of evidence to show that AF type, namely nonparoxysmal AF, is predictive of a higher rate of AF recurrence. Univariable analyses within 31 studies that reported recurrence rates for PAF vs. other types of AF were clinically and statistically heterogeneous, but meta-analysis found statistically significant higher rates of recurrence in patients with nonparoxysmal AF, with relative risks of about 1.6. However, only a minority of multivariable analyses bear this out. Overall, 25 studies reported multivariable analyses of the association between patient-level characteristics and AF recurrence. Among these, 17 evaluated AF type but only 6 of them found statistically significant independent associations between AF type and recurrence rates. In the 8 studies that reported hazard ratios, these ranged from 1.1 to 22, suggesting lower recurrence rates in patients with PAF. Among 11 comparisons that reported both univariable and multivariable analyses, 6 found statistically significant crude and adjusted higher recurrence rates in patients with nonparoxysmal AF, 3 found significant crude but nonsignificant adjusted associations, and 2 found nonsignificant crude and adjusted associations. In both univariable and multivariable analyses reported, no study or population factors were found to explain the	**Cycle 2 (July 2012)**					Up to date	Up to date
	1 non-RCT[6]	**No signal** In agreement with findings from the original CER, one study[6] using a multivariable analysis reported significantly higher rates of AF recurrence in participants with long-standing persistent AF vs. PAF or persistent AF (HR=1.90, 95% CI: 1.00, 3.50)	No MA in the original CER	None	Still valid		
	Cycle 1 (November 2011)						
	1 non-RCT on type of AF[28]	**No signal** In agreement with findings from the original CER, one study[28] using a multivariable analysis reported significantly higher rates of AF	**No signal** The MA for the risk of AF recurrence in the original CER was updated by pooling results from 1 RCT[28]	None	Still valid		

heterogeneity among the studies.		recurrence in participants with NPAF vs. PAF (HR=1.53, 95% CI: 1.15, 2.03)	<u>Original pooled</u> **NPAF vs. PAF** RR=1.59 95% CI: 1.38, 1.82 <u>Updated pooled</u> **NPAF vs. PAF** RR=1.54 95% CI: 1.38, 1.71 There was no change in statistical significance; % increase in RR<5				
There is a moderate level of evidence to show that among patients with approximately normal EF or LAD, these parameters are not independent predictors of AF recurrence. In multivariable analyses, 5 of 17 studies found an association between lower EF and AF recurrence, and 4 of 20 found an association between larger LAD and AF recurrence. However, the reported data suggest that only a small proportion of patients included in the analyses had EFs below about 40 percent or LADs above about 60 mm. The evidence is insufficient to estimate the predictive value of abnormal EF or LAD on recurrence rates.	**Cycle 2 (July 2012)**					Up to date	Up to date
	Non-RCTs[8,10,12]	**No Signal** In agreement with the original CER, in 2 studies,[10,12] multivariable analyses showed larger LAD as a significant predictor of AF recurrence rate: HR=1.45, 95% CI: 1.06, 1.98 [10] HR=1.009, 95% CI: 1.002, 1.017)[12] One study[8] similarly showed larger LVEDD as a significant predictor	NA	None	Still valid		

		of AF recurrence rate -59% (SD 7) vs. 52% (SD 6), p=0.005					
	Cycle 1 (November 2011)						
	No new evidence on EF 4 non-RCTs on LAD [28-31]	**No Signal** In 4 studies,[28-31] multivariable analyses showed consistently that larger LAD was a significant predictor of increased AF recurrence rate.	No MA in the original CER	None	Still valid		
There is a high level of evidence to show that sex, the presence of structural heart disease, and duration of AF are not associated with AF recurrence. None of the 23 studies found an independent association between sex and AF recurrence. Only 1 of 21 studies found a consistent association between structural heart disease and AF recurrence. Only 3 of 16 studies found a statistically significant association between duration and recurrence of AF, with hazard ratios of 1.03 and 1.08 for longer duration.	**Cycle 2 (July 2012)**					Possibly out of date	Probably out of date
	2 Non-RCTs[8-10]	**1 Signal (Other)** In 2 studies,[9,10] female gender was associated with either a significantly increased[10] or reduced rate[9] of AF recurrence: HR=0.092, 95% CI: 0.022, 0.386[9] HR=1.67, 95% CI: 1.34, 3.05 [10] **1 Signal (Other)** In 1 study,[9] longer duration of AF (> 6 mo) was shown as a significant predictor of increased AF recurrence rate. HR=1.644, 95% CI: 1.210, 2.235[9]	No MA in the original CER	None	Still valid		

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		1 Signal (Other) In 3 studies,[8-10] the presence of heart disease was shown as a significant predictor of AF recurrence: HR (presence of CHF) =10.903, 95% CI: 2.602, 45.694[9] HR (absence of CAD)=0.58, 95% CI: 0.36, 0.94[10] OR (presence of HTN)=4.8, 95% CI: 1.0, 22.7[8]					
	Cycle 1 (November 2011)						
	2 non-RCTs [28,32] 1 non-RCT[33]	**1 Signal (Other)** In 2 studies,[28,32] female gender was associated with a significantly increased rate of AF recurrence. **No Signal** In 1 study,[33] longer duration of AF (> 21 days) was shown to be a significant predictor of increased AF recurrence rate.	No MA in the original CER	None	Still valid		
There is a high level of evidence to show that age,	**Cycle 2 (July 2012)**					Up to date	Up to date

within the approximate range of 40 to 70 years, is not independently associated with AF recurrence. Only 1 of 24 studies found an association (that higher age was associated with lower rates of AF recurrence). However, the reported data suggest that only a small proportion of patients included in the analyses were younger than about 40 years or older than about 70 years. The evidence is insufficient to estimate the predictive value of young or very old age.	2 non-RCTs[10,12]	**No Signal** Results agreed with those in the original CER regarding the absence of significant effect of age on AF recurrence. Specifically, the independent effect of age on recurrence of AF was reported in two studies in both of which the observed effects were statistically non-significant (p=0.14 and p=0.37)[10,12]	NA	None	Still valid		
	Cycle 1 (November 2011)						
	No new evidence on age	**No Signal**	No MA in the original CER	None	Still valid		
There is insufficient evidence for other potential predictors of AF recurrence, as other predictors were only rarely evaluated.	**Cycle 2 (July 2012)**					Possibly out of date	Probably out of date
	6 non-RCTs[5,7-9,11,12]	**1 Signal (Other)** In the following studies, higher AF recurrence was associated with increased levels of $CHADS_2$ score[7] TRI/SRI levels[8] monocyte CD36FL (> 200),[11] presence of CKD,[12] presence of metabolic syndrome[5] Increased levels of AFCL[9] and	NA	None	Still valid		

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		monocyte CD36FL[11] were associated with significantly reduced AF recurrence					
	Cycle 1 (November 2011)						
	15 non-RCTs [28-42]	**1 Signal (Other)** In the following studies, higher AF recurrence was associated with increased levels of BNP,[34] EAT volume,[35] pericardial fat,[36] % of continuous electrical activity,[41] BMI,[40] plasma ET,[39] DROM,[38] reduced levels of ECG AFCL,[33] the presence of hematoma,[32] normal right-sided PV anatomy,[29] hypertension,[28,37,39] number of co-morbidities,[30] non-PV ectopy,[31] early AF recurrence,[42] and MS[40]	No MA in the original CER	None	One expert noted a recent study[42] showing an early AF recurrence as a predictor of late AF recurrence		
There is insufficient evidence to show that intervention-level characteristics, such as operator experience or setting, are predictors of AF recurrence, as no study addressed this question.	**Cycle 2 (July 2012)**					Up to date	Up to date
	No new evidence	**No Signal**	NA	None	Still valid		
	Cycle 1 (November 2011)						
	1 non-RCT [43]	**No Signal** In one study,[43] ablation of DFmax sites found as a	No MA in the original CER	None	Still valid		

		protective factor against AF recurrence					
Key question 3: How does the effect of RFA on short- and long-term rhythm control differ among the various techniques or approaches used?							
PVI vs. WACA. There is a moderate level of evidence to show that WACA may result in lower rates of AF recurrence than ostial PVI in patients with either PAF or persistent AF, with followup ranging from 6 to 15 months. Five RCTs of ostial PVI vs. WACA with or without additional ablation lines compared their efficacy to maintain sinus rhythm. Only two studies reported results after a single procedure and off AADs. Both studies found that patients who had WACA had a higher rate of success (freedom from AF recurrence) than patients who had ostial PVI (67 percent vs. 49 percent, P≤0.05; 88 percent vs. 67 percent, P=0.02). Of the three studies that included patients who had reablation during followup, two reported similar findings.	**Cycle 2 (July 2012)**					Possibly out of date	Possibly out of date
	No new evidence	**No signal**	NA	None	Still valid		
	Cycle 1 (November 2011)						
	1 RCT [44] and 1 non-RCT[45]	**1 Signal (A7)** 1 non-RCT (non-pivotal study),[45] found no difference in the rates of being free from AF between PVI (non-circumferential) vs. circumferential PVI (73% vs. 73%, p=0.97) 1 RCT (non-pivotal study),[44] found significant difference in the rates of being free from AF between PVI (non-circumferential) vs. circumferential PVI (40% vs. 11%, p<0.001)	No MA in the original CER	None	Still valid		
RFA with or without additional left-sided ablation lines. There is insufficient evidence to make definitive conclusions concerning the effects of the addition of left-sided ablation lines to RFA.	**Cycle 2 (July 2012)**					Up to date	Up to date
	No new evidence	**No signal**	NA	None	Still valid		
	Cycle 1 (November 2011)						

The substantive heterogeneity of the different types of additional left-sided ablation lines that were used by the studies preclude meaningful comparisons. Six RCTs compared the efficacy of one RFA technique with vs. without the addition of left-sided ablation lines (e.g., mitral-isthmus line (MIL), roof or posterior left atrial lines). The majority of the studies reported AF recurrence rates that included patients who had reablation or were continued on AADs. Three of five studies on patients with PAF or nonparoxysmal AF found that patients who had additional left-sided ablation lines had less AF or atrial arrhythmia recurrence at followup than patients who did not (MIL 71 percent vs. 53 percent, P=0.01; roof line 87 percent vs. 69 percent, ES-6 P=0.04; MIL 74 percent vs. 83 percent, no P value reported). Two studies did not find a significant difference in AF recurrence with the addition of left-sided ablation lines.	No new evidence	**No signal**	No MA in the original CER	None	Still valid		
PVI vs. PVI with right-sided lines. There is insufficient evidence concerning the effects of adding right-sided lines on AF recurrence after RFA. One RCT examined the incremental benefit of adding a cavotricuspid isthmus ablation line in patients undergoing RFA for AF. This study, which included patients with AF and at least one episode of atrial flutter, found no significant difference in AF recurrence at 12 months followup between the group that had ostial-antral PVI and the group that had ostial-antral PVI with cavotricuspid isthmus ablation. Another RCT compared WACA with vs. without additional ablation of the superior vena cava. This study of patients with PAF found no significant difference at 12 months followup in the recurrence of atrial tachyarrhythmia between the patients who had WACA with superior vena cava ablation and the patients who had only WACA.	**Cycle 2 (July 2012)**					Up to date	Up to date
	No new evidence	**No signal**	NA	None	Still valid		
	Cycle 1 (November 2011)						
	No new evidence	**No signal**	No MA in the original CER	None	Still valid		
Different approaches in retrospective studies.	**Cycle 2 (July 2012)**					Up to date	Up to date

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There is insufficient evidence to draw conclusions from this group of retrospective studies. These observational studies compared many different approaches to RFA. They have limitations in the comparability among groups. Historical controls were used in the majority of the studies. In some instances, the proportions of patients with different types of AF differed between groups, and the length of followup also differed. None of the studies adjusted for potential confounders.	2 RCTs [13,14]	**No Signal** 2 RCTs [13,14] reported on the comparison between Following RFA techniques: Duty-cycled bipolar/unipolar vs. 3D point-by-point[13] with no significant difference in AF termination Catheter ablation vs. surgical ablation[14] with greater AF termination rate in favor of surgical ablation	NA	None	Still valid		
	Cycle 1 (November 2011)						
	7 RCTs [42,46-51] 2 non-RCTs [52,53]	**No Signal** In one RCT,[46] PVI combined with GP was significantly more beneficial for AF recurrence than PVI alone (26.5% vs. 54.5%). In another RCT,[50] anatomical LA ablation was significantly better for AF recurrence than selective GP ablation (22.5% vs. 57.5%, p=0.02). **No Signal** The remaining 7	No MA in the original CER	None	Still valid		

		studies [42,47-49,51-53] reported on the effects of comparisons between various RFA techniques (e.g., cryoballoon vs. RFA; GP-RFA vs. C-PVI; antral PVI vs. antral PVI + CFAE; hand-navigated catheter vs. RMN; all PVI vs. arrhythmogenic PVI)					
Key question 4: What are the short- and long-term complications and harms associated with RFA?							
There is a low level of evidence that adverse events associated with RFA are relatively uncommon. The level of evidence was rated low because the studies reviewed employed nonuniform definitions and assessments of adverse events. There were 84 studies that reported at least one adverse event associated with RFA. Most of the studies did not report the time of occurrence of the adverse events. Based on the study description, we surmised that most of the adverse events either took place in a peri-procedural timeframe or shortly after being discharged home postprocedure. The only exception was the diagnosis of PV stenosis, which was routinely screened for at around 3 months. Major adverse events included PV stenosis, cardiac tamponade, stroke and/or transient ischemic attack, and peripheral vascular complications such as bleeding/hematoma, pseudoaneurysm, femoral vein thrombosis, or arteriovenous fistula. Seventy-eight studies assessed the rates of asymptomatic or symptomatic PV stenosis. The majority of these studies reported asymptomatic PV stenosis rates of between 0 percent and 19 percent (median 0.3 percent); 36 studies did not identify a single case of	**Cycle 2 (July 2012)**					Up to date	Up to date
	19 studies [5-7,9,10,13-26]	**No Signal** Overall, the rates of specific complications and harms in participants receiving RFA were similar to those reported in the original CER. The overall rates of complications/major adverse events were under 7%.[9,10,15,18-20,25] <u>PV stenosis</u> < 1%[6,7,10,13,15,23] <u>Tamponade</u> ≤ 5% [6,7,9,14,15,18,21,22] <u>TIA</u> 1 (0.23%)[10] 1 (0.25%)[9] 6 (1.06%)[20]	NA	None	Still valid		

PV stenosis. Symptomatic PV stenosis requiring interventions occurred in less than 1 percent of patients in six studies. Cardiac tamponade was reported to occur in 0 percent to 5 percent (median 1 percent) of patients in the 70 studies that reported this adverse event. Cerebrovascular events were reported in 0 percent to 7 percent (median 0.9 percent) of patients in 72 studies; 19 studies reported no cerebrovascular events. Atrioesophageal fistula was reported in 26 studies: 5 studies reported 1 case each, with event rates ranging from 0.1 percent to 0.9 percent; the remainder did not identify any cases. Among 16 studies, five deaths were reported within 30 days postprocedure: one patient died from a pulmonary infection, one died from anaphylaxis after the procedure, and three died from atrioesophageal fistulas. (Three publications from the same group of investigators each reported one death from atrioesophageal fistula.) Major adverse events associated with RFA are relatively uncommon. Overall, they occurred in less than 5 percent of patients in most studies. However, it is difficult to compare the rates of adverse events across studies, as the descriptions of the various adverse events were not always comparable.		Pulmonary embolism 2 (0.35%)[20] 11 (0.7%)[19] Death <2%[6,10,14,18-20,22,25] Pericardial effusion 5 (1.5%)[17] 2 (0.43%)[23] 11 (0.73%)[5] 3 (3%)[6] Pulmonary hypertension 19 (1.4%)[23] Rate of esophageal injury 22/219 (10%)[16] Excessive transmural injury 10 (9.6%)[24]					
	Cycle 1 (November 2011)						
	13 studies [27,28,37,42,44,49,51,54-59]	**No Signal** Overall, the rates of specific complications and harms in participants receiving RFA were similar to those reported in the original CER. The rates of major adverse events in studies identified through the update search were under 5%. Symptomatic PV	No MA in the original CER	None	Still valid Two experts mentioned Cappato et al.2010 study which reported similar results		

		stenosis 18/1404 (1.28%)[28] 2/144 (1.38%)[44] Asymptomatic PV stenosis 2/41 (4.87%)[49] Tamponade 5/1404 (0.35%)[28] 1/50 (2.0%)[55] Arteriovenous fistula 1/50 (2.0%)[51] 1/53 (1.9%)[42] 1/50 (2.0%) [55] Deaths 1/106 (0.94%)[27] 1/1404 (0.07%)[28] 1/53 (1.9%)[42] 32/32569 (0.1%)[56] 30-d post-procedure n=25[56] >30-d post-procedure n=7[56] Stroke 1/232 (0.43%)[58] 6/1404 (0.4%)[28] 1/53 (1.88%)[42] 27/2488 (1.1%)[57] 12/1348 (0.9%)[57]					
CER=comparative effectiveness review; RCT=randomized controlled trial; AF=atrial fibrillation; RFA=radiofrequency catheter ablation; AAD=anti-arrhythmic drug; PAF=paroxysmal atrial fibrillation; non-PAF=non-paroxysmal atrial fibrillation; LAD=left atrial diameter; EF=ejection fraction; CAD= coronary artery disease; BMI= body mass index; LSAL= left-sided ablation lines; RSAL= right-sided ablation lines; WACA=wide area circumferential ablation; PVI=pulmonary vein isolation; DROM=derivatives of reactive oxidative metabolites; ET=endothelin; AFCL=electrocardiogram atrial fibrillation cycle length; EAT= epicardial adipose tissue; BNP= B-type natriuretic peptide; DFmax=dominant frequency of maximal sites; MS=metabolic syndrome; MA=meta-analysis; HR=hazard ratio: CHF=congestive heart disease; TRI=temporal regularity index; SRI: spacial regularity index; CKD=chronic kidney disease; HTN=hypertension; CAD=coronary artery disease							

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Published online: May 16, 2013

References

1. Ip, S., Terasawa, T., Balk, E. M., et al. Comparative effectiveness of radiofrequency catheter ablation for atrial fibrillation [Internet]. Available at: http://www.ncbi.nlm.nih.gov/books/NBK43190/. Last Accessed: 28-11-2011. [PMID:PM:20704038]

2. Shojania KG, Sampson M, Ansari MT, et al. How quickly do systematic reviews go out of date? A survival analysis. Ann Intern Med 2007 Aug 21;147(4):224-33. [PMID: PM:17638714]

3. Shekelle, P., Newberry, S., Maglione, M., et al. Assessment of the need to update comparative effectiveness reviews: Report of an initial rapid program assessment (2005–2009) [Internet]. Available at: http://www.ncbi.nlm.nih.gov/books/NBK49457/pdf/TOC.pdf. Last Accessed: 29-11-2011. [PMID:PM:21204320]

4. Shekelle, P. G., Newberry, S. J., Wu, H., et al. Identifying signals for updating systematic reviews: A comparison of two methods [Internet]. Available at: http://www.ncbi.nlm.nih.gov/books/NBK56774/. Last Accessed: 29-11-2011. [PMID:PM:21834176]

5. Mohanty S, Mohanty P, Di BL, et al. Impact of metabolic syndrome on procedural outcomes in patients with atrial fibrillation undergoing catheter ablation. J Am Coll Cardiol 2012 Apr 3;59(14):1295-301. [PMID: 22464257]

6. Weerasooriya R, Khairy P, Litalien J, et al. Catheter ablation for atrial fibrillation: are results maintained at 5 years of follow-up? J Am Coll Cardiol 2011 Jan 11;57(2):160-6. [PMID: 21211687]

7. Chao TF, Cheng CC, Lin WS, et al. Associations among the CHADS(2) score, atrial substrate properties, and outcome of catheter ablation in patients with paroxysmal atrial fibrillation. Heart Rhythm 2011 Aug;8(8):1155-9. [PMID: 21402172]

8. Forclaz A, Narayan SM, Scherr D, et al. Early temporal and spatial regularization of persistent atrial fibrillation predicts termination and arrhythmia-free outcome. Heart Rhythm 2011 Sep;8(9):1374-82. [PMID: 21699850]

9. Rostock T, Salukhe TV, Steven D, et al. Long-term single- and multiple-procedure outcome and predictors of success after catheter ablation for persistent atrial fibrillation. Heart Rhythm 2011 Sep;8(9):1391-7. [PMID: 21699825]

10. Winkle RA, Mead RH, Engel G, et al. Relation of early termination of persistent atrial fibrillation by cardioversion or drugs to ablation outcomes. Am J Cardiol 2011 Aug 1;108(3):374-9. [PMID: 21600534]

11. Hu YF, Yeh HI, Tsao HM, et al. Impact of circulating monocyte CD36 level on atrial fibrillation and subsequent catheter ablation. Heart Rhythm 2011 May;8(5):650-6. [PMID: 21195211]

12. Naruse Y, Tada H, Sekiguchi Y, et al. Concomitant chronic kidney disease increases the recurrence of atrial fibrillation after catheter ablation of atrial fibrillation: a mid-term follow-up. Heart Rhythm 2011 Mar;8(3):335-41. [PMID: 21056121]

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Published online: May 16, 2013

13. Bittner A, Monnig G, Zellerhoff S, et al. Randomized study comparing duty-cycled bipolar and unipolar radiofrequency with point-by-point ablation in pulmonary vein isolation. Heart Rhythm 2011 Sep;8(9):1383-90. [PMID: 21457793]

14. Boersma LV, Castella M, van BW, et al. Atrial fibrillation catheter ablation versus surgical ablation treatment (FAST): a 2-center randomized clinical trial. Circulation 2012 Jan 3;125(1):23-30. [PMID: 22082673]

15. Hoyt H, Bhonsale A, Chilukuri K, et al. Complications arising from catheter ablation of atrial fibrillation: temporal trends and predictors. Heart Rhythm 2011 Dec;8(12):1869-74. [PMID: 21798230]

16. Contreras-Valdes FM, Heist EK, Danik SB, et al. Severity of esophageal injury predicts time to healing after radiofrequency catheter ablation for atrial fibrillation. Heart Rhythm 2011 Dec;8(12):1862-8. [PMID: 21782773]

17. Mohanty S, Mohanty P, Di BL, et al. Influence of body mass index on quality of life in atrial fibrillation patients undergoing catheter ablation. Heart Rhythm 2011 Dec;8(12):1847-52. [PMID: 21740879]

18. Shah RU, Freeman JV, Shilane D, et al. Procedural complications, rehospitalizations, and repeat procedures after catheter ablation for atrial fibrillation. J Am Coll Cardiol 2012 Jan 10;59(2):143-9. [PMID: 22222078]

19. Bohnen M, Stevenson WG, Tedrow UB, et al. Incidence and predictors of major complications from contemporary catheter ablation to treat cardiac arrhythmias. Heart Rhythm 2011 Nov;8(11):1661-6. [PMID: 21699857]

20. Chao TF, Lin YJ, Tsao HM, et al. CHADS(2) and CHA(2)DS(2)-VASc scores in the prediction of clinical outcomes in patients with atrial fibrillation after catheter ablation. J Am Coll Cardiol 2011 Nov 29;58(23):2380-5. [PMID: 22115643]

21. Yokokawa M, Sundaram B, Garg A, et al. Impact of mitral isthmus anatomy on the likelihood of achieving linear block in patients undergoing catheter ablation of persistent atrial fibrillation. Heart Rhythm 2011 Sep;8(9):1404-10. [PMID: 21699839]

22. Winkle RA, Mead RH, Engel G, et al. The use of a radiofrequency needle improves the safety and efficacy of transseptal puncture for atrial fibrillation ablation. Heart Rhythm 2011 Sep;8(9):1411-5. [PMID: 21699841]

23. Gibson DN, Di BL, Mohanty P, et al. Stiff left atrial syndrome after catheter ablation for atrial fibrillation: clinical characterization, prevalence, and predictors.[Erratum appears in Heart Rhythm. 2011 Nov;8(11):1828]. Heart Rhythm 2011 Sep;8(9):1364-71. [PMID: 21354332]

24. Yamasaki H, Tada H, Sekiguchi Y, et al. Prevalence and characteristics of asymptomatic excessive transmural injury after radiofrequency catheter ablation of atrial fibrillation. Heart Rhythm 2011 Jun;8(6):826-32. [PMID: 21315839]

25. Winkle RA, Mead RH, Engel G, et al. Safety of lower activated clotting times during atrial fibrillation ablation using open irrigated tip catheters and a single

transseptal puncture. Am J Cardiol 2011 Mar 1;107(5):704-8. [PMID: 21185007]

26. Guglin M, Chen R, Curtis AB. Sinus rhythm is associated with fewer heart failure symptoms: insights from the AFFIRM trial. Heart Rhythm 2010 May;7(5):596-601. [PMID: 20159046]

27. Wilber DJ, Pappone C, Neuzil P, et al. Comparison of antiarrhythmic drug therapy and radiofrequency catheter ablation in patients with paroxysmal atrial fibrillation: a randomized controlled trial. JAMA 2010 Jan 27;303(4):333-40. [PMID: 20103757]

28. Bhargava M, Di BL, Mohanty P, et al. Impact of type of atrial fibrillation and repeat catheter ablation on long-term freedom from atrial fibrillation: results from a multicenter study. Heart Rhythm 2009 Oct;6(10):1403-12. [PMID: 19716348]

29. den Uijl DW, Tops LF, Delgado V, et al. Effect of pulmonary vein anatomy and left atrial dimensions on outcome of circumferential radiofrequency catheter ablation for atrial fibrillation. Am J Cardiol 2011 Jan 15;107(2):243-9. [PMID: 21211601]

30. Helms AS, West JJ, Patel A, et al. Relation of left atrial volume from three-dimensional computed tomography to atrial fibrillation recurrence following ablation. Am J Cardiol 2009 Apr 1;103(7):989-93. [PMID: 19327428]

31. Lo LW, Tai CT, Lin YJ, et al. Predicting factors for atrial fibrillation acute termination during catheter ablation procedures: implications for catheter ablation strategy and long-term outcome. Heart Rhythm 2009 Mar;6(3):311-8. [PMID: 19251203]

32. Patel D, Mohanty P, Di BL, et al. Outcomes and complications of catheter ablation for atrial fibrillation in females. Heart Rhythm 2010;7(2):167-72. [PMID: 20022814]

33. Matsuo S, Lellouche N, Wright M, et al. Clinical predictors of termination and clinical outcome of catheter ablation for persistent atrial fibrillation. J Am Coll Cardiol 2009 Aug 25;54(9):788-95. [PMID: 19695455]

34. Hussein AA, Saliba WI, Martin DO, et al. Plasma B-type natriuretic peptide levels and recurrent arrhythmia after successful ablation of lone atrial fibrillation. Circulation 2011 May 17;123(19):2077-82. [PMID: 21536999]

35. Tsao HM, Hu WC, Wu MH, et al. Quantitative analysis of quantity and distribution of epicardial adipose tissue surrounding the left atrium in patients with atrial fibrillation and effect of recurrence after ablation. Am J Cardiol 2011 May 15;107(10):1498-503. [PMID: 21414593]

36. Wong CX, Abed HS, Molaee P, et al. Pericardial fat is associated with atrial fibrillation severity and ablation outcome. J Am Coll Cardiol 2011 Apr 26;57(17):1745-51. [PMID: 21511110]

37. Sawhney N, Anousheh R, Chen WC, et al. Five-year outcomes after segmental pulmonary vein isolation for paroxysmal atrial fibrillation. Am J Cardiol 2009 Aug 1;104(3):366-72. [PMID: 19616669]

38. Shimano M, Shibata R, Inden Y, et al. Reactive oxidative metabolites are associated with atrial conduction disturbance in patients with atrial

fibrillation. Heart Rhythm 2009 Jul;6(7):935-40. [PMID: 19560081]

39. Nakazawa Y, Ashihara T, Tsutamoto T, et al. Endothelin-1 as a predictor of atrial fibrillation recurrence after pulmonary vein isolation. Heart Rhythm 2009 Jun;6(6):725-30. [PMID: 19467500]

40. Chang SL, Tuan TC, Tai CT, et al. Comparison of outcome in catheter ablation of atrial fibrillation in patients with versus without the metabolic syndrome. Am J Cardiol 2009 Jan 1;103(1):67-72. [PMID: 19101232]

41. Takahashi Y, O'Neill MD, Hocini M, et al. Characterization of electrograms associated with termination of chronic atrial fibrillation by catheter ablation. J Am Coll Cardiol 2008 Mar 11;51(10):1003-10. [PMID: 18325439]

42. Dixit S, Gerstenfeld EP, Ratcliffe SJ, et al. Single procedure efficacy of isolating all versus arrhythmogenic pulmonary veins on long-term control of atrial fibrillation: a prospective randomized study. Heart Rhythm 2008 Feb;5(2):174-81. [PMID: 18242535]

43. Atienza F, Almendral J, Jalife J, et al. Real-time dominant frequency mapping and ablation of dominant frequency sites in atrial fibrillation with left-to-right frequency gradients predicts long-term maintenance of sinus rhythm. Heart Rhythm 2009 Jan;6(1):33-40. [PMID: 19121797]

44. Elayi CS, Verma A, Di BL, et al. Ablation for longstanding permanent atrial fibrillation: results from a randomized study comparing three different strategies. Heart Rhythm 2008 Dec;5(12):1658-64. [PMID: 19084800]

45. Sy RW, Gula LJ, Leong-Sit P, et al. Complete antral encirclement is not required for pulmonary vein isolation. Heart Rhythm 2011 Jan;8(1):16-22. [PMID: 20884380]

46. Katritsis DG, Giazitzoglou E, Zografos T, et al. Rapid pulmonary vein isolation combined with autonomic ganglia modification: a randomized study. Heart Rhythm 2011 May;8(5):672-8. [PMID: 21199686]

47. Tamborero D, Mont L, Berruezo A, et al. Circumferential pulmonary vein ablation: does use of a circular mapping catheter improve results? A prospective randomized study. Heart Rhythm 2010 May;7(5):612-8. [PMID: 20193794]

48. Kuhne M, Suter Y, Altmann D, et al. Cryoballoon versus radiofrequency catheter ablation of paroxysmal atrial fibrillation: biomarkers of myocardial injury, recurrence rates, and pulmonary vein reconnection patterns. Heart Rhythm 2010 Dec;7(12):1770-6. [PMID: 20817019]

49. Khan MN, Jais P, Cummings J, et al. Pulmonary-vein isolation for atrial fibrillation in patients with heart failure. N Engl J Med 2008 Oct 23;359(17):1778-85. [PMID: 18946063]

50. Pokushalov E, Romanov A, Shugayev P, et al. Selective ganglionated plexi ablation for paroxysmal atrial fibrillation. Heart Rhythm 2009 Sep;6(9):1257-64. [PMID: 19656736]

51. Oral H, Chugh A, Yoshida K, et al. A randomized assessment of the incremental role of ablation of complex fractionated atrial electrograms after antral pulmonary vein isolation for long-lasting persistent atrial fibrillation. J Am

Coll Cardiol 2009 Mar 3;53(9):782-9. [PMID: 19245970]

52. Katsiyiannis WT, Melby DP, Matelski JL, et al. Feasibility and safety of remote-controlled magnetic navigation for ablation of atrial fibrillation. Am J Cardiol 2008 Dec 15;102(12):1674-6. [PMID: 19064022]

53. Katritsis D, Giazitzoglou E, Sougiannis D, et al. Anatomic approach for ganglionic plexi ablation in patients with paroxysmal atrial fibrillation. Am J Cardiol 2008 Aug 1;102(3):330-4. [PMID: 18638596]

54. Martinek M, Hassanein S, Bencsik G, et al. Acute development of gastroesophageal reflux after radiofrequency catheter ablation of atrial fibrillation. Heart Rhythm 2009 Oct;6(10):1457-62. [PMID: 19716773]

55. Scharf C, Boersma L, Davies W, et al. Ablation of persistent atrial fibrillation using multielectrode catheters and duty-cycled radiofrequency energy. J Am Coll Cardiol 2009 Oct 6;54(15):1450-6. [PMID: 19796739]

56. Cappato R, Calkins H, Chen SA, et al. Prevalence and causes of fatal outcome in catheter ablation of atrial fibrillation. J Am Coll Cardiol 2009 May 12;53(19):1798-803. [PMID: 19422987]

57. Di Biase L, Burkhardt JD, Mohanty P, et al. Periprocedural stroke and management of major bleeding complications in patients undergoing catheter ablation of atrial fibrillation: the impact of periprocedural therapeutic international normalized ratio. Circulation 2010 Jun 15;121(23):2550-6. [PMID: 20516376]

58. Gaita F, Caponi D, Pianelli M, et al. Radiofrequency catheter ablation of atrial fibrillation: a cause of silent thromboembolism? Magnetic resonance imaging assessment of cerebral thromboembolism in patients undergoing ablation of atrial fibrillation. Circulation 2010 Oct 26;122(17):1667-73. [PMID: 20937975]

59. Martinek M, Meyer C, Hassanein S, et al. Identification of a high-risk population for esophageal injury during radiofrequency catheter ablation of atrial fibrillation: procedural and anatomical considerations. Heart Rhythm 2010 Sep;7(9):1224-30. [PMID: 20188859]

60. Wissner E, Tilz R, Konstantinidou M, et al. Catheter ablation of atrial fibrillation in patients with persistent left superior vena cava is associated with major intraprocedural complications. Heart Rhythm 2010 Dec;7(12):1755-60. [PMID: 20708711]

Appendix A: Search Methodology

All MEDLINE searches were limited to the following journals:

General biomedical – Annals of Internal Medicine, BMJ, JAMA, Lancet, and New England Journal of Medicine

Specialty journals – Circulation, Heart Rhythm, Am J Cardiol, and Journal of the American College of Cardiology

Database: MEDLINE

Cycle 2 (2nd assessment)

Time period covered: March 20, 2011- June 5, 2012

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present> Search Strategy:

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1 atrial fibrillation.mp. or exp Atrial Fibrillation/ (39540)
2 pulmonary vein$.mp. or exp Pulmonary Veins/ (12678)
3 1 or 2 (49153)
4 exp Catheter Ablation/ or radiofrequency ablation.mp. (19390)
5 radiofrequency catheter ablation.mp. or exp Catheter Ablation/ (18053)
6 ablation.mp. (51708)
7 radiofrequency.mp. (17678)
8 (catheter adj ablation).mp. (19015)
9 or/4-8 (57563)
10 3 and 9 (6481)
11 limit 10 to human (5812)
12 limit 11 to yr="2008 -Current" (2562)
13 limit 12 to (addresses or bibliography or biography or case reports or comment or editorial or lectures or legal cases or letter or news or newspaper article or "review") (1068)
14 12 not 13 (1494)
15 jama.jn. (62284)
16 "annals of internal medicine".jn. (27329)
17 bmj.jn. (73258)
18 "new england journal of medicine".jn. (65341)
19 lancet.jn. (122133)
20 circulation.jn. (36922)
21 Heart Rhythm.jn. (2920)
22 american journal of cardiology.jn. (31914)
23 "journal of the american college of cardiology".jn. (18507)
24 or/15-23 (440608)
25 14 and 24 (252)
26 (2011032* or 2011033* or 201104* or 201105* or 201106* or 201107* or 201108* or 201109* or 201110* or 201111* or 201112* or 2012*).ed. (1167673)
27 25 and 26 (92)

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Database: MEDLINE

Cycle 1 (1st assessment)

Time period covered: 01 January 2008 to September 23, 2011

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present> Search Strategy:

1 atrial fibrillation.mp. or exp Atrial Fibrillation/ (37642)
2 pulmonary vein$.mp. or exp Pulmonary Veins/ (12419)
3 1 or 2 (47231)
4 exp Catheter Ablation/ or radiofrequency ablation.mp. (18224)
5 radiofrequency catheter ablation.mp. or exp Catheter Ablation/ (17017)
6 ablation.mp. (49330)
7 radiofrequency.mp. (16716)
8 (catheter adj ablation).mp. (17952)
9 or/4-8 (54892)
10 3 and 9 (5992)
11 limit 10 to human (5386)
12 limit 11 to yr="2008 -Current" (2103)
13 limit 12 to (addresses or bibliography or biography or case reports or comment or editorial or lectures or legal cases or letter or news or newspaper article or "review") (881)
14 12 not 13 (1222)
15 jama.jn. (61339)
16 "annals of internal medicine".jn. (26749)
17 bmj.jn. (51763)
18 "new england journal of medicine".jn. (64179)
19 lancet.jn. (120502)
20 circulation.jn. (36447)
21 Heart Rhythm.jn. (2725)
22 american journal of cardiology.jn. (31517)
23 "journal of the american college of cardiology".jn. (18034)
24 or/15-23 (413255)
25 14 and 24 (214)

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Database: Cochrane Central Register of Clinical Trials

Cycle 2 (2nd assessment)

Date of search: June 3, 2012

ID	Search	Hits	Edit	Delete
#1	MeSH descriptor **Atrial Fibrillation** explode all trees	2161	edit	delete
#2	"atrial fibrillation":ti,ab,kw	3351	edit	delete
#3	MeSH descriptor **Pulmonary Veins** explode all trees	194	edit	delete
#4	pulmonary NEXT vein*:ti,ab,kw	283	edit	delete
#5	(#1 OR #2 OR #3 OR #4)	3413	edit	delete
#6	MeSH descriptor **Catheter Ablation** explode all trees	915	edit	delete
#7	"radiofrequency ablation" or "radiofrequency catheter ablation":ti,ab,kw	465	edit	delete
#8	ablation or radiofrequency:ti,ab,kw	2759	edit	delete
#9	catheter NEXT ablation:ti,ab,kw	965	edit	delete
#10	(#6 OR #7 OR #8 OR #9)	2759	edit	delete
#11	(#5 AND #10)	420	edit	delete
#12	(#11), from 2008 to 2011	204	edit	delete
#13	(#12), from 2011 to 2012	38	edit	delete

CENTRAL – 29, *after journal selection – 5 records*

Only CENTRAL was part of original strategy

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Database: Cochrane Central Register of Clinical Trials

Cycle 1 (1st assessment)

Date of search: September 22, 2011

#1	MeSH descriptor Atrial Fibrillation explode all trees (2014)
#2	"atrial fibrillation":ti,ab,kw (3159)
#3	MeSH descriptor Pulmonary Veins explode all trees (176)
#4	pulmonary NEXT vein*:ti,ab,kw (253)
#5	(#1 OR #2 OR #3 OR #4) (3221)
#6	MeSH descriptor Catheter Ablation explode all trees (846)
#7	"radiofrequency ablation" or "radiofrequency catheter ablation":ti,ab,kw (400)
#8	ablation or radiofrequency:ti,ab,kw (2542)
#9	catheter NEXT ablation:ti,ab,kw (890)
#10	(#6 OR #7 OR #8 OR #9) (2542)
#11	(#5 AND #10) (377)
#12	(#11), from 2008 to 2011(164)

Reduced to 11 records based on selected journals

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Appendix B: Updating Signals

Qualitative signals*

Potentially invalidating change in evidence

This category of signals (A1-A3) specifies findings from a pivotal trial**, meta-analysis (with at least one new trial), practice guideline (from major specialty organization or published in peer-reviewed journal), or recent textbook (e.g., *UpToDate*):

- Opposing findings (e.g., effective vs. ineffective) – **A1**
- Substantial harm (e.g., the risk of harm outweighs the benefits) – **A2**
- A superior new treatment (e.g., new treatment that is significantly superior to the one assessed in the original CER) – **A3**

Major change in evidence

This category of signals (A4-A7) refers to situations in which there is a clear potential for the new evidence to affect the clinical decision making. These signals, except for one (A7), specify findings from a pivotal trial, meta-analysis (with at least one new trial), practice guideline (from major specialty organization or published in peer-reviewed journal), or recent textbook (e.g., *UpToDate*):

- Important changes in effectiveness short of "opposing findings" – **A4**
- Clinically important expansion of treatment (e.g., to new subgroups of subjects) – **A5**
- Clinically important caveat – **A6**
- Opposing findings from meta-analysis (in relation to a meta-analysis in the original CER) or non-pivotal trial – **A7**

* Please, see Shojania et al. 2007[2] for further definitions and details

**A pivotal trial is defined as: 1) a trial published in top 5 general medical journals such as: Lancet, JAMA, Annals of Intern Med, BMJ, and NEJM. Or 2) a trial not published in the above top 5 journals but have a sample size of at least triple the size of the previous largest trial in the original CER.

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Appendix B: Updating Signals (Continued)

Quantitative signals (B1-B2)*

Change in statistical significance (B1)

Refers to a situation in which a statistically significant result in the original CER is now NOT statistically significant or vice versa- that is a previously non-significant result become statistically significant. For the 'borderline' changes in statistical significance, at least one of the reports (the original CER or new updated meta-analysis) must have a p-value outside the range of border line (0.04 to 0.06) to be considered as a quantitative signal for updating.

Change in effect size of at least 50% (B2)

Refers to a situation in which the new result indicates a relative change in effect size of at least 50%. For example, if relative risk reduction (RRR) new / RRR old <=0.5 or RRR new / RRR old >=1.5. Thus, if the original review has found RR=0.70 for mortality, this implies RRR of 0.3. If the updated meta-analytic result for mortality were 0.90, then the updated RRR would be 0.10, which is less than 50% of the previous RRR. In other words the reduction in the risk of death has moved from 30% to 10%. The same criterion applied for odds ratios (e.g., if previous OR=0.70 and updated result were OR=0.90, then the new reduction in odds of death (0.10) would be less 50% of the magnitude of the previous reduction in odds (0.30). For risk differences and weighted mean differences, we applied the criterion directly to the previous and updated results (e.g., RD new / RD old <=0.5 or RD new / RD old >=1.5).

* Please, see Shojania et al. 2007[2] for further definitions and details

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Appendix C: Evidence Table

Author year Study name (if applicable)	Study design	Subjects	Treatment groups (n; dose)	Treatment duration	Outcomes and findings
Key Question # 1: What is the effect of RFA on short-term (6 to 12 months) and long-term (>12 months) rhythm control, rates of congestive heart failure, left atrial and ventricular size changes, rates of stroke, quality of life, avoiding anticoagulation, and readmissions for persistent, paroxysmal, and long-standing persistent (chronic) atrial fibrillation?					
Cycle 2					
No new evidence	NA	NA	NA	NA	NA
Cycle 1					
Wilber 2010[60]	RCT	167 pts with symptomatic AF (at least 3 episodes within 6 mo before randomization) not responding to at least one AAD; Mean age: 55 yrs; Male: 66%	RFA (n=106) vs. AAD (n=61; dose: NR)	3 months (AAD)	RFA vs. AAD (FU=9 mo) **Symptomatic paroxysmal AF** 34% vs. 84%, p=NR (HR=0.30, 95% CI: 0.19, 0.47) **Symptomatic recurrent AF** 30% vs. 81%, p=NR (HR=0.24, 95% CI: 0.15, 0.39) **Any recurrent AF** 37% vs. 83%, p=NR (HR=0.29, 95% CI: 0.18, 0.45) **QOL (SF-36 mental)** MD=6.9, 95% CI: 2.6, 11.2 (favors RFA) **QOL (SF-36 physical)** MD=6.6, 95% CI: 3.6, 9.4 (favors RFA) **Major AEs** 5/103 (4.9%) vs. 5/57 (8.8%), p=NR
Key question # 2: What are the patient-level and intervention-level characteristics associated with RFA effect on short- and long-term rhythm control?					
Cycle 2					
Mohanty 2012[5]	Non-RCT	1496 pts with AF undergoing first ablation (29% PAF, 26% persistent AF, 45%	RFA (n=1496; circular mapping catheter and a 3.5-mm open-irrigation-tip catheter)	NA	**AF recurrence** (FU=21 mo) MS vs. no MS 189 (39%) vs. 319 (32%), p=0.005

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Author year Study name (if applicable)	Study design	Subjects	Treatment groups (n; dose)	Treatment duration	Outcomes and findings
		long-standing persistent AF); mean age: 62 yrs; male: 73.6%			(MS as a predictor of AF recurrence) Stratification by type of AF(MS vs. no MS) NPAF: 150 (46%) vs. 257 (35%), p=0.002 PAF: 39 (25%) vs. 62 (22%), p=0.295 (MS as a predictor of AF recurrence in NPAF but not PAF patients) **QOL-**(FU=12 mo) MS group Improvement in mean SFA-mental component summary score 5.7 (p<0.001) and SFA-physical component summary score 9.1 (p<0.001) No MS group Improvement in mean SFA-mental component summary score only 4.6 (p<0.036) (MS as a predictor of improvement in QOL when compared to 'no MS')
Weerasooriya 2011[6]	Non-RCT	100 pts with AF undergoing first ablation (63% PAF, 22% persistent AF, 14% long-standing persistent AF); mean age: 55.7 yrs; male: 86.0%	RFA (n=100; a steerable quadripolar catheter 2-5-2 mm)	NA	**AF recurrence** (FU=60 mo) Long-standing persistent AF vs. PAF (or persistent AF) HR=1.90, 95% CI: 1.00, 3.50 (type of AF - long-standing persistent AF as a predictor of AF recurrence)
Chao 2011[7]	Non-RCT	247 pts with symptomatic drug-refractory PAF undergoing first ablation; mean age: 52.8 yrs; male: 72.0%	RFA (n=247; 4 mm tip or internal irrigated-tip catheter)	NA	**AF recurrence** (FU=17 mo) $CHADS_2 \geq 3$ vs. $CHADS_2 = 1\text{-}2$ vs. $CHADS_2 = 0$ 17 (45.9%) vs. 24 (27.6%) vs. 16 (13.0%), p<0.01 ($CHADS_2$ score ≥ 3 as a predictor of AF recurrence)
Forclaz 2011[8]	Non-RCT	75 pts with persistent AF undergoing first ablation; mean age: 58	RFA-PVI (n=75; 3.5 mm externally irrigated-tip catheter)	NA	**AF termination** (FU=36 mo) AF termination vs. no AF termination

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Author year Study name (if applicable)	Study design	Subjects	Treatment groups (n; dose)	Treatment duration	Outcomes and findings
		yrs; male: 85.3%			TRI: 119% (SD 23) vs. 98% (SD 15), p<0.001 [UVA] (Increased TRI as a predictor of AF termination) SRI: 111% (SD 12) vs. 94% (SD 17), p<0.01[UVA] (Increased SRI as a predictor of AF termination) LVEDD: 52% (SD 6) vs. 59% (SD 7), p=0.005 [UVA] (Decreased LVEDD as a predictor of AF termination) OR=14.1, 95% CI: 2.9, 68.5 [MVA] (101% increased TRI from baseline as a predictor of AF termination) OR=4.8, 95% CI: 1.0, 22.7 [MVA] (Absence of hypertension as a predictor of AF termination)
Rostock 2011[9]	Non-RCT	395 pts with persistent AF undergoing first ablation; mean age: 61 yrs; male: 83.0%	RFA-PVI (n=395; steerable decapolar catheter, circumferential decapolar diagnostic catheter, nonsteerable quadripolar diagnostic catheter, and 3.5 mm external irrigated-tip ablation catheter)	NA	**AF recurrence** (FU=27 mo) AF recurrence vs. no AF recurrence Female gender: HR=0.092, 95% CI: 0.022, 0.386 (female gender as a protective factor against AF recurrence, i.e., predictor of AF termination) AFCL at baseline: HR=0.983, 95% CI: 0.977, 0.989 (longer baseline AFCL as a protective factor against AF recurrence, i.e., predictor of AF termination) AF termination during the index procedure: HR=0.280, 95% CI: 0.185, 0.425 (AF termination during the index procedure as a protective factor against AF recurrence, i.e., predictor of AF termination) Duration of AF>6 mo: HR=1.644, 95% CI: 1.210, 2.235 (AF>6 mo as a predictor of AF recurrence) Congestive heart failure: HR=10.903, 95% CI: 2.602, 45.694 (presence of congestive heart failure as a predictor of AF recurrence)
Winkle 2011[10]	Non-RCT	423 pts with persistent AF (lasting from 1week	Circumferential RFA-PVI and LA roof line	NA	**AF recurrence** (FU=36 mo)

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Author year Study name (if applicable)	Study design	Subjects	Treatment groups (n; dose)	Treatment duration	Outcomes and findings
		to 1 year); mean age: 62 yrs; male: 75.0%	(n=423; 3.5mm irrigated-tip catheter)		AF terminated by electrical/pharmacological means in <1 week vs. AF that lasted from 1 week to 1 year: 25% vs. 36%, p=0.042 HR=1.45, 95% CI: 1.06, 1.98 [MVA] (LA size as a predictor of AF recurrence) HR=1.67, 95% CI: 1.34, 3.05 [MVA] (female gender as a predictor of AF recurrence) HR=0.58, 95% CI: 0.36, 0.94 [MVA] (absence of coronary disease as a protective factor against AF recurrence) Age (p=0.14), body mass index (p=0.93), duration of AF (p=0.32), hypertension (p=0.67) , or diabetes (p=0.90) did not significantly predict AF recurrence [MVA]
Hu 2011[11]	Non-RCT	87 pts with AF (PAF 78% and persistent/permanent AF 22%); mean age: 55 yrs; male: 73.6%	NR	NA	**AF termination** (FU=12 mo) Monocyte CD36FL > 200 vs. Monocyte CD36FL ≤ 200 20/25 (80%) vs. 29/54 (53.7%), p=0.02 [KMA] (monocyte CD36FL > 200 units as a protective factor against AF recurrence, i.e., predictor of AF termination)
Naruse 2011[12]	Non-RCT	221 pts with drug-refractory AF (PAF 58%); mean age: 59 yrs; male: 81%	RFA-PVI (n=221; 7F quadripolar catheter with 8mm distal electrode and deflectable tip)	NA	**AF recurrence** (FU=32 mo) CKD (eGFR<60mL/min) vs. no CKD (eGFR≥60mL/min) 57.4% vs. 33.5%, p<0.01 HR=2.05, 95% CI: 1.32, 3.19 [KMA] HR=2.09, 95% CI: 1.29, 3.38 [MVA] (presence of CKD as a predictor of AF recurrence) HR=1.009, 95% CI: 1.002, 1.017 [MVA] (LA volume as a predictor of AF recurrence) Age (p=0.37), persistent AF (p=0.08), male gender (p=0.25) , LVMI (p=0.21), or LVEF (p=0.43) did not significantly predict AF recurrence [MVA]
Cycle 1					

Author year Study name (if applicable)	Study design	Subjects	Treatment groups (n; dose)	Treatment duration	Outcomes and findings
Patel 2010[32]	Non-RCT	3265 pts highly symptomatic and drug-refractory AF; Mean age: 57.5 yrs; Male: 84%	RFA (n=3265; circular mapping catheter and a 3.5-mm open-irrigation-tip catheter)	NA	**Ablation failure** (FU=12+ mo) 31.5% vs. 22.5% p=0 .001 (female gender as a predictor for ablation failure) 11 (2.1%) vs. 27 (0.9%), p=NR (hematomas as a predictor for ablation failure)
Hussein 2011[34]	Non-RCT	726 pts with lone AF ; Mean age: 56.9 yrs; Male: 70.7%	RFA (n=726)	NA	**Recurrent AF** (FU= 24 mo) HR=1.6 (2nd quintile vs. lowest quintile) HR=2.7 (3rd quintile vs. lowest quintile) HR=4.3 (4th quintile vs. lowest quintile) HR=5.7 (5th quintile vs. lowest quintile) (increased BNP level as a predictor of recurrent AF; test for trend p<0.001)
Tsao 2011[35]	Non-RCT	68 pts with AF and 34 controls; Mean age: 55 yrs; Male: 76%	RFA (n=68)	NA	**AF recurrence** (FU= 3 mo) Increased EAT volume as a predictor of AF recurrence, p = 0.038 (MVA)
Wong 2011[36]	Non-RCT	100 AF patients & 20 controls; Mean age: 58 yrs; Male: 76%	RFA (n=100)	NA	**AF recurrence** (FU= 24 mo) OR=1.71, 95% CI: 0.79, 2.64 (pericardial fat level as a predictor of AF recurrence)
Uijl 2011[29]	Non-RCT	100 pts with AF (paroxysmal 72%, persistent 28%); Mean age: 56 yrs; Male: 77%	Circumferential RFA (n=100)	NA	**AF recurrence** (FU=12 mo) OR= 1.08, p = 0.027 (anteroposterior LA diameter as a predictor of AF recurrence) OR= 6.71, p =0.006 (normal right-sided PV anatomy as a predictor of AF recurrence)
Bhargava 2009[28]	Non-RCT	1404 pts with symptomatic drug resistant AF; Mean age: 56 yrs; Male: 76%	RFA (n=1404)	NA	**Primary AF recurrence** (FU=59 mo) HR=1.53, 95% CI: 1.15, 2.03 (NPAF as predictor of AF recurrence; MVA) HR=1.30, 95% CI: 1.01, 1.67 (LA size > 40 mm as predictor of AF recurrence; MVA) **Secondary AF recurrence** (FU=59 mo) HR=2.19, 95% CI: 1.08, 4.46 (female gender as predictor of secondary AF recurrence; MVA)

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Author year Study name (if applicable)	Study design	Subjects	Treatment groups (n; dose)	Treatment duration	Outcomes and findings
					HR=2.13, 95% CI: 1.11, 4.10 (hypertension as predictor of secondary AF recurrence; MVA)
Matsuo 2009[33]	Non-RCT	90 pts with persistent AF; Mean age: 57 yrs; Male: 84.4%	RFA (n=90)	NA	**AF presence** (FU=28 mo) HR=0.93, 95% CI: 0.88, 0.98 (ECG AFCL > 142 mc as a protective factor against AF; MVA) **AF recurrence** (FU=28 mo) HR=6.0, 95% CI: 2.0, 18.5 (ECG AFCL < 142 mc as a predictor of AF recurrence; MVA) HR=0.13, 95% CI: 0.06, 0.51 (AF duration < 21 mo as a protective factor against AF recurrence; MVA)
Sawhney 2009[37]	Non-RCT	71 pts with paroxysmal AF; Mean age: 60 yrs; Male: 79%	PVI (n=71)	NA	**AF recurrence** (FU=60 mo) HR=2.9, 95% CI: 2.6, 3.1 (hypertension as predictor of AF recurrence; MVA)
Shimano 2009[38]	Non-RCT	306 pts with AF (225 paroxysmal and 81 persistent); Mean age: 59 yrs; Male: 74%	RFA (n=306)	NA	**AF recurrence** (FU=12+ mo) High DROM levels (> 355 Carr units) as a predictor of AF recurrence, p<0.05; KMA
Nakazava 2009[39]	Non-RCT	51 pts with symptomatic and drug-refractory paroxysmal or persistent AF; Mean age: 58 yrs; Male: 88%	PVI (n=75)	NA	**AF recurrence** (FU=6 mo) OR=8.71, p<0.01 (plasma ET-1 level>1.68 pg/ml as a predictor of AF recurrence; MVA) OR=6.10, p<0.05 (diastolic blood pressure as a predictor of AF recurrence; MVA)
Helms 2009[30]	Non-RCT	73 pts with AF (52 paroxysmal and 21 persistent); Mean age: 56 yrs; Male: 82%	C-PVI (n=73)	NA	**AF recurrence** (FU=12 mo) OR=7.6, 95% CI: 1.1, 53.0 (LA volume> 135 ml as a predictor of AF recurrence; MVA) OR=NR, p=0.03 (total number of co-morbidities as a predictor of AF recurrence; MVA)
Lo 2009[31]	Non-RCT	85 pts with AF (33 PAF and 52 NPAF); Mean age: 53 yrs; Male: 79%	Stepwise: C-PVI, LA linear ablation, LA/RA ECG-based ablation (n=85)	NA	**AF termination** (FU=13 mo) AF termination vs. No AF termination 38(5) vs. 44(8); smaller LA diameter [mm] as a protective factor against AF, MVA, p=0.037

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Author year Study name (if applicable)	Study design	Subjects	Treatment groups (n; dose)	Treatment duration	Outcomes and findings
					5.8(0.6) vs. 6.8(0.9); lower RA-DF [Hz] as a protective factor against AF, MVA, p=0.009 **AF recurrence** (FU=13 mo) AF recurrence vs. No AF recurrence 44(8) vs. 39(6); larger LA diameter as a predictor of AF recurrence, MVA, p=0.02 6(24%) vs. 2(3%); the presence of RA non-PV ectopy as a predictor of AF recurrence, MV, p=0.03
Atienza 2009[43]	Non-RCT	50 pts with AF (32 PAF and 18 persistent); Mean age: 52 yrs; Male: 74%	RFA (n=50)	NA	**AF recurrence** (FU=9.3 mo) OR=0.14, 95% CI: 0.025, 0.833 (ablation of DFmax sites as a protective factor against AF recurrence, MVA) OR=0.051, 95% CI: 0.008, 0.338 (PAF as a protective factor against AF recurrence, MVA)
Chang 2009[40]	Non-RCT	282 pts with drug-refractory AF (216 PAF and 66 NPAF); Mean age: 51 yrs; Male: 75%	RFA (n=282)	NA	**AF recurrence** (FU=3.5 mo) HR=2.56, p=0.008 (the presence of metabolic syndrome as a predictor of AF recurrence) HR=2.40, p=0.006 (BMI>25 kg/m^2 as a predictor of AF recurrence)
Takahashi 2008[41]	Non-RCT	40 pts with persistent drug-refractory AF; mean age: 59 yrs; Male: 85%	RFA (n=40)	NA	**AF termination** (FU of at least 3 mo) OR=1.013, 95% CI: 1.003, 1.023 (greater % of continuous electrical activity as a predictor of AF termination, MVA) OR=2.526, 95% CI: 1.052, 6.069 (the presence of temporal gradient of activation as a predictor of AF termination, MVA)
Dixit 2008[42]	RCT	105 pts with drug-refractory AF undergoing their first ablation (77 pts with	All PVI (n=53) and arrhythmogenic PVI (n=52)	NA	**Long-term AF recurrence post single ablation** (FU=12 mo) OR=7.14, 95% CI: 2.5, 20.0 (early AF recurrence as a predictive factor for long-term AF recurrence, MVA, p<0.001)

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Published online: May 16, 2013

Author year Study name (if applicable)	Study design	Subjects	Treatment groups (n; dose)	Treatment duration	Outcomes and findings
		PAF); Mean age: 57 yrs; Male: 72.3%			
Key question # 3: How does the effect of RFA on short- and long-term rhythm control differ among the various techniques or approaches used?					
Cycle 2					
Bittner 2011[13]	RCT	80 pts with drug-refractory AF (PAF 55% and persistent AF 45%); mean age: 58 yrs; male: 62%	Duty-cycled bipolar and unipolar RFA with decapolar circular catheter (n=40) vs. point-by-point antral ablation with 3D mapping system (n=40)	NA	Duty-cycled bipolar/unipolar vs. 3D point-by-point **AF termination** (FU=8 mo) 29/40 (72%) vs. 27/40 (68%), p=0.48
Boersma 2012[14]	RCT	124 pts with drug-refractory AF (PAF 66% and persistent AF 34%); mean age: 56 yrs; male: 80.6%	CA (n=63) vs. SA (n=61)	NA	CA vs. SA **AF termination** (FU=12 mo) 23/63 (36.5%) vs. 40/61 (65.6%), p=0.0022
Cycle 1					
Katritsis 2011[46]	RCT	67 pts with paroxysmal AF; Mean age: 54 yrs; Male: 77%	PV (n = 33) vs. PV+GP (n = 34)	NA	PV vs. PV+GP (FU=NR) **AF Recurrence** 18 (54.5%) vs. 9 (26.5%), p=NR **Arrhythmia-free** 20 (60.6%) vs. 29 (85.3%), log rank test p = 0.019
Tamborero 2010[47]	RCT	146 consecutive pts, 53% with paroxysmal AF; Mean age: 53 yrs; Male: 83%	CPVA (n=73) vs. CPVA- CM (n=73)	NA	CPVA vs. CPVA- CM (FU=9 mo) **Arrhythmia-free** 31 (42.5%) vs. 47(64.4%), p=0.008
Kühne 2010[48]	RCT	50 pts with paroxysmal AF; Mean age: 59 yrs; Male: 86%	Cryoballoon (n=25) vs. RFA (n=25)	NA	Cryoballoon vs. RFA (FU=12 mo) **Stable sinus rhythm** 88% vs. 92%, p=NR
Khan 2008[49]	RCT	81 pts with symptomatic, drug-resistant AF, an EF of	PVI (n=41) vs. AV-node ablation (n=40)	NA	PVI vs. AV-node ablation (FU=6 mo) **Progression of AF** 0% vs. 30%, p<0.001

Author year Study name (if applicable)	Study design	Subjects	Treatment groups (n; dose)	Treatment duration	Outcomes and findings
		40% or less, and HF; Age: 60.5 yrs; Male: 91.5%			**From NPAF to PAF** 100% vs. 5%, p<0.001
Katritsis 2008[53]	Non-RCT	38 pts with symptomatic, paroxysmal AF; Mean age: 51.7 yrs; Male: 84%	GP-RFA (n=19) vs. C-PVA (n=19)	NA	GP-RFA vs. C-PVA (FU=12 mo) **AF recurrence** 14 (74%) vs. 7 (37%), p= 0.017 HR= 2.5, 95% CI: 1.0 to 6.6
Sy 2011[45]	Non-RCT	99 pts with paroxysmal AF; Mean age: 56.5 yrs Male: 71%	Circumferential (n=37) vs. non-circumferential (n=62)	NA	Circumferential vs. non-circumferential (FU=12 mo+) **Freedom from symptomatic recurrence** 73% vs. 73%, p=0.97 **Organized tachycardia** More common in Circumferential groups
Pokushalov 2009[50]	RCT	80 pts with PAF; Mean age: 53 yrs Male: 82.5%	Selective GP ablation (n=40) vs. LA ablation at anatomic sites (n=40)	NA	Selective GP vs. LA anatomic (FU=13 mo) **PAF recurrence** 23/40 (57.5%) vs. 9/40 (22.5%), p=0.02
Oral 2009[51]	RCT	100 pts with long-lasting persistent AF who did not terminate AF after antral PVI; Mean age: 60 yrs Male: 80.6%	Antral PVI (n=50) vs. Antral PVI + CFAE RFA (n=50)	NA	Antral PVI vs. Antral PVI + CFAE RFA (FU=10 mo) **Maintaining sinus rhythm after 1st ablation** 19/50(38%) vs. 18/50(36%), p=0.84 **Maintaining sinus rhythm after last ablation** 34/50(68%) vs. 30/50(60%), p=0.40
Elayi 2008[44]	RCT	144 pts with long-lasting persistent AF; Mean age: 59 yrs Male: 66%	CPVA (n=47) vs. PVAI (n=48) vs. CFAE+PVAI (n=49)	NA	CPVA vs. PVAI (FU=16 mo) **Freedom from AF after a single procedure** 5/47(11%) vs. 19/48(40%), p<0.001 **Freedom from AF after 2 procedures** 8/47(17%) vs. 27/48(56%), p<0.001 **Freedom from AF after 1-2 procedures plus AAD** 13/47(28%) vs. 41/48(83%), p<0.001 PVAI vs. CFAE+PVAI (FU=16 mo) **Freedom from AF after a single procedure** 19/48(40%) vs. 30/49(61%), p<0.033 **Freedom from AF after 2 procedures**

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Author year Study name (if applicable)	Study design	Subjects	Treatment groups (n; dose)	Treatment duration	Outcomes and findings
					27/48(56%) vs. 39/49(80%), p<0.013 **Freedom from AF after 1-2 procedures plus AAD** 41/48(83%) vs. 46/48(94%), p<0.17
Katsiyiannis 2008[52]	Non-RCT	40 pts with AF (13 pts with persistent AF and 27 with paroxysmal AF); Mean age: NR; Male: NR	Conventional hand-navigated 8mm-tip bidirectional catheter with RF (n=20) vs. RMN 4mm-tip magnetic catheter with RF (n=20)	NA	Conventional hand-navigated vs. RMN (FU=12 mo) **Freedom from AF** 15/20 (75%) vs. 16/20 (80%), p>0.05
Dixit 2008[42]	RCT	105 pts with drug-refractory AF undergoing their first ablation (77 pts with PAF); Mean age: 57 yrs; Male: 72.3%	All PVI (n=53) vs. Arrhythmogenic PVI (n=52)	NA	All PVI vs. Arrhythmogenic PVI (FU=12 mo) **Freedom from AF after a single ablation** 38/53(75%) vs. 37/52(71%), p=0.70 OR=1.18, 95% CI: 0.50, 2.83 **Freedom from AF after a single ablation off AAD** 30/53(59%) vs. 31/52(60%), p=0.93 OR=1.03, 95% CI: 0.47, 2.27 **AF recurrence** 10/53(19%) vs. 15/52(29%), p=0.25 OR=1.70, 95% CI: 0.68, 4.26
Key question 4: What are the short- and long-term complications and harms associated with RFA?					
Cycle 2					
Hoyt 2011[15]	Non-RCT	931 pts with drug-refractory AF (PAF 58%, persistent AF 27%, long-standing 15%); mean age: 58 yrs; male: 73%	RFA (n=931; 4mm tipped irrigated catheter)	NA	**Major complications** (FU=9 yrs) Overall rate: 55/931 (6.0%) 56 events per 1190 ablations (vascular n=18, stroke n=9, TIA n=3, respiratory compromise n=5, pericardial tamponade n=13, hemothorax n=2, phrenic nerve injury n=3, complete heart block n=1, mitral valve injury n=1, pulmonary stenosis n=1)
Contreras-Valdes 2011[16]	Non-RCT	219 pts with drug-refractory AF (PAF and persistent AF); mean age: 60 yrs; male: 80%	RFA (n=219; externally irrigated 3.5mm-tip quadripolar catheter)	NA	**Rate of esophageal injury** 22/219 (10%)
Boersma 2012[14]	RCT	124 pts with drug-refractory AF (PAF 66% and persistent AF 34%);	CA (n=63) vs. SA (n=61)	NA	CA vs. SA **Procedural complications** (FU=NA) 2/63 (3.2%) vs. 14/61 (23%), p=0.001

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Author year Study name (if applicable)	Study design	Subjects	Treatment groups (n; dose)	Treatment duration	Outcomes and findings
		mean age: 56 yrs; male: 80.6%			CA group: pericardial effusion/tamponade (n=1), TIA/stroke (n=1), groin hematoma/bleed (n=4) SA group: pericardial effusion/tamponade (n=1), TIA/stroke (n=1), pneumothorax (n=6), hematothorax (n=1), rib fracture (n=1), sternotomy for bleeding (n=1), pneumonia (n=1), PM implant (n=1) **Complications during FU** (FU=12 mo) 8/63 (12.6%) vs. 7/61 (11.5%), p=1.0 CA group: stroke (n=1), TIA (n=1), pneumonia (n=2), heart failure (n=2), death due to subarachnoid hemorrhage (n=1), ileus (n=1), groin hematoma/bleed (n=2) SA group: pneumonia (n=2), hydrothorax (n=2), pericarditis (n=1), fever (n=1), ileus (n=1) **Significant adverse events** (FU=12 mo) 10/63 (15.9%) vs. 21/61 (34.4%), p=0.027
Bittner 2011[13]	RCT	80 pts with drug-refractory AF (PAF 55% and persistent AF 45%); mean age: 58 yrs; male: 62%	Duty-cycled bipolar and unipolar RFA with decapolar circular catheter (n=40) vs. point-by-point antral ablation with 3D mapping system (n=40)	NA	Duty-cycled bipolar/unipolar vs. 3D point-by-point **Complications** (FU=8 mo) No late complications; no PV stenosis
Chao 2011[7]	Non-RCT	247 pts with symptomatic drug-refractory PAF undergoing first ablation; mean age: 52.8 yrs; male: 72.0%	RFA (n=247; 4 mm tip or internal irrigated-tip catheter)	NA	**Complications** Hematoma of the vascular access: 4 (1.61%) Cardiac tamponade: 2 (0.80%) Symptomatic PV stenosis: 1 (0.40%)
Mohanty 2011[17]	Non-RCT	660 pts with symptomatic drug-refractory AF (PAF 27%, persistent AF 31%, long-standing persistent AF 42%); mean age: 62 yrs; male:	RFA (n=660; circular mapping catheter and 3.5mm open-irrigation tip catheter)	NA	**Complications** Pericardial effusion: 5 (1.5%)

Author year Study name (if applicable)	Study design	Subjects	Treatment groups (n; dose)	Treatment duration	Outcomes and findings
		69.0%			
Mohanty 2012[5]	Non-RCT	1,496 pts with AF undergoing first ablation (29% PAF, 26% persistent AF, 45% long-standing persistent AF); mean age: 62 yrs; male: 73.6%	RFA (n=1,496; circular mapping catheter and a 3.5-mm open-irrigation-tip catheter)	NA	**Complications** Pericardial effusion: 11 (0.73%) Groin hematoma: 1 (0.06%) Pseudoaneurysm: 2 (0.13%)
Shah 2012[18]	Non-RCT	4,156 pts with AF; mean age: 61.7 yrs; male: 67.8%	RFA (n=4,156 pts; ablation catheter type: NR)	NA	**Any complications** Overall rate: 211/4,156 (5.1%) Vascular complication 110 (52.1%), hematoma 93 (44.1%), perforation/tamponade 104 (49.3%), stroke 10 (4.7%), pneumothorax 4 (1.9%), transient ischemic attack 3 (1.4%), death 1 (0.5%) **30-day re-hospitalization** Overall rate: 390/4,156 (9.4%) AF/atrial flutter 105 (26.9%), procedural complication 76 (19.5%), pneumothorax 3 (0.8%), vascular complication 45 (11.5%), perforation/tamponade 12 (3.1%), acute stroke 19 (4.9%), death 9 (2.3%)
Weerasooriya 2011[6]	Non-RCT	100 pts with AF undergoing first ablation (63% PAF, 22% persistent AF, 14% long-standing persistent AF); mean age: 55.7 yrs; male: 86.0%	RFA (n=100; a steerable quadripolar catheter 2-5-2 mm)	NA	**Complications** 11 pts (cardiac tamponade n=3, pericardial effusion n=3, asymptomatic 70% PV stenosis n=1, arteriovenous femoral fistulae n=1, femoral false aneurysm n=1, anaphylactic shock secondary to propofol n=1, and ventricular fibrillation secondary to direct current cardioversion n=1) No procedure-related deaths. Three deaths due to lung cancer, cerebral hematoma, or suicide
Bohnen 2011[19]	Non-RCT	1,676 pts with AF undergoing ablation; mean age: 57.6 yrs; male: 66.0%	RFA (n=1,676; ablation catheter type: NR)	NA	**Complications** Overall major complication rate: 64/1,676 (3.8%) Death 2 (0.1%), perforation 21 (1.3%), thromboembolic event 11 (0.7%), access complication 23 (1.4%), deep vein thrombosis 1 (0.1%), aspiration pneumonia 3 (0.2%), pulmonary edema 2 (0.1%), conduction system damage 1 (0.1%), genitourinary trauma 2 (0.1%)

Author year Study name (if applicable)	Study design	Subjects	Treatment groups (n; dose)	Treatment duration	Outcomes and findings
Chao 2011[20]	Non-RCT	565 pts AF (PAF 75%); mean age: 55 yrs; male: 75.0%	RFA (n=565; ablation catheter type: NR)	NA	**Complications** (FU=39 mo) Overall rate: 27/565 (4.8%) Death n=9 (1.6%), ischemic stroke n=9 (1.6%), TIA n=6 (1.06%), pulmonary embolism n=2 (0.35%), peripheral embolism n=1 (0.17%) 15.2% vs. 2.4%, p<0.001 [KMA] ($CHADS_2$ score > 2 as a predictor of adverse event)
Winkle 2011 [22]	Non-RCT	1,550 pts with AF; mean age: 62 yrs; male: 71%	RF needle (n=575) vs. standard needle (n=975)	NA	**Complications** RF needle No pericardial tamponade No death Standard needle Pericardial tamponade n=9 (0.92%) No death
Yokokawa 2011[21]	Non-RCT	55 pts with persistent AF; mean age: 61 yrs; male: 75%	RFA needle (n=55; ablation or ring catheter)	NA	**Complications** Pericardial tamponade n=3 (5%) No arterial injury, thromboembolism, or esophageal/phrenic nerve injury
Winkle 2011[10]	Non-RCT	423 pts with persistent AF (lasting from 1week to 1 year); mean age: 62 yrs; male: 75.0%	Circumferential RFA-PVI and LA roof line (n=423; 3.5mm irrigated-tip catheter)	NA	**Complications** TIA: 1 (0.23%) Major complications: 3.2% of the pts Minor complications: 3.5% of the pts No deaths, atrial esophageal fistula, or pulmonary vein stenosis
Rostock 2011[9]	Non-RCT	395 pts with persistent AF undergoing first ablation; mean age: 61 yrs; male: 83.0%	RFA-PVI (n=395; steerable decapolar catheter, circumferential decapolar diagnostic catheter, nonsteerable quadripolar diagnostic catheter, and 3.5 mm external irrigated-tip ablation catheter)	NA	**Complications** Sinus arrest: 7 (1.77%) Cardiac tamponade: 4 (1.01%) TIA with paresthesia and motor weakness the left upper limb: 1 (0.25%)
Gibson 2011[23]	Non-RCT	1,380 pts with AF (29%	RFA (n=1,380; PV	NA	**Complications**

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Author year Study name (if applicable)	Study design	Subjects	Treatment groups (n; dose)	Treatment duration	Outcomes and findings
		PAF, 45% persistent AF, 26% long-standing persistent AF); mean age: 62 yrs; male: 75.0%	antrum isolation guided by circular mapping catheter)		Pericardial effusion: 2 (0.43%) No atrioesophageal fistula or PV stenosis **Pulmonary hypertension (PH)** Overall rate: 19 (1.4%) Mild PH: 10 (0.72%) Moderate PH: 6 (0.43%) Severe: 3 (0.21%) <u>Predictors of PH</u> OR=6.13, 95% CI: 1.2, 32.5 [MVA] (LA ≤ 45 mm as a predictor of PH) OR=1.14, 95% CI: 1.1, 1.4 [MVA] (Mean LA pressure as a predictor of PH) OR=4.4, 95% CI: 1.1, 22.2 [MVA] (severe LA scarring as a predictor of PH) OR=9.49, 95% CI: 2.0, 44.2 [MVA] (baseline presence of diabetes as a predictor of PH) OR=6.23, 95% CI: 1.6, 24.4 [MVA] (baseline presence of obstructive sleep apnea as a predictor of PH)
Yamasaki 2011[24]	Non-RCT	104 pts with drug-resistant AF (50% persistent AF); mean age: 59 yrs; male: 81.0%	Extensive encircling PV vein isolation (n=104; 7-Fr decapolar ring catheter, non-irrigation ablation catheter with 4mm distal electrode, or irrigation catheter with 3.5mm distal electrode)	NA	**Excessive transmural injury (ETI)** Overall rate: 10 (9.6%) Esophageal erythema: 2 (1.9%) Necrotic ulcerations: 2 (1.9%) Gastric hypomotility after periesophageal nerve injury: 6 (5.8%) <u>Predictors of ETI</u> OR=0.76, 95% CI: 0.59, 0.97 [MVA] (lower BMI as a predictor of ETI) Age, gender, and type of AF did not predict ETI
Winkle 2011[25]	Non-RCT	843 pts with	Circumferential RFA	NA	**Complications (# events per ablations)**

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Author year Study name (if applicable)	Study design	Subjects	Treatment groups (n; dose)	Treatment duration	Outcomes and findings
		symptomatic AF (32% PAF, 50% persistent AF, 18% long-standing persistent AF); mean age: 62 yrs; male: 72.0%	(n=843; closed-tip and open irrigated tip 7-Fr duodeca catheter)		Overall # of vascular/hemorrhagic events: 28/1,122 (2.5%) No death, atrio-esophageal fistula, or PV stenosis Vascular/hemorrhagic events by activated clotting time (ACT) ACT (<250 sec): 9/557 (1.62%) ACT (251-299 sec): 10/331 (3.02%) ACT (300-349 sec): 7/196 (3.57%) ACT (>350 sec): 2/36 (5.55%) P=0.024 [MVA] (the use of open irrigated-tip catheter as a protective factor against vascular/hemorrhagic events) Gender and ACT levels did not predict the complications [MVA]
Guglin 2010[26]	Non-RCT	3,218 pts with AF; mean age: 69 yrs; male: 60.0%	RFA (n=3,218; catheter type: NR)	NR	**Complications** Rate of heart failure (HF) symptoms more common in the rate control vs. rhythm group
Cycle 1					
Oral 2009[51]	RCT	100 pts with long-lasting persistent AF who did not terminate AF after antral PVI; Mean age: 60 yrs Male: 80.6%	Antral PVI (n=50) vs. Antral PVI + CFAE RFA (n=50)	NA	Antral PVI (FU=10 mo) **Complications** 5 pts (transient pericarditis n=2; pericardial effusion without tamponade n=1; self-limited extraperitoneal bleed n=1; femoral arteriovenous fistula n=1)
Wilber 2010[27]	RCT	167 pts with symptomatic AF (at least 3 episodes within 6 mo before randomization) not responding to at least one AAD; Mean age: 55 yrs; Male: 66%	RFA (n=106) vs. AAD (n=61; dose: NR)	NA	RFA vs. AAD (FU=30 d) **Major treatment related AEs** 5/103 (4.9%) vs. 5/57 (8.8%), p=NR RFA: 5 pts (pericardial effusion n=1; pulmonary edema n=1; pneumonia n=1; vascular complication n=1; heart failure n=1) AAD: 5 pts (life-threatening arrhythmias and disabling drug intolerance n=3) **Events not related to treatment** RFA: 1 pt (death 284 d after PVI due to acute MI)

Author year Study name (if applicable)	Study design	Subjects	Treatment groups (n; dose)	Treatment duration	Outcomes and findings
Bhargava 2009[28]	Non-RCT	1404 pts with symptomatic drug resistant AF; Mean age: 56 yrs; Male: 76%	RFA (n=1404)	NA	RFA (FU=57 mo) **Complications** RFA: 46 pts (tamponade n=5; thromboembolic including transient ischemic attack or stroke events n=6; severe PV stenosis n=18; pulmonary embolism/death n=1; diaphragmatic paralysis n=5; transient altered mental status n=2; optic neuritis n=1; major vascular bleed n=3; deep venous thrombosis n=1; hemothorax n=1; retroperitoneal bleeding n=1; coronary embolism n=1; lasso entrapment in mitral valve n=1)
Sawhney 2009[37]	Non-RCT	71 pts with paroxysmal AF; Mean age: 60 yrs; Male: 79%	PVI (n=71)	NA	PVI (FU=57 mo) **Complications** PVI: 3 pts (femoral hematoma n=2; femoral pseudoaneurysm n=1)
Khan 2008[49]	RCT	81 pts with symptomatic, drug-resistant AF, an EF of 40% or less, and HF; Age: 60.5 yrs; Male: 91.5%	PVI (n=41) vs. AV-node ablation (n=40)	NA	PVI vs. AV-node ablation (FU=6 mo) **Complications** 7/41 (17%) vs. 7/40 (17.5%), p>0.05 PVI: 7 pts (groin bleeding n=3; pericardial effusion n=1; pulmonary edema n=1; mild asymptomatic stenosis of a single pulmonary vein n=2). AV-node ablation: 7 pts (left ventricular-lead dislodgment n=2; high left ventricular threshold n=2; pocket hematoma n=2; and pneumothorax n=1)
Elayi 2008[44]	RCT	144 pts with long-lasting persistent AF; Mean age: 59 yrs Male: 66%	CPVA (n=47) vs. PVAI (n=48) vs. CFAE+PVAI (n=49)	NA	**Complications** (FU=16 mo) CFAE+PVAI: 3 pts (pericardial effusions n=2; PV stenosis n=1) PVAI: 1 pt (PV stenosis)
Dixit 2008[42]	RCT	105 pts with drug-refractory AF undergoing their first ablation (77 pts with PAF); Mean age: 57 yrs; Male: 72.3%	All PVI (n=53) vs. Arrhythmogenic PVI (n=52)	NA	**Serious adverse events** (FU=12 mo) All PVI: 3 pts (cerebrovascular stroke n=1; LA esophageal fistula n=1; death=1) Arrhythmogenic PVI: no serious adverse event
Martinek 2009[54]	Non-RCT	31 pts (25 pts with PAF); Mean age: 56 yrs; Male: 90%	RFA (n=31)	NA	**Gastroesophageal events** (FU=24 hrs) 1 pt with esophageal ulceration

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Published online: May 16, 2013

Author year Study name (if applicable)	Study design	Subjects	Treatment groups (n; dose)	Treatment duration	Outcomes and findings
Scharf 2009[55]	Non-RCT	50 pts with long-standing persistent AF; Mean age: 58 yrs; Male: NR	RFA (n=50)	NA	RFA (FU=20 mo) **Serious adverse events** 4 pts (groin hematoma n=1; arteriovenous fistula n=1; cardiac tamponade n=1; ischemic neurologic ataxia n=1) **Other adverse events** 2 pts (pain and fever associated with pericardial and pleural effusions n=1; heart failure secondary to recurrent AF)
Cappato 2009[56]	Non-RCT	32569 pts with AF; Age range: 18-90 yrs; Male: 62%	Catheter ablation: CARTO- and Lasso-guided (n=32569)	NA	**Early deaths (within 30 days of procedure) -**FU=11 yrs 25 pts (tamponade n=7; stroke n=3; atrioesophageal fistula n=5; massive pneumonia n=2; myocardial infarction n=1; septicemia n=1; sudden respiratory arrest n=1; extrapericardial PV perforation n=1; both lateral PV occlusion n=1; hemothorax n=1; anaphylaxis n=1; irreversible torsades de pointes n=1) **Late deaths (after 30 days of procedure)** - FU=11 yrs 7 pts (stroke n=2; asphyxia from tracheal compression secondary to subclavian hematoma n=1; intracranial bleeding n=1; acute respiratory distress syndrome n=1; esophageal perforation n=1; tamponade with subsequent cardiac arrest n=1) CARTO-guided ablation vs. Lasso-guided ablation **Death rates** 0.18% (of 4665 pts) vs. 0.08% (of 2385 pts), p=0.51 4mm-tip catheter vs. irrigated/cooled-tip catheter **Death rates** 0.19% (of 13470 pts) vs. 0.23% (of 5271 pts), p=0.19
Biase 2010[57]	Non-RCT	6454 pts with persistent, paroxysmal or long standing persistent AF; Mean age: 57 yrs; Male: 76%	Ablation with an 8-mm catheter (n= 2488) vs. Ablation with an open irrigated catheter-off warfarin (n=1348) vs. Ablation with an open irrigated catheter-on	NA	8-mm vs. open irrigated-off warfarin vs. open irrigated-on warfarin (FU=12mo) **Stroke/transient ischemic attack** 27 (1.1%) vs. 12 (0.9%) vs. 0, p<0.05 [8 mm or open irrigated-off warfarin vs. open irrigated-on warfarin] **Major bleeding** 10 (0.4%) vs. 11 (0.8%) vs. 10 (0.4%), p<0.05 [open irrigated-off warfarin vs. open irrigated-on warfarin] **Pericardial effusion**

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Author year Study name (if applicable)	Study design	Subjects	Treatment groups (n; dose)	Treatment duration	Outcomes and findings
			warfarin (n=2618)		11 (0.4%) vs. 11 (0.8%) vs. 12 (0.5%), p>0.05 [8 mm vs. open irrigated-off warfarin vs. open irrigated-on warfarin]
Gaita 2010[58]	Non-RCT	232 pts with paroxysmal or persistent AF; Mean age: 58 yrs; Male: 78%	RFA (n=232)	NA	**Adverse Events** (FU=NR) 1 pt (periprocedural symptomatic cerebrovascular accident) , 33 pts (embolic lesions) **Cardioversion** OR= 2.75, 95% CI: 1.29, 5.89; p=0.009
Martinek 2010[59]	Non- RCT	267 pts (34.5% of those with esophageal ulceration had persistent atrial fibrillation and 83.3% of those without esophageal ulceration had persistent atrial fibrillation); Mean age: 59.6 yrs; Male: 73%	RFA	NA	FU=9.2 mo **LA-to-esophagus distance** Regression coefficient for esophageal ulcerations: β= -0.159, p=0 .0176

pts=patients; yr(s)=years; HR=hazard ratio; KMA=Kaplan-Meier analysis MVA=multivariable analysis; UVA=univariate analysis; NR=not reported; CER=comparative effectiveness review; RCT=randomized controlled trial; AF=atrial fibrillation; RFA=radiofrequency catheter ablation; AAD=anti-arrhythmic drug; PAF=paroxysmal atrial fibrillation; NPAF=non-paroxysmal atrial fibrillation; LAD=left atrial diameter; EF=ejection fraction; CAD= coronary artery disease; BMI= body mass index; WACA=wide area circumferential ablation; PVI=pulmonary vein isolation; LA= left atrium; RA=right atrium; CPVA= circumferential pulmonary vein ablation; GP= ganglionated plexi; PVA=pulmonary vein ablation; CPVA-CM= circumferential pulmonary vein ablation circular mapping; AE=adverse event; QOL=quality of life; FU=follow-up; MD=mean difference; PVAI=pulmonary vein antrum isolatation; MS=metabolic syndrome; CHADS=congestive heart failure, hypertension, age>75 years, diabetes, and previous stroke/transient ischemic attack; TRI=temporal regularity index; SRI: spacial regularity index; LVEDD=left ventricular/diastolic diameter; RECORDAF=Registry on Cardiac Rhythm Disorders Assessing the Control of Atrial Fibrillation; CKD=chronic kidney disease; LVMI=left ventricular mass index; LVEF= left ventricular ejection fraction; CA=catheter ablation; SA=surgical ablation; AFCL= AF cycle length

Appendix D: Questionnaire Matrix

Comparative Effectiveness of Radiofrequency Catheter Ablation for Atrial Fibrillation

AHRQ Publication No. 09-EHC015-EF July 2009
Access to full report: http://www.ncbi.nlm.nih.gov/books/NBK43190/pdf/TOC.pdf

Clinical expert name:

Conclusions from CER (executive summary)	Is the conclusion(s) in this CER still valid? (Yes/No/Don't know)	Are you aware of any new evidence that is sufficient to invalidate the finding(s) in CER? (Yes/No/Don't know) If yes, please provide references	Comments
Key Question # 1: What is the effect of RFA on short-term (6 to 12 months) and long-term (>12 months) rhythm control, rates of congestive heart failure, left atrial and ventricular size changes, rates of stroke, quality of life, avoiding anticoagulation, and readmissions for persistent, paroxysmal, and long-standing persistent (chronic) atrial fibrillation?			
Rhythm control There is a moderate level of evidence to show that patients who received RFA as a second-line therapy (i.e., patients who did not respond to medical therapy) had a higher chance of maintaining sinus rhythm than those treated with medical therapy alone (relative risk (RR) 3.46, 95-percent confidence interval (CI) 1.97-6.09) at 12 months postprocedure. The summary estimate was derived from meta-analysis of three RCTs that assessed the rhythm control of patients exclusively after a single procedure. There is insufficient evidence to compare freedom from AF recurrence in patients who had RFA as first-line therapy vs. medically treated patients. One fair quality RCT of 67			

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Published online: May 16, 2013

patients (96 percent PAF) reported an increased freedom from AF recurrence at 12 months for RFA as first-line therapy compared with medical treatment (88 percent vs. 37 percent, P<0.001). Rates of congestive heart failure There is insufficient evidence to compare the rates of congestive heart failure between RFA and medical treatment. There was only one observational study with data. This study reported that patients who underwent RFA had a lower risk of developing congestive heart failure than those treated with medical therapy (5 percent vs. 10 percent, P value not reported) at a mean followup of 30 months. Left atrial and ventricular size changes There is a low level of evidence showing no statistically significant difference in the improvement of left atrial diameter (LAD), left ventricular end diastolic diameter (LVED), or ejection fraction (EF) at 12 months in patients who underwent RFA compared to those treated with medical therapy. Rates of stroke There is a low level of evidence showing no statistically significant difference in the risk of cerebrovascular events at 12 months in patients who underwent RFA compared to those treated with medical therapy (risk difference 0.6 percent, 95-percent CI -1.1 to 2.3 percent favoring AAD). The summary estimate was derived from meta-analysis of six RCTs. Quality of life There is a low level of evidence to suggest that RFA improves quality of life more than medical			

treatment. Three RCTs and one observational study reported more improvement in the general or physical functioning score of the SF-36 health survey in patients who underwent RFA than in patients who had medical treatment alone (net difference between the two treatments, +1 to +25 favoring RFA). However, these studies assessed the results at nonuniform time points and therefore the findings may be difficult to interpret. ES-4 Avoiding anticoagulation There is a low level of evidence suggesting that patients treated with RFA have a better chance of avoiding anticoagulation than those treated with AADs. There was only one RCT. It found a higher proportion of patients treated with RFA than patients treated with medical therapy reporting freedom from anticoagulation at 12 months (60 percent vs. 34 percent, P=0.02). Readmissions There is a low level of evidence on differences in readmission rates between patients treated with RFA and those treated with AADs. Two RCTs compared the rates or number of readmissions between RFA and medical treatment. One RCT reported a lower readmission rate in patients treated with RFA than medical treatment (9 percent vs. 54 percent, P<0.001), while the other RCT reported no statistically significant difference in the median number of readmissions between RFA and medical treatment (1 readmission vs. 2 readmissions, P=0.34). The findings on the rates of readmissions are inconsistent. This may be because readmission rates depend on many other factors besides the recurrence of disease			

(e.g., the particular health care system, bed availability, severity of illness)			
Key question # 2: What are the patient-level and intervention-level characteristics associated with RFA effect on short- and long-term rhythm control?			
There is a low level of evidence to show that AF type, namely nonparoxysmal AF, is predictive of a higher rate of AF recurrence. Univariable analyses within 31 studies that reported recurrence rates for PAF vs. other types of AF were clinically and statistically heterogeneous, but meta-analysis found statistically significant higher rates of recurrence in patients with nonparoxysmal AF, with relative risks of about 1.6. However, only a minority of multivariable analyses bear this out. Overall, 25 studies reported multivariable analyses of the association between patient-level characteristics and AF recurrence. Among these, 17 evaluated AF type but only 6 of them found statistically significant independent associations between AF type and recurrence rates. In the 8 studies that reported hazard ratios, these ranged from 1.1 to 22, suggesting lower recurrence rates in patients with PAF. Among 11 comparisons that reported both univariable and multivariable analyses, 6 found statistically significant crude and adjusted higher recurrence rates in patients with nonparoxysmal AF, 3 found significant crude but nonsignificant adjusted associations, and 2 found nonsignificant crude and adjusted associations. In both univariable and multivariable analyses reported, no study or population factors were found to explain the heterogeneity among the studies. There is a moderate level of evidence to show that among patients with approximately normal EF or LAD, these parameters are not			

independent predictors of AF recurrence. In multivariable analyses, 5 of 17 studies found an association between lower EF and AF recurrence, and 4 of 20 found an association between larger LAD and AF recurrence. However, the reported data suggest that only a small proportion of patients included in the analyses had EFs below about 40 percent or LADs above about 60 mm. The evidence is insufficient to estimate the predictive value of abnormal EF or LAD on recurrence rates. There is a high level of evidence to show that sex, the presence of structural heart disease, and duration of AF are not associated with AF recurrence. None of the 23 studies found an independent association between sex and AF recurrence. Only 1 of 21 studies found a consistent ES-5 association between structural heart disease and AF recurrence. Only 3 of 16 studies found a statistically significant association between duration and recurrence of AF, with hazard ratios of 1.03 and 1.08 for longer duration. There is a high level of evidence to show that age, within the approximate range of 40 to 70 years, is not independently associated with AF recurrence. Only 1 of 24 studies found an association (that higher age was associated with lower rates of AF recurrence). However, the reported data suggest that only a small proportion of patients included in the analyses were younger than about 40 years or older than about 70 years. The evidence is insufficient to estimate the predictive value of young or very old age.			

There is insufficient evidence for other potential predictors of AF recurrence, as other predictors were only rarely evaluated. There is insufficient evidence to show that intervention-level characteristics, such as operator experience or setting, are predictors of AF recurrence, as no study addressed this question			
Key question # 3: How does the effect of RFA on short- and long-term rhythm control differ among the various techniques or approaches used?			
PVI vs. WACA. There is a moderate level of evidence to show that WACA may result in lower rates of AF recurrence than ostial PVI in patients with either PAF or persistent AF, with followup ranging from 6 to 15 months. Five RCTs of ostial PVI vs. WACA with or without additional ablation lines compared their efficacy to maintain sinus rhythm. Only two studies reported results after a single procedure and off AADs. Both studies found that patients who had WACA had a higher rate of success (freedom from AF recurrence) than patients who had ostial PVI (67 percent vs. 49 percent, P≤0.05; 88 percent vs. 67 percent, P=0.02). Of the three studies that included patients who had reablation during followup, two reported similar findings. **RFA with or without additional left-sided ablation lines**. There is insufficient evidence to make definitive conclusions concerning the effects of the addition of left-sided ablation lines to RFA. The substantive heterogeneity of the different types of additional left-sided ablation lines that were used by the studies preclude meaningful comparisons. Six RCTs compared the efficacy of one RFA technique with vs. without the addition of left-sided			

ablation lines (e.g., mitral-isthmus line (MIL), roof or posterior left atrial lines). The majority of the studies reported AF recurrence rates that included patients who had reablation or were continued on AADs. Three of five studies on patients with PAF or nonparoxysmal AF found that patients who had additional left-sided ablation lines had less AF or atrial arrhythmia recurrence at followup than patients who did not (MIL 71 percent vs. 53 percent, P=0.01; roof line 87 percent vs. 69 percent, ES-6 P=0.04; MIL 74 percent vs. 83 percent, no P value reported). Two studies did not find a significant difference in AF recurrence with the addition of left-sided ablation lines. **PVI vs. PVI with right-sided lines.** There is insufficient evidence concerning the effects of adding right-sided lines on AF recurrence after RFA. One RCT examined the incremental benefit of adding a cavotricuspid isthmus ablation line in patients undergoing RFA for AF. This study, which included patients with AF and at least one episode of atrial flutter, found no significant difference in AF recurrence at 12 months followup between the group that had ostial-antral PVI and the group that had ostial-antral PVI with cavotricuspid isthmus ablation. Another RCT compared WACA with vs. without additional ablation of the superior vena cava. This study of patients with PAF found no significant difference at 12 months followup in the recurrence of atrial tachyarrhythmia between the patients who had WACA with superior vena cava ablation and the patients who had only WACA. **Different approaches in retrospective studies**.			

There is insufficient evidence to draw conclusions from this group of retrospective studies. These observational studies compared many different approaches to RFA. They have limitations in the comparability among groups. Historical controls were used in the majority of the studies. In some instances, the proportions of patients with different types of AF differed between groups, and the length of followup also differed. None of the studies adjusted for potential confounders			
Key Question #4.What are the short- and long-term complications and harms associated with RFA?			
There is a low level of evidence that adverse events associated with RFA are relatively uncommon. The level of evidence was rated low because the studies reviewed employed nonuniform definitions and assessments of adverse events. There were 84 studies that reported at least one adverse event associated with RFA. We surmised that most of the adverse events either took place in a peri-procedural timeframe or shortly after being discharged home postprocedure. The only exception was the diagnosis of PV stenosis, which was routinely screened for at around 3 months. Major adverse events included PV stenosis, cardiac tamponade, stroke and/or transient ischemic attack, and peripheral vascular complications such as bleeding/hematoma, pseudoaneurysm, femoral vein thrombosis, or arteriovenous fistula.			
CER=comparative effectiveness review; RCT=randomized controlled trial; AF=atrial fibrillation; RFA=radiofrequency catheter ablation; AAD=anti-arrhythmic drug; PAF=paroxysmal atrial fibrillation; non-PAF=non-paroxysmal atrial fibrillation; LAD=left atrial diameter; EF=ejection fraction; CAD= coronary artery disease; BMI= body mass index; LSAL= left-sided ablation lines; RSAL= right-sided ablation lines; WACA=wide area circumferential ablation; PVI=pulmonary vein isolation			

Source: www.effectivehealthcare.ahrq.gov
Published online: May 16, 2013