Research Article

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Comparative effectiveness of catheter ablation devices in the treatment of atrial fibrillation: a network meta-analysis

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Atrial fibrillation (AF) ablation is most commonly performed using radiofrequency (RF) and cryoballoon (CB) catheters. Ablation Index is a novel lesion-quality marker associated with improved outcomes in RF ablation. Due to lack of direct comparative evidence between the latest generations of technologies, there is uncertainty regarding the best treatment option. **Aim:** To conduct a network meta-analysis to evaluate the comparative effectiveness of RF with Ablation Index to other catheter ablation devices in the treatment of AF. **Methods:** Searches for randomized and nonrandomized prospective comparative studies of ablation catheters were conducted in multiple databases. The outcome of interest was 12-month freedom from atrial arrhythmias after a single ablation procedure. Studies were grouped as high-, low- and unclear-quality based on study design and balanced baseline patient characteristics. Bayesian hierarchical network meta-analysis was conducted and results presented as relative risk ratios with 95% credible intervals (CrIs). **Results:** 12 studies evaluating five different catheter ablation devices were included. Radiofrequency ablation with Ablation Index was associated with statistically significantly greater probability of 12-month freedom from atrial arrhythmias than Arctic Front (relative risk: 1.77; 95% CrI: 1.21–2.87), Arctic Front Advance™ (1.41; 1.06–2.47), THERMOCOOL™ (1.34; 1.17–1.48) and THERMOCOOL SMARTTOUCH™ (1.09; 1–1.3). Results were robust in multiple sensitivity analyses. **Conclusion:** Radiofrequency catheter with Ablation Index is superior to currently available options for 12-month freedom from atrial arrhythmias after AF ablation. This study provides decision-makers with robust, pooled, comparative evidence of the latest ablation technologies.

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Keywords: atrial fibrillation • catheter ablation • cryoballoon • network meta-analysis • radiofrequency

Catheter ablation is a minimally invasive option for the treatment of atrial fibrillation (AF) [1–3]. Ablation is routinely performed using radiofrequency (RF) and cryoballoon (CB) catheters, with RF catheters being the most widely used technology [1,4]. Radiofrequency catheters have evolved since their introduction to include contact force (CF) technology, which provides real-time feedback on the contact between the catheter tip and cardiac tissue during ablation. Ablation with CF catheters has improved freedom from atrial arrhythmia compared with non-CF catheters and has reduced complications, procedure time and fluoroscopy time [5–12].

More recently, use of a novel lesion-quality marker, Ablation Index (also referred to as VISITAG SURPOINT™), with CF catheters has been associated with improved outcomes of RF ablation. A recent meta-analysis reported a significant 57% reduction in the odds of acute pulmonary vein (PV) reconnection and significant 65% reduction

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in recurrence of atrial arrhythmias 12 months after an Ablation Index-guided procedure compared with use of CF catheters alone [13].

For CB catheters, three successive generations have followed the first-generation CB. The second-generation CB included a redesigned balloon that allowed for more uniform cooling across the surface, which led to improved effectiveness and safety when compared with first-generation CB [14,15]. Third and fourth generations of the CB catheter have been developed to include shorter tips to help improve assessment of time to PV isolation. Emerging evidence on these devices has shown similar effectiveness and safety as the second-generation device [16,17].

Direct comparative data between the advanced catheter ablation technologies are lacking, making assessments of the different ablation technologies challenging. Randomized trials have compared the effectiveness and safety of RF and CB catheters [18–23]; however, of these published studies, few have included advanced catheter ablation technologies [18,22]. To date, no studies comparing CF catheters with Ablation Index to CB have been published.

Although several meta-analyses have been published that compare RF and CB technologies, it is difficult to understand the comparative effectiveness of specific devices because analyses often combine catheters with different technologies (e.g., combine first- and second-generation devices and different CF technologies), include a broad range of patients (i.e., combine paroxysmal and persistent AF, drug-naive and drug-refractory), and do not have a clear follow-up period (i.e., combine studies that report outcomes at various follow-up periods). Network meta-analysis (NMA) enables the indirect comparison of treatments that have not been directly compared in clinical trials [24]. Network meta-analyses are robust and well established for the use of guideline development and decision-making at national (e.g., NICE, Canadian Agency for Drugs and Technologies in Health [CADTH]) and international (e.g., WHO) levels. The objective of this study was to conduct an NMA that considers the totality of prospective comparative evidence to evaluate the pooled clinical effectiveness of the THERMOCOOL SMARTTOUCH™ Catheter with Ablation Index compared with other available catheter ablation devices, including second-generation CB, in the treatment of AF.

Methods

A Bayesian statistical model was used to conduct the NMAs. The study protocol was registered on PROSPERO (registration number CRD42018093077, available online at: www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42018093077). Reporting of the analysis follows the Preferred Reporting Items of Systematic Reviews and Meta-analyses (PRISMA) Extension Statement for Reporting of Systematic Reviews Incorporating Network Meta-analyses of Health Care Interventions (Supplementary Material 1) [25].

Search strategy

A comprehensive search strategy was developed to search PubMed to identify relevant studies (Supplementary Material 2). Searches of relevant grey literature and key study bibliographies were also conducted. Only English-language articles published from 2008 onward were reviewed.

Eligibility criteria & study selection

Studies that included adult patients (≥18 years old) with paroxysmal AF (PAF) refractory and/or intolerant to antiarrhythmic drugs undergoing first-time catheter ablation were considered if they compared the use of one catheter ablation device of interest to another (Supplementary Material 3). The primary interventions of interest included the THERMOCOOL SMARTTOUCH SF Catheter with Ablation Index. Relevant comparators included THERMOCOOL SMARTTOUCH Catheter/THERMOCOOL SMARTTOUCH SF Catheter, THERMOCOOL™ Catheter/THERMOCOOL SF Catheter, Arctic Front Cryoballoon, Arctic Front Advance™ Cryoballoon, Arctic Front Advance-Short Tip and Arctic Front Advance Pro™. Studies must have reported on the outcome of interest: 12-month freedom from atrial arrhythmias, defined as AF, atrial tachycardia (AT) or atrial flutter (AFL) after a single procedure, excluding events that occurred during a 3-month blanking period, and without touch-up using a focal catheter. Randomized controlled trials (RCTs) and prospective observational studies were considered. Studies were excluded if they were retrospective or single arm in design or did not report freedom from or recurrence of atrial arrhythmias disaggregated by device. Study screening was conducted by a single reviewer K Eaton (KE) and validated by a second reviewer L Patel (LP). Conflicts were resolved by consensus through discussion or a third party D Grima (DG).

Data extraction

Data extracted included: study design, sample size, patient baseline characteristics, interventions and key outcomes. Some data were extracted by digitizing data (DigitizeIt version 2.2.2 digitizing software) for outcomes at 12 months, when available. No data imputation was required, and no attempt was made to contact study authors for clarification of results or to obtain missing data. Data were extracted by a single reviewer (KE) and verified for accuracy by a second reviewer K Dawkins (KD). Conflicts were resolved by consensus or a third party (LP).

Quality assessment & study hierarchy

Risk of bias of randomized and nonrandomized studies was assessed separately using two independent tools. For studies in which patients were randomized to device-level interventions, the Cochrane Risk of Bias Tool for Randomized Controlled Trials was used [26]. For nonrandomized studies or randomized studies that did not randomize for device-level comparisons, the Cochrane Risk of Bias in Nonrandomized Studies of Interventions (ROBINS-I) was used [27]. One reviewer (KE) scored studies according to the respective tool's grading scheme, and a second reviewer A Dineen (AD) confirmed scores; discrepancies were resolved by consensus or a third party (LP).

A single comprehensive classification scheme was developed to assess the overall hierarchy of studies, including studies for which subgroup data were extracted. The classification scheme assessed study design, adjustment for baseline differences between treatment groups, and balance in baseline characteristics between treatment groups, where balance was identified as the absence of significant differences. Studies were grouped as high-, low- or unclear-quality according to the following definitions: high-quality studies were RCTs or prospective observational studies that reported balanced baseline characteristics or adjusted to balance baseline characteristics between treatment groups; low-quality studies were those that reported unbalanced, unadjusted baseline characteristics; and unclear-quality studies were those that did not report baseline characteristics (i.e., for a treatment or patient subgroup).

Data synthesis & analysis

Devices were represented as individual nodes within the network to best reflect their variability in design, functionality and use in practice. Network meta-analyses were performed using methods as outlined in NICE Decision Support Unit Technical Support Series [28] with extensions to account for evidence from multiple study designs as described by Efthimiou *et al.* [29]. Specifically, analyses were conducted using a three-level Bayesian hierarchical model to incorporate both randomized and nonrandomized evidence (additional detail in Supplementary Material 4). The Bayesian hierarchical model provides estimates of treatment effect in each of the three subnetworks (i.e., high-, unclear- and low-quality), as well as an overall average across designs. Estimates for the primary analysis were taken from the high-quality subnetwork, which allows them to primarily be based on high-quality evidence while being influenced (i.e., borrowing strength) from the unclear- and low-quality subnetworks. Furthermore, low- and unclear-quality studies were weighted 50% compared with high-quality studies. The Bayesian hierarchical NMA was conducted using R Statistical Software version 3.5.3 and JAGS version 4.3.0. All analyses were conducted using a random-effects model with vague priors. Outcomes were modeled on the log-odds scale and converted to relative risk (RR) ratios with 95% credible intervals (CrIs) using the model-estimated average baseline event rate as described by NICE [28]. Absolute rates and 95% CrIs were calculated by adding the estimated treatment effect for each technology to the pooled reference treatment response estimated by the NMA.

Risk ratios <1 or >1 favor one of the catheter ablation devices over the other. CrIs can be interpreted as the Bayesian equivalent to confidence intervals, with CrIs excluding 1 indicating the Bayesian-equivalent of statistical significance. An advantage of Bayesian analyses is that they allow for calculation of the probability that a treatment is the best, second best – among others. These ranks are summarized using medians and their uncertainty is captured by the surface under the cumulative ranking curve area (SUCRA) statistic [30]. SUCRA is expressed as a percentage such that a treatment with a SUCRA of 100% is the best treatment with zero uncertainty. Available study and patient characteristics were assessed for similarity and to investigate the potential effect of heterogeneity. Inconsistency models for hierarchical NMAs have not been developed and tested, therefore an inconsistency analysis was not performed. In addition, NMA results were qualitatively compared with those from direct comparisons generated from traditional meta-analyses using R Statistical Software version 3.6.1. Detailed methods are included in Supplementary Material 4.

Secondary & sensitivity analyses

A secondary analysis was conducted to assess the overall average estimate from the hierarchical NMA, as this estimate would be relevant for decision-makers interested in the average effect across the populations included in each design.

Sensitivity analyses were conducted to assess the robustness of the primary analysis. To assess the influence of the evidence weighting (i.e., low- and unclear-quality studies) on results, sensitivity analyses where low- and unclear-quality studies were not downweighted and where low- and unclear-quality studies were downweighted 80% compared with high-quality studies were conducted. To assess the impact of variance in the subnetworks for low- and unclear-quality studies on primary analysis results, a sensitivity analysis using equivalent standard deviations across all three levels of the Bayesian hierarchical NMA was conducted, where the between-study heterogeneity was assumed to be equivalent in high-, unclear- and low-quality studies.

Results

Literature search & study characteristics

The literature search identified 897 potentially relevant studies, of which 631 were subsequently excluded during the title and abstract review process (Figure 1). Of the 103 eligible full-text articles assessed, 16 were identified for potential inclusion in the quantitative analysis [5–7,15,18,21–23,31–38]. Overall, 12 studies met the criteria for inclusion in the quantitative analyses [5–7,15,18,21,23,32–34,37,38].

Catheters examined in the 12 selected studies included: THERMOCOOL, THERMOCOOL SMARTTOUCH SF, THERMOCOOL SMARTTOUCH SF with Ablation Index, Arctic Front and Arctic Front Advance (Table 1). Males comprised 43–88% of patients, and mean patient age ranged from 56 to 65 years. Presence of paroxysmal AF was 48–100%, and mean duration of AF ranged from 45.6 to 56.4 months. Left atrial diameter, left ventricular ejection fraction and CHA_2DS_2-VASc score were similar across studies. History of coronary artery disease, stroke or transient ischemic attack, hypertension and diabetes varied broadly across studies. Two studies did not report patient baseline characteristics disaggregated by subgroup [18,34]. The definition of effectiveness used in included studies varied, including the type of recurrent arrhythmia measured (e.g., AF, AT and AFL) (Supplementary Material 5).

Risk of bias assessment & study hierarchy

Risk of bias assessment for studies in which patients were randomized to device-level interventions revealed that one RCT had high risk of performance bias [21] and one had low risk of attrition and reporting bias (Supplementary Material 6) [23]. The ROBINS-I tool revealed all nonrandomized studies to have a moderate overall risk of bias for the outcome of freedom from atrial arrhythmias at 12-month follow-up (Supplementary Material 7).

Further assessment of studies by design and balanced patient baseline characteristics identified seven studies of high quality [6,7,15,21,23,37,38], three of low quality [5,32,33] and two of unclear quality (Supplementary Material 8) [18,34].

Primary analysis

A total of 12 studies and 1722 patients were included in the primary analysis (Figure 2). The evidence network consisted primarily of multiple-study connections of two to four studies; single-study connections informed comparisons across device generations and ablation technologies (e.g., one study connecting the Arctic Front and THERMOCOOL SMARTTOUCH nodes and one study connecting the THERMOCOOL and Arctic Front Advance nodes). Evidence plots for each subnetwork (i.e., high-, unclear- and low-quality) are presented in Supplementary Material 9.

THERMOCOOL SMARTTOUCH with Ablation Index was associated the highest absolute probability (95.8%) of 12-month freedom from atrial arrhythmias, followed by THERMOCOOL SMARTTOUCH (87.5%), THERMOCOOL (71.5%), Arctic Front Advance (66.3%) and Arctic Front (54.0%). When compared with all other catheter ablation devices, results favored THERMOCOOL SMARTTOUCH with Ablation Index for the probability of 12-month freedom from atrial arrhythmias (Figure 3; Supplementary Material 10). THERMOCOOL SMARTTOUCH with Ablation Index was associated with a significantly greater (77%) likelihood of freedom from atrial arrhythmias than Arctic Front (RR: 1.77, 95% CrI: 1.21–2.87).

Similarly, THERMOCOOL SMARTTOUCH with Ablation Index was associated with a statistically significantly greater (41%) likelihood of 12-month freedom from atrial arrhythmias than Arctic Front Advance (RR: 1.41; 95% CrI: 1.06–2.47). Additionally, THERMOCOOL SMARTTOUCH with Ablation Index was associ-

Table 1. Summary of baseline patients characteristics.

Study (year)	Treatment device	N	Age (years)	PAF (%)	Males (%)	Duration of AF (months)	LAD (mm)	LVEF (%)	CHA_2DS_2-VASc score	CHADS2 score	BMI	Stroke or TIA (%)	HT (%)	Diabetes (%)	Ref.
Andrade *et al.* (2014)	THERMOCOOL™	50	58.6	100	86	–	39.2	59.9†	–	–	–	–	–	–	[5]
	THERMOCOOL SMARTTOUCH™	25	58.8	100	76	–	32.4	63.3†	–	–	–	–	–	–	
Davtyan *et al.* (2018)	Arctic Front Advance™	44	57.6	100	48.9	–	41	–	1.3	–	29.9	11.1	77.8	4.4	[23]
	THERMOCOOL SMARTTOUCH	45	55.6	100	43.2	–	40	–	1.3	–	29.8	9.1	77.3	13.6	
Dhillon *et al.* (2018)	THERMOCOOL SMARTTOUCH	50	59.9	100	48†	Median: 42	38.7	–	1.68	–	–	–	34	6	[33]
	THERMOCOOL SMARTTOUCH + AI	50	60.1	100	70†	Median: 24	37.6	–	1.3	–	–	–	38	12	
Hussein *et al.* (2017)	THERMOCOOL SMARTTOUCH	89	62	48	73	–	41	–	–	0.65	29	9	30	9	[34]
	THERMOCOOL SMARTTOUCH + AI	89	62	50	75	–	42	–	–	0.65	29	3	34	15	
Itoh *et al.* (2016)‡	THERMOCOOL	50	61	100	62	–	38	65	1.8	1.0	–	8	52	16	[7]
	THERMOCOOL SMARTTOUCH	50	65	100	60	–	37	65	2.3	1.3	–	14	64	10	
Jourda *et al.* (2015)‡	Arctic Front Advance	75	59.9	100	73.3	45.6	–	64.4	1.3	0.7	28.2†	4	34.7	8.0	[32]
	THERMOCOOL SMARTTOUCH	75	62.5	100	76.0	52.8	–	65.5	1.5	0.9	26.5†	10.7	48.0	4.0	
Koektuerk *et al.* (2017)	Arctic Front	21	62	100	71.4	–	–	58.7	1.8	–	–	–	52.4	9.5	[15]
	Arctic Front Advance	93	61	100	60.2	–	–	59.9	1.8	–	–	–	58.1	5.4	
Kuck *et al.* (2016)	Radiofrequency	376	60.1	100	63	56.4	40.6	–	1.8	–	27.8	–	58.8	5.9	[18]
	Cryoballoon	374	59.9	100	59	55.2	40.8	–	1.9	–	28.0	–	57.5	9.9	
Marijon *et al.* (2014)	THERMOCOOL	30	61.0	100	73.3	–	–	65.4	0.58	–	–	–	–	–	[6]
	THERMOCOOL SMARTTOUCH	30	59.9	100	70.0	–	–	64.7	0.86	–	–	–	–	–	
Perez-Castellano *et al.* (2014)	THERMOCOOL	25	Median: 56	100	88	–	Median: 42	–	–	–	–	–	32	8	[21]
	Arctic Front	25	Median: 58	100	68	–	Median: 42	–	–	–	–	–	24	16	
Phlips *et al.* (2018)	THERMOCOOL SMARTTOUCH	50	62	100	62	Median: 24	40.4	–	–	–	26.6	–	40	0	[38]
	THERMOCOOL SMARTTOUCH + AI	50	61	100	72	Median: 24	39.9	–	–	–	27.0	–	30	4	
Zhao *et al.* (2017)	Arctic Front	50	60.9	100	72	47.5	–	62.4	0.89	–	–	–	38	12	[37]
	Arctic Front Advance	50	60.4	100	80	51.3	–	61	0.82	–	–	–	36	14	

Data are expressed as means or proportion of patients (%) except where otherwise noted. Blank cells represent unreported data.

†Differences between baseline characteristics within in each treatment group are significant ($p < 0.05$).

‡Data were reported for vascular disease.

AF: Atrial fibrillation; AI: Ablation Index; BMI: Body mass index; HT: Hypertension; LAD: Left atrial diameter; LVEF: Left ventricular ejection fraction; PAF: Paroxysmal atrial fibrillation; TIA: Transient ischemic attack.

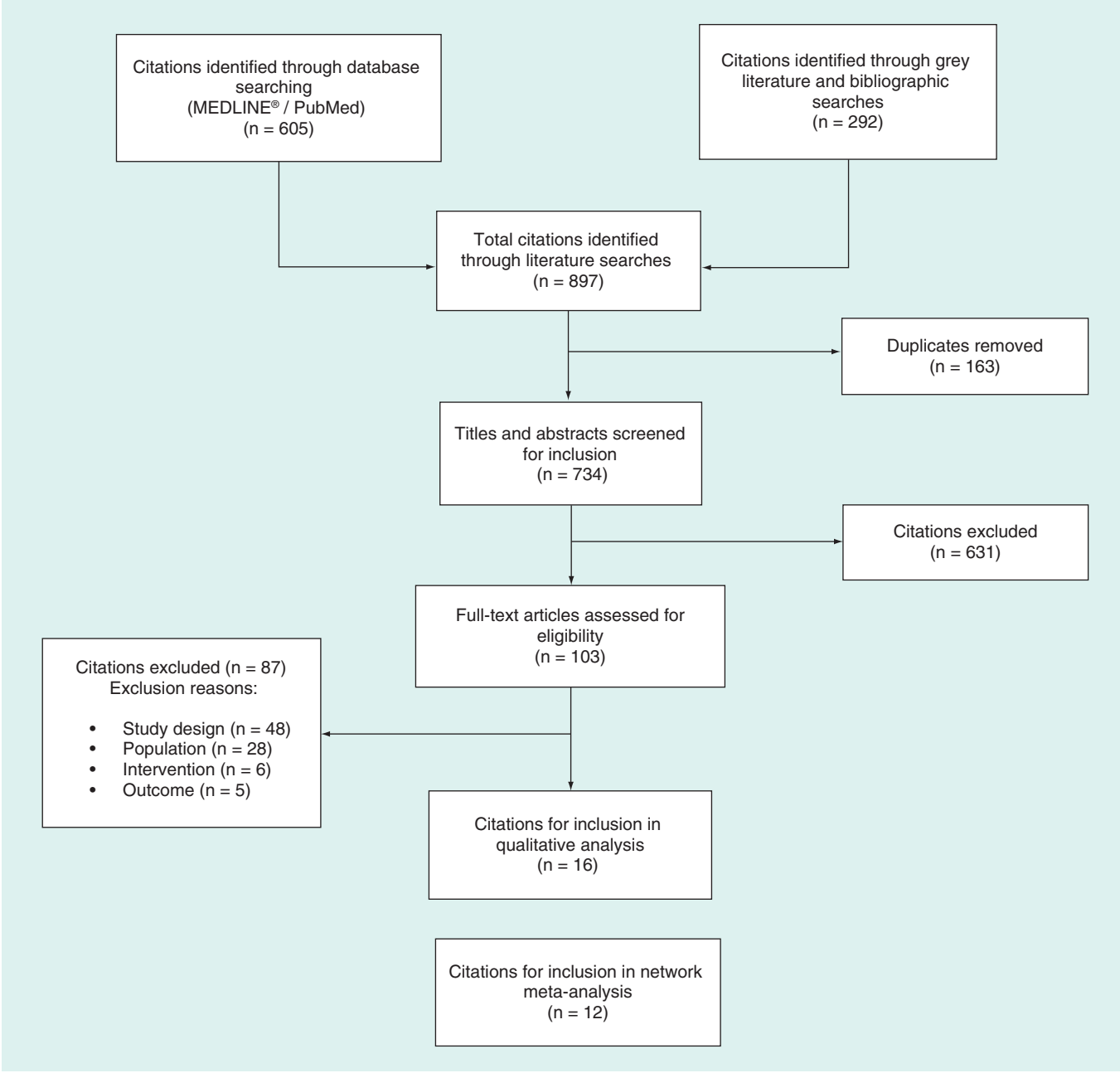

Figure 1. Preferred reporting items of systematic reviews and meta-analyses flow diagram.

ated with a significantly greater (34%) likelihood of freedom from atrial arrhythmias than THERMOCOOL (RR: 1.34; 95% CrI: 1.17–1.48) and a significantly greater (9%) likelihood of freedom from atrial arrhythmias than THERMOCOOL SMARTTOUCH (RR: 1.09; 95% CrI: 1–1.3). THERMOCOOL SMARTTOUCH with Ablation Index was ranked first among treatments (median rank 1; 95% CI: 1–2), followed by THERMOCOOL SMARTTOUCH (median rank 2; 95% CI: 2–3), THERMOCOOL (median rank 3; 95% CI: 3–5), Arctic Front Advance (median rank 4; 95% CI: 2–5) and Arctic Front (median rank 5; 95% CI: 4–5) (Supplementary Material 11). Furthermore, THERMOCOOL SMARTTOUCH with Ablation Index had the highest SUCRA (99.2%), followed by THERMOCOOL SMARTTOUCH (73.0%), THERMOCOOL (39.5%), Arctic Front Advance (33.6%) and Arctic Front (4.7%) (Supplementary Material 12).

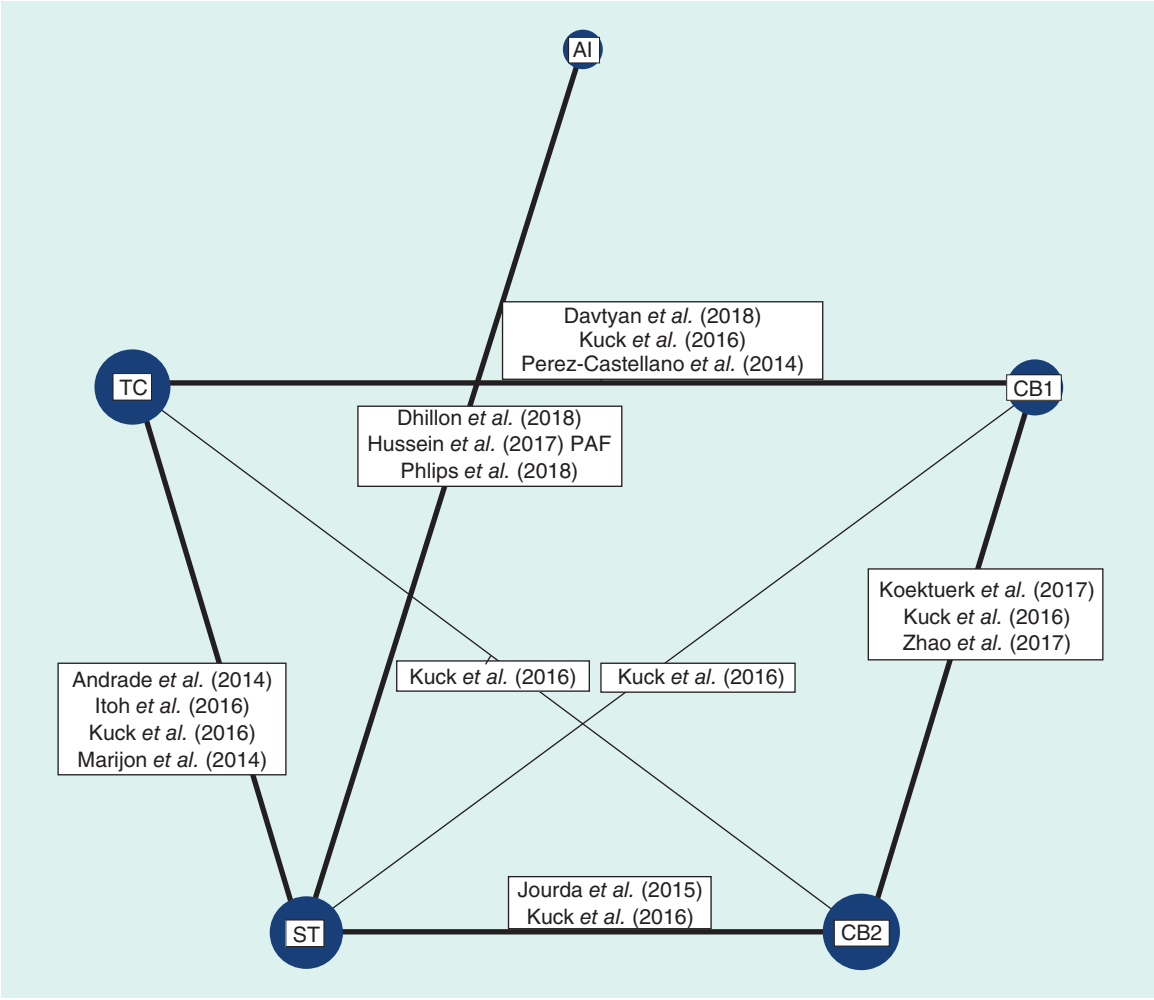

Figure 2. Evidence network of studies included in the primary analysis. In the evidence network, the width of the lines for each connection is proportional to the number of studies comparing each pair of treatments. The size of each treatment node is proportional to the number of participants.
AI: THERMOCOOL SMARTTOUCH™ with Ablation Index; CB1: Arctic Front; CB2: Arctic Front Advance™; ST: THERMOCOOL SMARTTOUCH™; TC: THERMOCOOL™.

Secondary & sensitivity analyses

Secondary and sensitivity analyses included all studies from the primary analysis. The overall average effect across populations was similar to the results of the primary analysis (Figure 4; Supplementary Material 13). THERMOCOOL SMARTTOUCH with Ablation Index continued to have a statistically significantly greater likelihood of freedom from atrial arrhythmias than all catheter ablation devices except THERMOCOOL SMARTTOUCH, as well as the highest median rank and SUCRA (Supplementary Appendices 11 & 12).

Results of the primary analysis were reasonable and robust to changes in downweighting of low- and unclear-quality studies and the uncertainty in the low- and unclear-quality study levels due to low number of studies (Figure 4; Supplementary Material 13). When low- and unclear-quality studies were not downweighted or were downweighted 80%, THERMOCOOL SMARTTOUCH with Ablation Index continued to have a statistically significantly greater probability of freedom from atrial arrhythmias than all other catheter ablation devices. Additionally, results were consistent when an equivalent standard deviation was used across all three levels of the Bayesian hierarchical model. In all sensitivity analyses, THERMOCOOL SMARTTOUCH with Ablation Index continued to have the highest median rank and SUCRA (Supplementary Materiales 11 & 12).

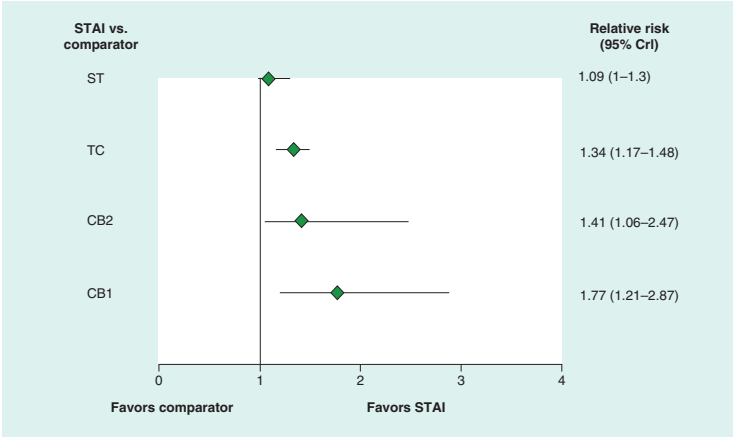

Figure 3. Forest plot summarizing results of the primary analysis for THERMOCOOL SMARTTOUCH™ with Ablation Index vs comparators.
CB1: Arctic Front; CB2: Arctic Front Advance™; CrI: Credible interval; ST: THERMOCOOL SMARTTOUCH™; STAI: THERMOCOOL SMARTTOUCH™ with Ablation Index; TC: THERMOCOOL™.

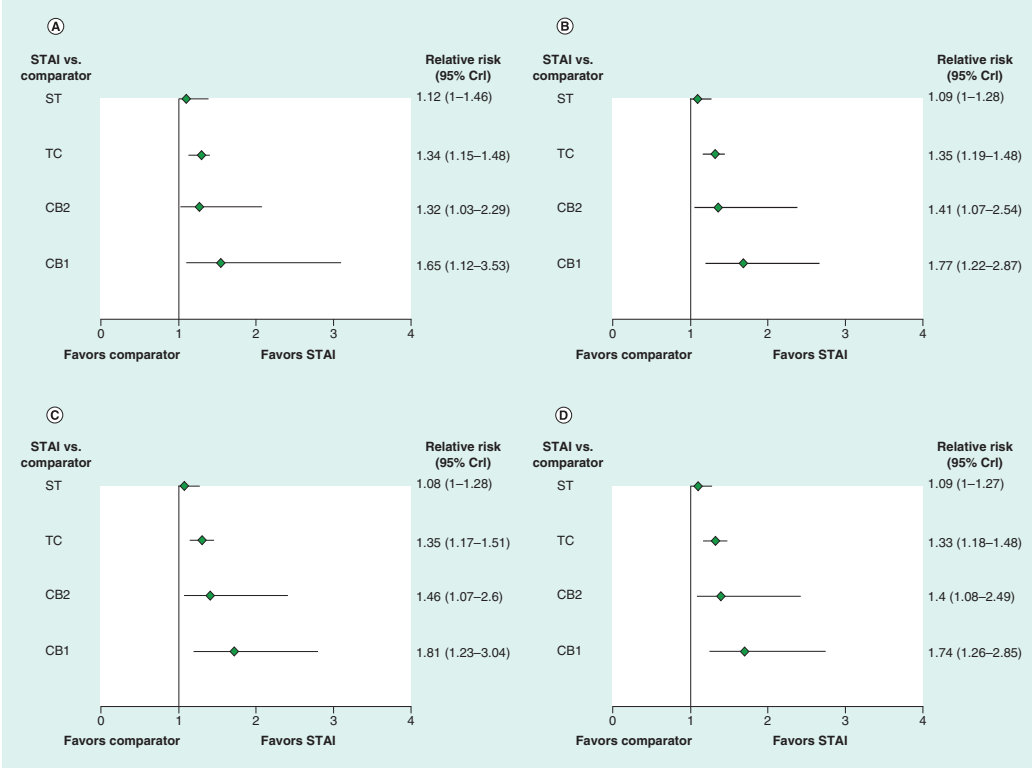

Figure 4. Summary of results from the secondary and sensitivity analyses for THERMOCOOL SMARTTOUCH™ with Ablation Index vs comparators. (A) Bayesian hierarchical model with 50% downweighting (overall average effect); **(B)** Bayesian hierarchical model without downweighting (high quality); **(C)** Bayesian hierarchical model with 80% downweighting (high quality); **(D)** Bayesian hierarchical model where all three levels shared standard deviation and low- and unclear-quality studies are weighted by 50% of high-quality studies (high quality).
CB1: Arctic Front; CB2: Arctic Front Advance™; CrI: Credible interval; ST: THERMOCOOL SMARTTOUCH™; STAI: THERMOCOOL SMARTTOUCH™ with Ablation Index; TC: THERMOCOOL™.

Discussion

Advancements to catheter ablation technology are continually emerging; however, contemporary, high-quality evidence comparing these advanced technologies such as the THERMOCOOL SMARTTOUCH with Ablation Index are lacking. The objective of this study was to evaluate the comparative effectiveness of THERMOCOOL SMARTTOUCH with Ablation Index using the totality of currently available prospective comparative evidence for RF and CB ablation.

Overall, results from this analysis showed that THERMOCOOL SMARTTOUCH with Ablation Index provides significantly greater likelihood of freedom from recurrent atrial arrhythmias at 12-month follow-up than other catheter ablation devices. Additionally, THERMOCOOL SMARTTOUCH with Ablation Index was ranked first among all treatments and was associated with the highest probability of being ranked among the best treatments (SUCRA) for freedom from atrial arrhythmias at 12 months. Results of the primary analysis were robust in sensitivity analyses. Our results are consistent with those of a meta-analysis that compared THERMOCOOL SMARTTOUCH with Ablation Index to THERMOCOOL SMARTTOUCH, which found use of Ablation Index was associated with significant reductions in acute PV reconnection and arrhythmia recurrence at 12-month follow-up [13]. However, studies directly comparing CB to advanced RF technology are lacking; specifically, no studies directly compare CB to RF technology with the use of Ablation Index.

The lack of direct comparative data between alternative treatments makes assessments of various technologies challenging. This analysis provides decision-makers with robust, pooled, comparative evidence for the latest generations of catheter ablation devices used in the treatment of AF, namely THERMOCOOL SMARTTOUCH with Ablation Index and Arctic Front Advance, that reflects the totality of published evidence.

One limitation of this study is that results may be biased due to inclusion of poor-quality studies (i.e., low- or unclear-quality). Although the aim of a Bayesian hierarchical model is to incorporate the additional uncertainty related to biases introduced by pooling different study designs, the ability to estimate the true effect may be limited by an immature network and/or a lack of high-quality studies. Methods have been developed to manually adjust potentially biased studies based on the results of meta-epidemiological literature, but their application to this problem would be inappropriate owing to the lack of such studies specific to medical devices [29]. Another limitation was the lack of homogeneity across studies. The conduct of an NMA assumes there is homogeneity between studies being compared; however, heterogeneity was unavoidably introduced, for example, through differences in patient baseline characteristics, in the type of recurrent arrhythmia measured (i.e., AF, AT and AFL), and in the method used to monitor arrhythmias (Supplemental Material 16). This may affect the generalizability and applicability of results.

A major strength of the present study is that it is the first NMA to compare the effectiveness of AF ablation across several catheter ablation devices, with a focus on the most current technologies of Ablation Index and second-generation CB. Furthermore, the results of this analysis are highly comprehensive, including 12 prospective comparative studies. The majority of NMAs are conducted using RCTs; however, nonrandomized studies may be considered if RCT data are limited [39]. Specifically, conduct of a Bayesian hierarchical NMA is a rigorous statistical approach used to incorporate randomized and nonrandomized studies [40]. Incorporation of both randomized and nonrandomized studies helps to improve the generalizability and applicability of results to real-world scenarios important in clinical and health economic decision-making [41].

Conclusion

Overall, catheter ablation using the THERMOCOOL SMARTTOUCH Catheter with Ablation Index is statistically significantly more favorable for freedom from atrial arrhythmias at 12 months than first- and second-generation RF and CB catheters. This is the first study to provide decision-makers with robust, pooled, comparative evidence of the latest ablation technologies that reflects the totality of evidence available, particularly contemporary, high-quality studies.

Supplementary data

To view the supplementary data that accompany this paper please visit the journal website at: www.futuremedicine.com/doi/suppl/10.2217/cer-2019-0165

Summary points

- Ablation Index is a novel lesion-quality marker associated with improved outcomes in radiofrequency ablation; however, there is a lack of direct comparative evidence between the latest generations of catheter ablation devices and uncertainty regarding the best treatment option.
- We conducted a Bayesian hierarchical network meta-analysis of 12 prospective studies to evaluate the comparative effectiveness of radiofrequency ablation with Ablation Index to other catheter ablation devices in the treatment of atrial fibrillation (AF).
- Radiofrequency ablation using the THERMOCOOL SMARTTOUCH™ Catheter with Ablation Index was associated the highest absolute probability (95.8%) of 12-month freedom from atrial arrhythmias, followed by THERMOCOOL SMARTTOUCH (87.5%), THERMOCOOL™ (71.5%), Arctic Front Advance™ (66.3%) and Arctic Front (54.0%).
- THERMOCOOL SMARTTOUCH with Ablation Index was associated with statistically significantly greater probability of 12-month freedom from atrial arrhythmias than Arctic Front (relative risk: 1.77; 95% credible interval: 1.21–2.87), Arctic Front Advance (1.41; 1.06–2.47), THERMOCOOL (1.34; 1.17–1.48) and THERMOCOOL SMARTTOUCH (1.09; 1–1.3).
- THERMOCOOL SMARTTOUCH with Ablation Index was ranked first among all treatments and was associated with the highest probability of being ranked among the best treatments (SUCRA) for freedom from atrial arrhythmias at 12 months.
- In secondary and sensitivity analyses, the overall average effect across populations was similar to the results of the primary analysis.
- The present study conducted a Bayesian hierarchical network meta-analysis, which is a rigorous statistical approach used to incorporate randomized and nonrandomized studies and improves the generalizability and applicability of results to real-world scenarios.
- This analysis provides decision-makers with robust, pooled, comparative evidence for the latest generations of catheter ablation devices used in the treatment of atrial fibrillation.

Author contributions

L Goldstein, M Velleca and G Costa contributed to the conception and design of the research and provided critical revisions and intellectual content to the manuscript. D Gupta and T De Potter provided substantial intellectual content, and revisions to the manuscript. T Disher, L Patel, D Grima and K Eaton conducted analyses, discussed the results, drafted the manuscript and contributed to the final version of the manuscript. All authors provided critical and intellectual feedback of the research, analysis and manuscript.

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Ethical conduct of research

This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

Data sharing statement

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

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