CJC Open 5 (2023) 965–970

Original Article

Half-Normal Saline vs Normal Saline for Cavotricuspid Isthmus-Dependent Atrial Flutter Ablation

Ana de Leon, MD, Matthew Hanson, MD, Nasser Alhammad, MD, David Bakker, RCT, Sanoj Chacko, MB, BS, Christopher Simpson, MD, Hoshiar Abdollah, MB, ChB, Adrian Baranchuk, MD, Damian Redfearn, MD, Benedict Glover, MD, Andres Enriquez, MD, and Victor Neira, MD

Division of Cardiology, Queen's University, Kingston, Ontario, Canada

ABSTRACT

Background: Cavotricuspid isthmus (CTI) ablation requires permanent bidirectional block to prevent recurrence of typical atrial flutter (AFL). Catheter irrigation with half-normal saline (HNS) produces larger and deeper lesions in experimental models compared with normal saline (NS). This study was performed to compare the clinical efficacy and safety of HNS vs NS irrigation for typical AFL ablation.

Methods: Sixty patients undergoing catheter ablation of typical AFL were randomized 1:1 to NS or HNS irrigation. Endpoints included time to CTI block, acute reconnection, incidence of steam pops, and recurrence of AFL during follow-up.

Results: Baseline characteristics were comparable between both arms. The mean age of the patients was 68.5 ± 8.2 years, 20% were female, and 32% had atrial fibrillation before being enrolled. Bidirectional CTI block was obtained in all patients with no difference in time

RÉSUMÉ

Contexte : Pour prévenir la récurrence d'un flutter auriculaire (flutter) typique, l'ablation de l'isthme cavotricuspidien exige un bloc de conduction bidirectionnel permanent. Dans des modèles expérimentaux, l'irrigation par cathéter au moyen d'un soluté demi-salin produit des lésions plus larges et plus profondes, comparativement à un soluté physiologique salin. La présente étude a été réalisée dans le but de comparer l'efficacité clinique et l'innocuité de l'irrigation au moyen d'un soluté demi-salin à celles de l'irrigation par un soluté physiologique salin dans les cas d'ablation d'un flutter.

Méthodologie : Soixante patients soumis à une ablation d'un flutter typique par cathéter ont été répartis au hasard dans un rapport de 1:1 en deux groupes d'irrigation, soit par soluté demi-salin, soit par soluté physiologique salin. Les critères d'évaluation de l'étude étaient les suivants : temps écoulé jusqu'au bloc de l'isthme cavotricuspidien,

Typical atrial flutter (AFL) is a common supraventricular arrhythmia with a re-entrant circuit localized to the right atrium. It has a critical area of slow conduction in the cavotricuspid isthmus (CTI), which is also the narrowest part of the circuit, located between the tricuspid valve anteriorly and the inferior vena cava posteriorly.[1,2]

Because of its well-defined anatomic substrate for catheter ablation, high rate of procedural success, low risk of complications, and relative resistance to antiarrhythmic therapy, catheter ablation of CTI-dependent AFL is considered a first line therapy.[3,4] The principle of catheter ablation is to create an effective and durable transmural lesion in the isthmus, demonstrated by bidirectional conduction block. Despite a high acute success rate of 90% to 98%, up to 10% of patients have a long-term recurrence.[3,5,6] An effective radiofrequency (RF) ablation lesion depends on many variables such as RF power, contact force, delivery time, and type of catheter (irrigated vs not irrigated). The type of irrigant solution may also influence the RF efficacy. Previous ex vivo and in vivo studies have demonstrated that the use of half normal saline (HNS) produces deeper and larger lesions.[7,8] In the last few years, HNS used by open irrigated RF catheter has been compared with standard normal saline (NS) in different ablation scenarios.[9,10] The purpose of this study was to determine the safety and efficacy of HNS irrigation for ablation of CTI-dependent AFL and to see if long-term rates of recurrence were lower with this technique.

Methods

This single-centre double-blind randomized clinical study included 60 patients with documented typical AFL who were referred for CTI ablation between January 2018 and

Received for publication August 18, 2023. Accepted September 21, 2023.

Corresponding author: Dr Victor Neira, Division of Cardiology, Queen's University, 76 Stuart Street, Kingston, Ontario K7L 2V7, Canada. Tel.: +1-613-549-6666, ext 3801; fax: +1-613-548-1387.

E-mail: victor.neiravidal@KingstonHSC.ca

See page 969 for disclosure information.

https://doi.org/10.1016/j.cjco.2023.09.013

to CTI block between groups (6.4 ± 4.4 minutes vs 7.6 ± 4.5 minutes, respectively; $P = 0.15$). There was a trend to less acute reconnection in the HNS group compared with NS (13.3% vs 26.6%; $P = 0.46$). Steam pops occurred in 4 patients using HNS vs none in the NS group, but no major complications were observed. During the follow-up, rate of AFL recurrence was similar between groups (6.7% with HNS vs 10% with NS; $P = 0.5$). There was no difference in time to recurrence (7.6 ± 6.9 vs 4.9 ± 4.5 months; $P = 0.6$).

Conclusions: In this small pilot randomized controlled trial, there was no significant difference between HNS and NS for CTI ablation; however, HNS may increase the incidence of steam pops.

reconnexion aiguë, jet de vapeur sonore (*steam pop*) et récidive de flutter durant le suivi.

Résultats : Les caractéristiques initiales étaient comparables dans les deux groupes. Les patients avaient une moyenne d'âge de 68,5 ± 8,2 ans, 20 % étaient des femmes et 32 % présentaient une fibrillation auriculaire avant leur admission à l'étude. Un bloc bidirectionnel dans l'isthme cavotricuspidien a été obtenu chez tous les patients, sans différence entre les groupes en ce qui a trait au temps écoulé jusqu'à l'obtention du bloc isthmique (6,4 ± 4,4 minutes *vs* 7,6 ± 4,5 minutes, respectivement; $p = 0{,}15$). Une tendance vers un nombre plus faible de cas de reconnexion aiguë a été notée dans le groupe d'irrigation par soluté demi-salin, comparativement au soluté physiologique salin (13,3 % *vs* 26,6 %; $p = 0{,}46$). Un jet de vapeur sonore est survenu chez 4 patients recevant un soluté demi-salin contre aucun dans le groupe sous soluté physiologique salin, mais aucune complication importante n'a été relevée. Durant le suivi, le taux de récidive de flutter a été similaire dans les deux groupes (6,7 % sous soluté demi-salin *vs* 10 % sous soluté physiologique salin; $p = 0{,}5$). Aucune différence n'a été notée pour ce qui est du temps écoulé jusqu'à la survenue d'une récidive (7,6 ± 6,9 *vs* 4,9 ± 4,5 mois; $p = 0{,}6$).

Conclusions : Dans cette petite étude pilote contrôlée et avec répartition aléatoire, aucune différence significative n'a été observée entre le soluté demi-salin et le soluté physiologique salin pour l'ablation de l'isthme; toutefois, le soluté demi-salin augmenterait la fréquence des cas de jet de vapeur sonore.

September 2019 at Kingston Health Science Centre (KHSC). Randomization was performed using random number generation (from 0-60) for irrigant solution and ablation slot. Consecutive patients meeting inclusion criteria then underwent ablation according to the predetermined randomized schedule known only to the study coordinator. Blinding of the operator was maintained through fluid preparation outside of the procedure room by the circulating nurse's use of opaque bags covering the irrigant during the cases. The study was approved by the institutional Health Sciences Research Ethics Board.

Patients were eligible if they met all of the inclusion criteria: age ≥18 years, documented typical AFL, and ability to provide informed consent. Patients were excluded if they met any of the exclusion criteria: previous CTI ablation, presence of left atrial thrombus, or inability to provide consent.

Eligible patients were randomly assigned to HNS (0.45% sodium chloride [NaCl] concentration) or NS (0.9% NaCl concentration) as a catheter ablation irrigant solution. Both patient and operator were blinded to the irrigant solution. The primary endpoints were acute and long-term ablation efficacy and acute procedural safety. Secondary endpoints included number of lesions, duration of ablation, and time to recurrence.

Procedures were performed under conscious sedation, guided by 3-dimensional (3D) electroanatomic mapping (NavX Ensite Precision, Abbott, St Paul, MN) using an open irrigated 4-mm contact-force RF ablation catheter (Tacticath SE, Abbott). In some cases, a deflectable sheath (Agillis, Abbott) was used at the operator's discretion. A fast anatomic map was created before ablation to characterize the CTI anatomy. In those patients presenting in AFL, entrainment manoeuvres were conducted to confirm a CTI-dependent mechanism. Patients in sinus rhythm had differential pacing from proximal coronary sinus and lateral right atrium for pre- and postablation comparison.

Catheter ablation was delivered by operator preference using anatomic or maximum voltage-guided method,[5] in a point-by-point fashion with 40-second lesions at a power of 30 watts and a contact force of at least 10 g. Radiofrequency delivery was interrupted before 40 seconds if any of the following occurred: impedance drop > 30 Ohms, impedance rise > 10 Ohms, temperature rise > 42° C, or steam-pop. After each ablation lesion, local electrograms were assessed for CTI block. This was confirmed by double potentials separated by an isoelectric line measuring ≥ 110 ms and evidence of bidirectional block using differential pacing from proximal coronary sinus and the CTI lateral to the ablation line. Activation and propagation map during proximal coronary sinus pacing was also performed to show the line of block. Once bidirectional block was achieved, a 30-minute waiting period was started, during which differential pacing was performed to confirm the durability of bidirectional block. If, during that period, a reconnection was observed, ablation was resumed until block was achieved and a new waiting period was started.

After ablation, patients were monitored in hospital for at least 4 hours before discharge. Bedside echocardiography was performed to rule out pericardial effusion. After discharge, patients were followed-up for at least 1 year with clinic visits at 3, 6, and 12 months to detect recurrence of AFL, incidence of atrial fibrillation (AF), and to monitor for any complications. For arrhythmia surveillance, a 12-lead electrocardiogram (ECG) and 24-hour Holter monitor were performed at each visit. Antiarrhythmic drugs were discontinued unless they were deemed necessary because of coexisting AF.

Statistical analysis was conducted using Stata 13.0 software (StataCorp, College Station, TX). Continuous data with a

Table 1. Baseline characteristics of study population

Characteristic	HNS group	NS group
Randomized subjects (n)	30	30
Age (years)	68.9 ± 7.0	68.0 ± 9.4
Female (n)	8 (26.6)	4 (13.3)
Comorbidities		
Hypertension	19 (63.3)	18 (60)
Type II diabetes	12 (40)	6 (20)
Sleep apnea	11 (36.6)	10 (33.3)
Chronic heart failure	7 (23.3)	4 (13.3)
Chronic kidney disease	3 (10)	2 (6.6)
History of CVA or TIA	2 (6.6)	1 (3.3)
CHA_2DS_2-VASc score	3.0 ± 1.6	2.4 ± 1.4
BMI (kg/m^2)	31.1 ± 6.5	30.5 ± 4.8
Echocardiogram parameters		
LVEF (%), mean ± SD	54.5 ± 14.5	56.8 ± 14.3
LA diameter (mm)	40.8 ± 6.8	40.9 ± 6.0
LA indexed volume (mL/m^2)	39.2 ± 6.2	38.9 ± 10.7
RA volume (mL/m^2)	28 ± 6.2	27.5 ± 7.9
Antiarrhythmic drugs treatment		
Beta blockers	21 (70)	19 (63.3)
Amiodarone	10 (33.3)	9 (30)
Calcium channel blockers	6 (20)	6 (20)
Digoxin	2 (6.6)	2 (6.6)
Sotalol	3 (10)	1 (3.3)
IC antiarrhythmic drugs	2 (6.7)	0 (0)
Dronedarone	0 (0)	1 (3.3)

Values are presented as mean ± SD, median, or as n (%). *P* value by Fisher's exact test for categorical variables and for continuous variables; Student's *t*-test for equal variances and unequal variances, as appropriate.

BMI, body mass index; $CHAD_2DS_2$-VASc, **C**ongestive Heart Failure, **H**ypertension, **A**ge [≥ 75 Years] [doubled], **D**iabetes Mellitus, **S**troke [doubled], **V**ascular Disease, **A**ge [65-74] Years, **S**ex **C**ategory [Female]; CVA, cerebrovascular accident; HNS, half-normal saline; LA, left atrium; LVEF, left ventricular ejection fraction; NS, normal saline; RA, right atrium; SD, standard deviation; TIA, transient ischemic attack.

normal distribution were presented as mean ± standard deviation and were compared using Student's *t*-test for equal variances and unequal variances, as appropriate. Categorical variables were expressed as frequencies and were compared using the Fisher's exact test. Differences between the groups in terms of time to AFL recurrences were depicted with Kaplan-Meier curves, compared using *P* value by log-rank test, and the hazard ratios were tested with Mantel-Cox regression log-rank test. A *P* value < 0.05 was considered statistically significant.

Results

Sixty-patients were enrolled in the study and randomized 1:1 to HNS or NS. Baseline characteristics are summarized in Table 1. The patients were comparable between both arms; the mean age was 68.5 ± 8.2 years, and 20% were female. AF was documented in 31.7% of patients before enrollment. The mean $CHAD_2DS_2$-VASc (**C**ongestive Heart Failure, **H**ypertension, **A**ge [≥ 75 Years] [doubled], **D**iabetes Mellitus, **S**troke [doubled], **V**ascular Disease, **A**ge [65-74] Years, **S**ex **C**ategory [Female]) score was 2.7 ± 1.5 points. Baseline echocardiographic characteristics did not differ between groups with respect to atrial size or left ventricular (LV) function.

The presenting rhythm at the time of CTI ablation was sinus rhythm in 46.6% and typical AFL in 53.4% of patients. Ninety percent of patients were on medical therapy with aortic valve (AV) nodal blocking agents or antiarrhythmic drugs, with 41.6% on more than 2 medications. The most frequently used medications were beta blockers in 66.6%, amiodarone in 31.6%, calcium channel blockers in 20%, digoxin in 6.7%, sotalol in 6.7%, class IC antiarrhythmic drugs in 3.3%, and dronedarone in 1.7%.

Table 2. Analysis of intraoperative results and complications in both arms of the study

Characteristic	HNS group (n = 30)	NS group (n = 30)	*P* value
Ablation lesion parameters			
CF (g)	12.0 ± 3.2	12.3 ± 3.0	0.72
LSI	5.3 ± 0.63	5.4 ± 0.68	0.27
FTI (gs)	425.2 ± 116.4	430.3 ± 128.6	0.87
Time to CTI block (min)	6.4 ± 4.4	7.6 ± 4.5	0.15
Number of lesions (n)	12.2 ± 7.8	16.7 ± 9.4	0.02
Procedure outcomes			
Bidirectional block	30 (100)	30 (100)	1.0
Acute reconnection	4 (13.3)	8 (26.6)	0.46
Annular region	0 (0)	2 (6.6)	0.26
Middle region	3 (10)	5 (16.6)	0.38
Caval region	1 (3.3)	1 (3.3)	0.75
Procedure time (min)	105.6 ± 22.7	117.5 ± 39.4	0.15
Acute complications			
Steam pop	4 (13.3)	0 (0)	0.06
Pericardial effusion	0 (0)	0 (0)	1.0

Values are presented as mean ± SD, median, or as n (%). *P* value by Fisher's exact test for categorical variables and for continuous variables; Student's *t*-test for equal variances and unequal variances, as appropriate.

CF, contact force; CTI, cavotricuspid isthmus FTI, force-time integral; HNS, half-normal saline; LSI, lesion size index; NS, normal saline; SD, standard deviation.

The analysis of intraoperative results and outcomes are presented in Table 2. The average CTI length was 31.2 ± 5.4 mm, and bidirectional CTI block was achieved with ablation in all patients. There was a trend to shorter ablation time to achieve bidirectional CTI block in the HNS group compared with the NS group, but it was not statistically significant (6.4 ± 4.4 minutes vs 7.6 ± 4.5 minutes, respectively; $P = 0.15$). The impedance drop during ablation was higher in the HNS group (26.7 ± 7.3 vs 23.1 ± 4.3 Ohms, respectively; $P = 0.02$), whereas the overall number of RF lesions was lower with HNS (12.2 ± 7.8 vs 16.7 ± 9.4, respectively; $P = 0.02$). Use of deflectable sheath was similar between groups: used in 19 cases with HNS compared with 15 cases of NS ($P = 0.42$). In both groups, the time to block and number of radiofrequency lesions were reduced when a maximum voltage-guided technique was used (Fig. 1). There was 50% less acute reconnection in HNS group compared with NS, but this was not statistically significant (13.3% vs 26.6%, respectively; $P = 0.46$). Acute reconnections were more frequent in the middle CTI region in both groups (10% HNS group vs 16.6% NS group; $P = 0.38$). There were 4 steam pops in the HNS group: 2 at the middle CTI region and 2 at the caval CTI region, and none in the NS group (13.3% vs 0%, respectively; $P = 0.06$); however, no pericardial effusions were observed.

The outcomes during the follow-up showed similar acute and long-term efficacy and safety despite a higher steam pop rate, which was not related to major complications (Table 3). During the follow-up, 13.3% of the patients in both arms remained on single antiarrhythmic drug treatment, used as a

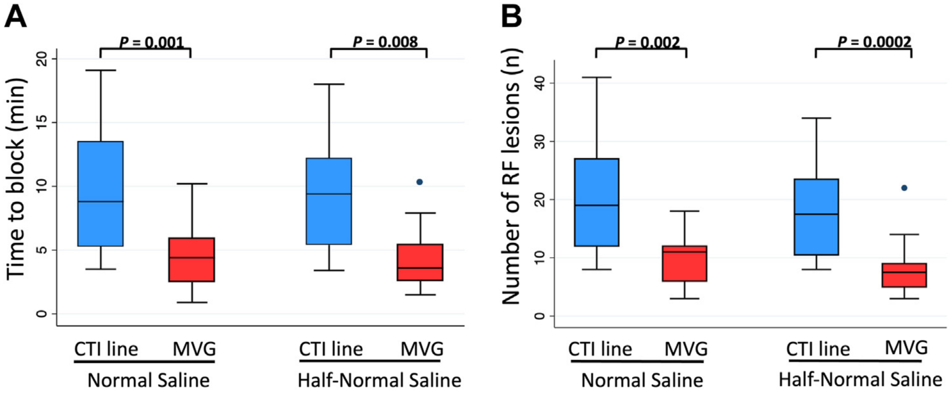

Figure 1. Comparison of ablation parameters among HNS vs NS arms, according to the ablation technique. (**A**) Time to block and (**B**) number of RF lesions. *P* value for continuous variables, using Student's *t*-test for equal variances. CTI, cavotricuspid isthmus; HNS, half normal saline; MVG, maximum voltage guided; NS, normal saline; RF, radiofrequency.

rhythm control strategy in patients with concomitant atrial fibrillation.

During a mean follow up time of 35 months, there were no significant differences in recurrence of AFL between the HNS and NS arms (Fig. 2). Two patients in the HNS group and 3 patients in the NS group had recurrence of typical AFL (6.7% vs 10%, respectively; $P = 0.5$). One additional patient in the HNS group came back with an atypical left-sided AFL, and long-term reconnection of the CTI was documented. In addition, the time to recurrence in the HNS and NS arms was not significantly different (7.6 ± 6.9 months vs 4.9 ± 4.5 months, respectively; $P = 0.6$). No deaths were observed during follow-up.

Discussion

To our knowledge this is the first randomized study comparing HNS with NS as irrigant solution for ablation of typical AFL. Our study shows that ablation using HNS required fewer lesions to achieve CTI block but did not translate into better acute or long-term success and was associated with a trend toward more steam pops.

Use of low-ionic irrigant solutions such as HNS or 5% dextrose increases the impedance surrounding the tissue-catheter interface, reducing current dispersion to the surrounding environment and increasing RF current delivery to the tissue. In experimental models, RF ablation using HNS compared with standard ablation increases the lesion volume by 25% to 30% and the lesion depth by 10% to 12%.[7]

Table 3. Analysis of outcomes during the follow-up period

Characteristic	HNS group (n = 30)	NS group (n = 30)	*P* value
Atrial flutter recurrence	2 (6.7)	3 (10)	0.5
Time to recurrence (months)	7.56 ± 6.9	4.9 ± 4.5	0.6
Incidence of atrial fibrillation	5 (16.5)	3 (10)	0.4
Discontinue antiarrhythmic drug	9 (30)	9 (30)	1.0
Cardiovascular death	0 (0)	0 (0)	1.0
Global mortality	2 (6.7)	1 (3.3)	1.0

Values are presented as mean ± SD, median, or as n (%). *P* value by Fisher's exact test for categorical variables and for continuous variables. Student's *t*-test for equal variances and unequal variances, as appropriate.

HNS, half-normal saline; NS, normal saline; SD, standard deviation.

HNS-irrigated ablation has proved to be beneficial in certain clinical scenarios, particularly for ventricular arrhythmias when standard ablation with NS is ineffective. A multicentre series including 94 cases of ventricular tachycardia or premature ventricular complexes refractory to standard ablation showed that HNS-irrigated ablation resulted in 83% acute success.[10] More than one-half of these cases involved the interventricular septum or LV summit, whereas the remainder originated from the papillary muscles (13%), LV free wall (15%), or right ventricle (16%). In another study including 31 patients with outflow tract arrhythmias and initially failed RF ablation, the use of HNS provided an additional success rate of 68%.[11] The incremental benefit of HNS in these cases is likely explained by an intramural origin of some ventricular arrhythmias, which require deeper lesion formation to reach the arrhythmogenic foci.

The benefits of HNS irrigation for treatment of atrial arrhythmias are less clear. A randomized trial of patients with AF undergoing first-time catheter ablation ($n = 99$) showed that irrigation with HNS was associated with shorter RF times but no significant difference with respect to total procedure duration or recurrence of atrial arrhythmias during follow-up.[9] The overall rate of complications was low and comparable between the 2 arms.

Our results suggest that routine use of HNS irrigation is not warranted in most ablations of typical AFL. Considering the thickness of the CTI (3-6 mm),[12] lesion transmurality is achieved in most cases with standard NS ablation, whereas the challenges to achieve CTI block have more to do with anatomic obstacles (prominent Eustachian ridge, presence of pouches) or a heat-sink effect caused by proximity to coronary vessels. HNS irrigation may eventually have a role as a bailout strategy in refractory cases when deeper lesions are desired, especially if significant tissue edema is suspected after extensive ablation, but this needs to be investigated further. Other strategies that can be considered when CTI block cannot be achieved include the use of intracardiac echocardiography to assess for anatomic variants,[13] bipolar ablation,[14] modulation of the circuit impedance by repositioning or adding a second dispersive patch, or balloon occlusion of the small cardiac vein to minimize the heat-sink effect.[15]

In terms of safety, no serious procedure-related complications were observed in this study. Steam pops were

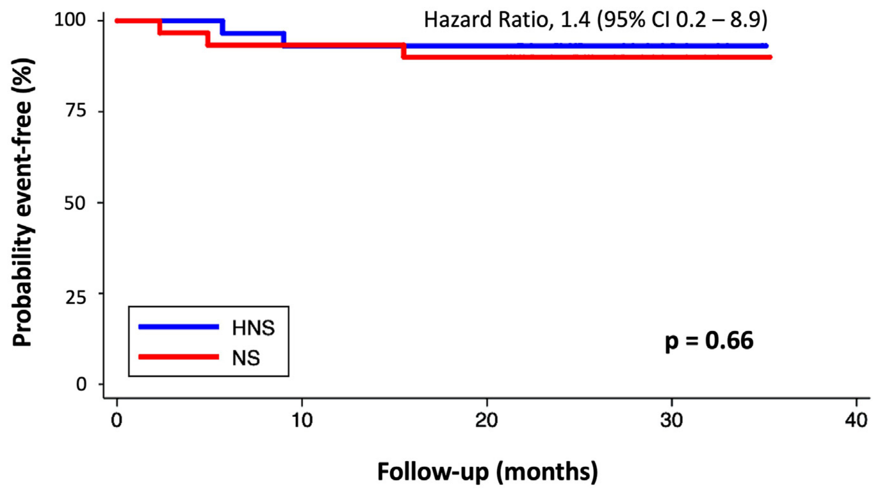

Figure 2. Probability of freedom from atrial flutter recurrences in HNS and NS arms, during the follow-up period. *P*-value by log-rank test and hazard ratio by Mantel-Cox test. HNS, half-normal saline; NS, normal saline.

documented in 4 patients in the HNS group (13%) vs none in the NS group. Although none of these resulted in pericardial effusion, this raises some safety concerns and is consistent with previous observations.[14] When HNS is used, careful titration of power should be exercised, starting at lower power and gradually titrating up based on impedance drops. RF should be stopped in case of impedance rise or exaggerated impedance drops.

Limitations

The sample size is relatively small, which may have reduced the power to detect significant differences in some outcomes. For example, despite a 50% relative risk reduction in acute reconnection, this difference did not reach statistical significance. As there were no previous clinical studies at the time of enrollment, previous sample size estimation was not possible. On a larger scale, it is possible that the lower rate of acute reconnections, fewer RF lesions, and similar long-term efficacy seen in the HNS group could lead to improved clinical outcomes. However, this must be balanced against the increased risk of steam pops and the potential complications therein, as these were only seen in the HNS group. The ablation approach was not homogeneous among the different operators, with some of them opting for a contiguous ablation line, whereas others used a maximum voltage-guided technique. Also, a deflectable sheath was not routinely used in most cases and typically was resorted to when problems with catheter stability or contact were noticed, which may have contributed to some of the acute reconnections. Finally, a single ablation catheter was used in all included patients (Tacticath SE, Abbott), and our results may not be applicable to other catheters.[16]

Conclusions

HNS compared with NS as irrigant solution for ablation of typical AFL requires fewer RF lesions to achieve CTI block while demonstrating similar acute procedural success, safety, and long-term efficacy. Increased rates of steam pops were seen in the HNS group; however, no pericardial effusions were demonstrated in either group. A larger study may be warranted to confirm these findings with an aim to determine if durable bidirectional block and procedure times can be significantly shortened with the use of HNS irrigation.

Ethics Statement

The study was approved by the institutional Health Sciences Research Ethics Board.

Patient Consent

The authors confirm that patient consent form(s) have been obtained for this article.

Funding Sources

No funding was provided for this paper.

Disclosures

The authors have no conflicts of interest to disclose.

References

1. Cosio FG, Lopez-Gil M, Goicolea A, Arribas F, Barroso JL. Radiofrequency ablation of the inferior vena cava-tricuspid valve isthmus in common atrial flutter. Am J Cardiol 1993;71:705-9.

2. Nakagawa H, Lazzara R, Khastgir T, et al. Role of the tricuspid annulus and the eustachian valve/ridge on atrial flutter. Circulation 1996;94:407-24.

3. Brugada J, Katritsis DG, Arbelo E, et al. 2019 ESC guidelines for the management of patients with supraventricular tachycardia. Eur Heart J 2020;41:655-720.

4. Natale A, Newby KH, Pisanó E, et al. Prospective randomized comparison of antiarrhythmic therapy versus first- line radiofrequency ablation in patients with atrial flutter. J Am Coll Cardiol 2000;35:1898-904.

5. Gula LJ, Redfearn DP, Veenhuyzen GD, et al. Reduction in atrial flutter ablation time by targeting maximum voltage: results of a prospective randomized clinical trial. J Cardiovasc Electrophysiol 2009;20:1108-12.

6. Giehm-Reese M, Kronborg MB, Lukac P, et al. Recurrent atrial flutter ablation and incidence of atrial fibrillation ablation after first-time ablation for typical atrial flutter: a nation-wide Danish cohort study. Int J Cardiol 2020;298:44-51.

7. Nguyen DT, Gerstenfeld EP, Tzou WS, et al. Radiofrequency ablation using an open irrigated electrode cooled with half-normal saline. JACC Clin Electrophysiol 2017;3:1103-10.

8. Maan A, Bode WD, Heist EK, et al. Outcome of high-power short-duration radiofrequency ablation in combination with half-normal saline irrigation for the treatment of atrial fibrillation. Pacing Clin Electrophysiol 2022;45:43-9.

9. Gianni C, Gallinghouse GJ, Al-Ahmad A, et al. Half-normal saline versus normal saline for irrigation of open-irrigated radiofrequency catheters in atrial fibrillation ablation. J Cardiovasc Electrophysiol 2021;32:973-81.

10. Nguyen DT, Tzou WS, Sandhu A, et al. prospective multicenter experience with cooled radiofrequency ablation using high impedance irrigant to target deep myocardial substrate refractory to standard ablation. JACC Clin Electrophysiol 2018;4:1176-85.

11. Chung FP, Vicera JJB, Lin YJ, et al. Clinical efficacy of open-irrigated electrode cooled with half-normal saline for initially failed radiofrequency ablation of idiopathic outflow tract ventricular arrhythmias. J Cardiovasc Electrophysiol 2019;30:1508-16.

12. Cabrera JA, Sanchez-Quintana D, Ho SY, Medina A, Anderson RH. The architecture of the atrial musculature between the orifice of the inferior caval vein and the tricuspid valve: the anatomy of the isthmus. J Cardiovasc Electrophysiol 1998;9:1186-95.

13. Luani B, Ismail A, Kaese S, et al. Zero-fluoroscopy ablation of the cavotricuspid isthmus guided by intracardiac echocardiography in patients with typical atrial flutter. Eur Heart J 2022;43.

14. Futyma P, Futyma M, MacioŁek M, KuŁakowski P. Bipolar radiofrequency ablation of typical atrial flutter. J Cardiovasc Electrophysiol 2016;27:874-5.

15. Christopoulos G, Siontis KC, Kucuk U, Asirvatham SJ. Cavotricuspid isthmus ablation for atrial flutter: anatomic challenges and troubleshooting. HeartRhythm Case Rep 2020;6:115-20.

16. Yamaguchi J, Takigawa M, Goya M, et al. Impact of tip design and thermocouple location on the efficacy and safety of radiofrequency application. J Interv Card Electrophysiol 2023;6:885-96.