Atrioventricular nodal echoes over a wide echo window as a therapeutic end point for the catheter-guided radiofrequency ablation of atrioventricular nodal reentrant tachycardia: a prospective study

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Aims
In previous retrospective studies, it was shown that the presence of residual single atrioventricular node (AVN) echoes with an echo zone longer than 30 ms may increase the rate of recurrence after radiofrequency ablation (RFA) of slow pathway in patients with AVN reentrant tachycardia (AVNRT). Based on that, some centres perform additional RFA in these patients. However, this opinion has never been tested prospectively and many centres do not perform re-ablation in these patients. The purpose of this study was to test whether persistence of a single AVN echo over a wide echo zone is a valid end point for RFA.

Methods and results
In this prospective study, 576 patients who had a non-inducible arrhythmia post-RFA of AVNRT were divided into those with a remnant echo over a wide echo zone (case group) and those reaching classical end points (control group). The primary end point of the study was recurrence and patients were followed for 34.5 ± 18.8 months. In the control group (n = 510), 14 patients (2.7%) had a recurrence while no recurrence was seen in the case group (n = 66) (final cure rate, 97.3 vs. 100%; difference, 2.7%; upper bound of the 98% CI, 0.0488; P < 0.0001 for non-inferiority). Two complete heart blocks (0.4%) happened in the control group and none in the case group (P = 0.784).

Conclusion
Non-inducibility in the presence of a wide echo window is non-inferior to non-inducibility in the presence of narrow echo window or no AVN echoes. In general, the presence of a single echo beat is not an indication for further ablation and this applies for both narrow and wide windows.

Keywords
Atrioventricular node reentrant tachycardia • AVNRT • Radiofrequency • Ablation • End point • Wide echo zone

Introduction
Modification of dual atrioventricular (AV) node physiology by the application of radiofrequency (RF) current to atrial tissue near the AV node has become the main treatment for atrioventricular node reentrant tachycardia (AVNRT).1–3 Currently, non-inducibility of AVNRT with and without isoproterenol infusion in patients without residual evidence of dual atrioventricular node (AVN) pathways such as AVN

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What's new?

- This study is the first prospective study investigating the effect of a remnant atrioventricular (AV) nodal echo over a wide echo zone after ablation of slow pathway on the recurrence of AVN reentrant tachycardia (AVNRT).
- Following 576 patients for 34 ± 18 months for detecting recurrences, it was noticed that non-inducibility in the presence of a wide echo window is non-inferior to non-inducibility in the presence of narrow echo window or no AVN echoes.
- Our data does not support re-ablation strategies in the patients with a remnant wide echo zone.
- Patients who suffer AVNRT produced over a wide echo zone had a longer AH interval. This finding may demonstrate that these patients have a slower conduction over the fast pathway than control and a post-ablation wide echo zone may be an intrinsic characteristic of the AV node rather than a result of radiofrequency ablation.

Methods

Study design
This prospective, case-control, non-inferiority, multicentre study was performed on 616 consecutive patients with AVNRT referring to Faghihi and Kowsar Hospitals from February 2009 to November 2014. The Medical Ethics Committee of Shiraz University of Medical Sciences approved the protocol of the study, and a signed written informed consent was obtained from each participant. The study conformed with the declaration of Helsinki in working to human subjects. Flowchart diagram of the study is provided in Figure 1.

Participants
All patients had symptomatic episodes and in 90.5% of them the episode of AVNRT was documented by a 12-lead surface electrocardiogram before the ablation procedure. Patients with reduced ejection fractions (5 patients), congenital heart disease (3 patients), atypical AVNRT (Those with a VA interval longer than 90 ms; 12 patients), and additional arrhythmias (8 patients) were excluded. Eligible patients were transferred to catheterization laboratory and electrophysiological study was done. Atrioventricular node reentrant tachycardia was induced and documented. Ablation with RF wave was done and post-ablation study was performed. Non-inducibility was confirmed in all. Those with a non-inducible AVNRT and remnant single AVN echo over a wide echo zone after ablation were considered as the case group and no extra ablations were done in this group. The others were considered as the control group. Demographic and baseline characteristics are shown in Table 1.

Electrophysiological study and ablation
All anti-arrhythmic drugs were discontinued for duration equal to five half-life cycles for the specified drug before study. The procedure was done using a local anaesthesia. We used the femoral approach for 95.5% of patients and jugular punctures in 4.5%. Each patient had right atrial, right ventricular, HIS catheter (Marinr, Medtronic, Inc., USA), and coronary sinus (St Jude Medical, Inc., USA) in place during the study. A standard electrophysiological study was done and the diagnosis of typical AVNRT was confirmed considering the approved criteria. Presence of accessory pathways was checked and induction of atrioventricular reentrant tachycardia was excluded in each patient using standard electrophysiological criteria. During extra stimulus application (S2), the A2H2 interval was measured with each extra stimulus coupling interval. An increase in the A2H2 interval more than 50 ms in response to a decrease in the A1A2 coupling interval of 10 ms was considered as a jump and an evidence of dual anterograde AVN physiology. Arrhythmia induction was done using extra stimulus application and isoproterenol was used in the face of non-inducibility. After induction, RF was applied to modify the slow pathway using 4-mm deflectable solid tip catheter (Marinr, Medtronic, Inc., USA) with a power of 50 W and temperature limit of 60°C for 60 s. No junctional rhythm was noticed after 10 s, RF was stopped and the subsequent RF applications were made more anteriorly. The atrioventricular relationship was continuously monitored throughout the application. If any degree of block or rapid junctional rhythm was noticed, RF was discontinued immediately. Post-ablation study to confirm non-inducibility was done in all patients using staged atrial extra stimuli application. If arrhythmia was not re-induced another round of study using isoproterenol was done for all. If AVNRT was re-induced anyhow, another round of ablation was performed. Those who did not show any AVN echoes and jumps post-ablation were considered as complete slow pathway elimination and dual AVN physiology was eliminated in this group. These patients were included in the control group of the study. Those who had a residual evidence of dual AVN pathways and had a single AVN echo (AVN modification group) were categorized into two groups. Echo window was defined as the interval during programmed stimulation with 10-ms decrements over which a single echo was observed in the post-ablation period. Those who had an AVN echo in an echo zone (window) less than 30 ms faced the current accepted end points of ablation and were included in the control group of the study. If the AVN echo happened in a wider echo zone (longer than 30 ms), the patients were included in the case group. We did not perform the second round of ablation in any of the groups.
Post-ablation care and follow-up

All the participants had a 12-lead ECG before their discharge from the hospital. All anti-arrhythmic drugs were discontinued post-ablation. Recurrence was defined as occurrence of a documented new episode of AVNRT after successful ablation. Patients were followed in the 1st and 6th post-procedural months in the outpatient clinic. If the patients developed symptoms of arrhythmia, we tried to document the cause with standard 12-lead ECG during their symptomatic periods. Those who could not be visited in the symptomatic episodes underwent 24- to 48-h Holter monitoring. Late follow-up (34.4 ± 18.05 months) for checking the recurrence of tachycardia symptoms was done by telephone. If the patients developed symptoms identical to those before RFA, or if we found any evidence of AVNRT recurrence using ECG or a Holter recording, we repeated the EP studies and, if necessary, repeated catheter ablation.

Statistical analysis

We performed a non-inferiority analysis for the primary end point. Primarily efficacy was calculated as the proportion of patients achieving a final cure; an exact confidence interval for that proportion was computed; the exact, one-sided, upper bound of the 98% confidence interval for the difference in success probabilities was compared with the use of \( \delta = 0.10 \) (the chosen margin for non-inferiority) using Farrington and Manning test. Continuous variables are presented as mean ± SD. Categorical variables are expressed as absolute frequencies and percentages. For continuous variables, comparisons between the groups were performed by means of independent student \( t \)-test or the Mann–Whitney \( U \) test, wherever appropriate. Nominal variables were compared by means of the \( \chi^2 \) test. Patients who were lost to follow-up in whom no known event had occurred were not included in the denominator for calculations of binary
end points. All $P$ values except the value for non-inferiority were two-tailed. The $P$ values less than 0.05 were considered significant. Statistical Package for Social Sciences version 17.0 (SPSS, Inc., Chicago, IL, USA) was used for statistical analysis.

## Results

### Baseline characteristics

Clinical characteristics of the patients are shown in Table 1. Patients included in the study were 48.3 ± 17.3 years old. AVNRT was more frequent in women (407 patients, 70.6%). In 154 patients (26.7%), there was evidence of structural heart disease. Hypertensive heart disease, coronary artery disease, and valvular heart disease were more frequently encountered. In the remainder (73.3%), no clinically detectable structural heart disease was found.

### Electrophysiological findings

During RF application, 564 of the 576 patients (97.9%) developed a junctional rhythm. A total of 490 (85%) patients were in sinus rhythm during the electrophysiological study. Main electrophysiological findings are shown in Table 2. We could induce the arrhythmia in all the patients before ablation using electrical stimulation while 150 patients (26%) needed isoproterenol infusion for arrhythmia induction and/or maintenance.

### Results of radiofrequency ablation

Dual AV node physiology was eliminated completely in 236 patients (41%), persisted with inducible single AVN echoes over an echo zone less than 30 ms in 274 patients (47.5%) (a total of 510 patients were considered as the control group), and with inducible single AVN echoes over an echo window longer than 30 ms in 66 patients (11.5%; case group).

### Complications

Two complete heart blocks happened in the control group (0.4%) while none happened in the case group ($P = 0.78$). No other major complications were observed. In patients with third-degree AV block,
permanent pacemakers were implanted 1 and 6 days after ablation. No major vascular complications were noticed in any group.

**Follow-up results**

Follow-up data were available in 576 patients. Of the 510 patients with successful ablation in the control group, 14 (2.7%) had a recurrence. In the remaining 496 patients (97.3%) from the control group, no AVNRT was documented. No recurrence was seen in the case group (final cure rate, 97.3 vs. 100%; difference, 2.7% points; upper bound of the 98% CI, 0.0488; P < 0.0001 for non-inferiority). Among the 236 patient who had slow pathway elimination, 7 (2.96%) had recurrence which was not different from the 7 recurrences in the slow pathway modified patients (2.1%; P = 0.5). Thirteen patients in the control group (2.5%) reported symptoms suggestive of tachycardia, whereas none of the patients in the case group did. These symptoms were confirmed during Holter monitoring in all but one patient. The echo window was significantly lower in patients without recurrence (32 ± 21 ms) than in patients with recurrence (73 ± 44 ms). Then, they performed a post hoc analysis and reached an echo window cut-point of 30 ms. The presence of an AVN echo with an echo window lower than 30 ms had a negative predictive value for recurrence as 82%. An echo window of 0–30 ms carried a positive predictive value for recurrence of 63%. However, this cut-off was based on a low number of patients. So, whether the 30 ms cut off value is an appropriate one or not is uncertain. Consequently, a prospective evaluation deemed necessary. Our study was designed to answer this question in a prospective case–control study and we reached a contrary finding. This controversy may be explained in part, by different study designs. Here, we have noticed that patients who suffer AVNRT produced over a wide echo zone had a marginally longer AH interval during the sinus rhythm, a finding in favour of a slower conduction over the fast pathway than control. So, it may be hypothesized that reaching a post-ablation wide echo zone is more an intrinsic characteristics of the AV node in these patients than being a result of a RFA changes at the AV nodal site.

Our study faced some limitations. First, the number of patients in the case group was significantly lower than the control group. However, this finding was expected because the incidence of a wide echo zone is significantly lower. The lower rate of recurrence in the case group may be attributed to the lower sample size in this group. In addition, we could not analyse the effect of echo window duration in patient with a short echo window on the recurrence rate, probably because of the very low recurrence rates. Another limitation of our study was excluding the patients with concomitant congenital heart disease, reduced ejection fraction, those with atypical AVNRT, or with accompanying arrhythmia. So, our results cannot be generalized to these groups.

It can be concluded that post-ablation persistence of inducible single AVN echo beats over a wide echo zone in patients with non-inducible AVNRT is non-inferior to non-inducibility in the presence of a narrow echo window or no AVN echoes. Our data do not support re-ablation in the former group. In general, the presence of a single echo beat is not an indication for further ablation and this applies for both narrow and wide windows. Future, randomized trials are needed to see whether performing a repeated burn in these patients carries a higher risk for complications or not?

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