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A Composite Electrophysiological Descriptor of Atrioventricular Nodal Conduction and Non-inducible Atrioventricular Nodal Reentrant Tachycardia: Findings from a Retrospective Electrophysiological Cohort

ABSTRACT

Objective: To examine whether a simple electrophysiological descriptor derived from routinely measured antegrade atrioventricular nodal conduction parameters is associated with non-inducible atrioventricular nodal reentrant tachycardia (AVNRT).

Methods: This retrospective cohort included 387 consecutive patients undergoing electrophysiological study for clinically suspected AVNRT. The Total Antegrade Nodal Delay (TAND) index was defined as the sum of the atrio–His (AH) interval and antegrade Wenckebach cycle length (WBCL). Logistic regression, receiver operating characteristic analysis, and quadrant-based continuum analysis were performed. Because WBCL values were missing predominantly in inducible patients, complete-case and sensitivity analyses were conducted.

Results: Non-inducible AVNRT occurred in 106 patients (27.4%). In the complete-case TAND cohort (n = 329), higher TAND values were associated with non-inducibility (odds ratio [OR] per 50-ms increase: 1.26, 95% CI: 1.02-1.56, *P* = .032), remaining significant after adjustment for age and sex (adjusted OR: 1.31, 95% CI: 1.05-1.63, *P* = .016). Discrimination was modest (area under the curve: 0.592, 95% CI: 0.525-0.659). After multiple imputation, the association remained directionally consistent but was attenuated (adjusted OR: 1.21, 95% CI: 0.99-1.46, *P* = .056). Quadrant analysis demonstrated a graded increase in non-inducibility from the low-AH/low-WBCL to the high-AH/high-WBCL quadrant (25.0% vs. 42.3%; trend OR: 1.32, 95% CI: 1.07-1.61, *P* = .008).

Conclusion: Total Antegrade Nodal Delay was modestly associated with non-inducible AVNRT and may describe a group-level electrophysiological pattern characterized by slower antegrade nodal conduction and higher functional conduction thresholds. However, TAND should not be interpreted as a mechanistic requirement for AVNRT inducibility or as an individual-level prediction tool.

Keywords: AH interval, atrioventricular nodal reentrant tachycardia, electrophysiological pattern, electrophysiological study, slow pathway, Wenckebach cycle length

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INTRODUCTION

Atrioventricular nodal reentrant tachycardia (AVNRT) is the most common form of paroxysmal supraventricular tachycardia encountered in clinical practice.[1] The diagnosis is traditionally confirmed during an electrophysiological study (EPS) by reproducible induction of tachycardia using programmed atrial stimulation, often facilitated by pharmacological modulation of autonomic tone. Its initiation and maintenance depend on the existence of dual atrioventricular (AV) nodal pathways and a critical temporal alignment between conduction delay and refractory recovery, permitting reentrant activation within the AV node.[2-4] In most published studies, these patients are either excluded from analysis or considered procedural limitations, and the phenomenon of non-inducibility is rarely examined as a primary research question.[5,6]

At the substrate level, inducibility may be influenced by the temporal interplay between conduction delay and refractory recovery.[1,2] Atrioventricular nodal conduction and refractoriness are known to be influenced by age, autonomic tone, and intrinsic electrophysiological properties of the AV node and its nodal extensions.[7-9] Greater conduction delay and higher functional refractoriness may alter the temporal conditions required for sustained reentry. These factors may influence the likelihood of sustaining reentrant tachycardia during EPS despite clinically documented episodes. It has been hypothesized that inducibility may depend not only on procedural conditions but also on the balance between antegrade nodal conduction properties and functional conduction limits.

Conventional parameters such as the atrio–His (AH) interval and the antegrade Wenckebach cycle length (WBCL) describe isolated aspects of nodal conduction and refractoriness but do not capture their integrated interaction. It has been hypothesized that non-inducible AVNRT may be associated with a distinct electrophysiological pattern characterized by greater antegrade nodal delay and higher functional conduction thresholds.

To operationalize this concept, the Total Antegrade Nodal Delay (TAND) index was defined as the sum of baseline AH interval and induction WBCL. This composite parameter was designed as a simple exploratory summary of routinely measured electrophysiological variables potentially relevant to inducibility. The aim of this study was not to develop a clinical prediction score, but rather to explore whether TAND is associated with a graded electrophysiological pattern related to AVNRT inducibility.

METHODS

Study Design and Population

This retrospective observational study included consecutive patients who underwent EPS for documented paroxysmal supraventricular tachycardia (SVT) with clinical and electrocardiographic features highly suggestive of AVNRT at a tertiary referral center between 2013 and 2026. Patients were considered to have clinically suspected AVNRT based on documented narrow-complex tachycardia with sudden onset and termination, absence of manifest pre-excitation, and supportive clinical or electrophysiological features such as dual AV nodal physiology or AV nodal echo beats.[1] Patients with structural heart disease, prior AV nodal ablation, or incomplete baseline EPS data were excluded.

Electrophysiological Study

All electrophysiological studies were performed according to routine institutional electrophysiology laboratory practice under a shared procedural framework. However, induction maneuvers, pacing sequence, and pharmacological facilitation were not prospectively standardized across all patients. All studies were performed under local anesthesia (without sedation) with continuous hemodynamic and electrocardiographic monitoring. Antiarrhythmic and AV nodal–blocking medications, including beta-blockers and non-dihydropyridine calcium channel blockers when applicable, were discontinued for at least 5 drug half-lives prior to the procedure. All EPS procedures were performed using standard multipolar catheters positioned in the high right atrium, His bundle region, right ventricular apex, and coronary sinus. Baseline electrophysiological measurements included sinus cycle length (BCL), AH interval, and His-ventricular (HV) interval. Antegrade AV nodal function was assessed by determining the antegrade WBCL during incremental atrial pacing, while retrograde conduction was evaluated using the ventriculoatrial block cycle length (VABCL).

The presence of dual AV nodal physiology, defined as a ≥50 ms increase in the AH interval in response to a 10 ms decrement in the atrial extrastimulus coupling interval, along with the occurrence of single or multiple AV nodal echo beats, was also systematically evaluated.[1] For inclusion in the non-inducible cohort, patients were strictly required to have prior electrocardiogram (ECG) documentation of spontaneous SVT combined with the demonstration of at least one surrogate marker of dual AV nodal physiology (AH jump or echo beats) during EPS, which served as the clinical justification for empirical slow pathway modification. In patients where sustained AVNRT could not be induced, these findings served as critical surrogate markers, providing supportive electrophysiological evidence for the presence of an underlying AVNRT substrate.[6,10]

Induction attempts generally followed a stepwise institutional approach beginning with baseline measurements, followed by incremental atrial pacing and programmed atrial stimulation using atrial extrastimuli. When tachycardia was not induced under baseline conditions, pharmacological provocation with intravenous isoproterenol and/or atropine was applied at the operator's discretion. Because of the retrospective real-world nature of the study, the exact pacing sequence, stimulation intensity, number of extrastimuli, and use or dose of pharmacological facilitation were not prospectively standardized across all patients.[11,12] Therefore, inducibility was assessed under routine laboratory conditions rather than under a uniform experimental protocol. Empirical slow pathway modification was performed in patients with strong clinical suspicion and dual AV nodal physiology despite non-inducibility. Patients were classified as inducible if sustained AVNRT was reproducibly induced during EPS. Patients were classified as non-inducible if

HIGHLIGHTS

- Total Antegrade Nodal Delay (TAND) combines atrio–His (AH) interval and antegrade Wenckebach cycle length (WBCL).
- Total Antegrade Nodal Delay was modestly associated with non-inducible atrioventricular nodal reentrant tachycardia at the group level.
- Quadrant analysis supported a graded AH–WBCL continuum.
- Missing WBCL sensitivity analyses supported cautious interpretation.
- Total Antegrade Nodal Delay should not be interpreted as an individual-level prediction tool.

sustained tachycardia could not be induced after routine atrial pacing and programmed stimulation, including pharmacological provocation when applied, despite prior ECG documentation of SVT and supportive electrophysiological evidence of dual AV nodal physiology.

Novel Electrophysiological Parameters and Exploratory Clustering Analysis

To comprehensively assess the combined pattern of antegrade AV nodal conduction delay and functional conduction threshold, The TAND index was defined as the unweighted sum of the baseline AH interval and antegrade WBCL during induction (TAND = AH + WBCL). Total Antegrade Nodal Delay was intended as a pragmatic composite electrophysiological descriptor derived from routinely measured parameters, rather than as a direct mechanistic measure of AVNRT reentry or as a clinical prediction score.

Rationale for the Total Antegrade Nodal Delay Index

Sustained AVNRT depends on a complex interaction between dual AV nodal physiology, conduction delay, refractory recovery, autonomic tone, and procedural conditions during EPS.[1,13] Therefore, neither AH interval nor WBCL should be interpreted as a necessary or sufficient mechanistic determinant of AVNRT inducibility. The rationale for TAND was to summarize 2 routinely available antegrade AV nodal measurements into a simple exploratory descriptor. The rationale underlying TAND is that successful induction of AVNRT requires a favorable temporal interaction between antegrade conduction and recovery of the reentrant substrate. It has been hypothesized that patients with longer AH intervals and higher antegrade Wenckebach cycle lengths may exhibit slower antegrade nodal conduction and higher functional conduction thresholds, potentially reducing the likelihood of reproducible tachycardia induction during routine electrophysiological testing. Accordingly, TAND was conceived as an exploratory descriptor intended to summarize these antegrade nodal characteristics rather than to represent a mechanistic determinant of AVNRT inducibility.

Ethical Considerations

The study protocol was approved by İzmir Katip Çelebi University Atatürk Training and Research Hospital Ethics Committee (approval number: 0024, date: January 15, 2026) and was conducted in accordance with the Declaration of Helsinki.

Statistical Analysis

Statistical Software and Significance Threshold

Analyses were performed using SPSS (Statistical Package for the Social Sciences) version 30.0 (IBM Corp., Armonk, NY, USA) and the R programming language (R Foundation for Statistical Computing, Vienna, Austria, version 4.5.2) within the RStudio environment version 2025.09.2 (Posit PBC, Boston, MA, USA). All statistical tests were 2-sided, and a $P < .05$ was considered statistically significant.

Data Preparation, Imputation, and Missing-Data Analysis

A missing data analysis was performed for unrecorded WBCL values. The induction WBCL measurement required for TAND calculation was unavailable in 58 patients, resulting in a complete-case TAND cohort of 329 patients. These missing induction WBCL values were predominantly observed in inducible patients, most likely reflecting early tachycardia induction before Wenckebach periodicity could be reached. Therefore, the primary TAND analyses were performed as complete-case analyses.

To address the potential impact of missing WBCL values, additional sensitivity analyses were conducted. First, multiple imputation using predictive mean matching was performed using 20 imputed datasets for missing WBCL values, and TAND was recalculated within each imputed dataset. Second, deterministic sensitivity analyses were performed by assigning missing WBCL values to the observed first quartile, median, and third quartile values. These analyses were used to evaluate whether the association between TAND and non-inducibility remained directionally consistent under different assumptions regarding missing WBCL values.

Because missing WBCL values occurred predominantly among inducible patients and were likely related to early tachycardia induction before Wenckebach periodicity could be reached, the missing-data mechanism may not have been completely random. Accordingly, multiple imputation results should be interpreted in the context of its missing-at-random assumption, while the deterministic sensitivity analyses were performed to evaluate the robustness of findings under alternative missing-data scenarios. These missing induction WBCL values were predominantly observed in inducible patients, most likely reflecting early tachycardia induction before Wenckebach periodicity could be reached (Supplementary Table 1).

Descriptive and Comparative Analyses

Continuous variables were expressed as median and interquartile range (IQR) and compared using the Mann–Whitney *U*-test. Categorical variables were expressed as counts and percentages and compared using the chi-square test or Fisher's exact test, as appropriate.

Primary Association Analysis

Binary logistic regression was used to evaluate the association between TAND and non-inducible AVNRT. Because TAND was the predefined exploratory variable of interest and the number of events was limited, the primary adjusted model included age and sex as clinically relevant covariates. Total Antegrade Nodal Delay was modeled per 50-ms increase for clinical interpretability. Odds ratios (ORs) are presented with 95% CIs.

Discrimination, Internal Validation, and Secondary Analyses

Discrimination was assessed using receiver operating characteristic (ROC) curve analysis with area under the curve (AUC) and 95% CIs. The DeLong method was used to compare correlated ROC curves for TAND, AH interval, and WBCL. Internal validation was performed using bootstrap resampling with 1000 iterations to estimate optimism in apparent discrimination. Restricted cubic spline regression with 4 knots was used to explore potential nonlinear associations between TAND and non-inducibility.

For the AH–WBCL quadrant analysis, patients were categorized into 4 groups according to low and high AH interval and WBCL strata. The frequency of non-inducibility was compared across quadrants using the chi-square test. Logistic regression was used to compare each quadrant with the low-AH/low-WBCL reference quadrant and to evaluate the ordered trend in noninducibility across quadrants.

Exploratory Clustering Analysis

Exploratory AH–WBCL clustering was performed using k-means clustering based on standardized AH interval and induction WBCL values. Clustering was performed independently of inducibility status and was used as a descriptive analysis to assess whether AH and WBCL formed distinct group-level electrophysiological patterns.

Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline was used to draft this manuscript, and the STROBE reporting checklist was applied during editing, which is included as a supplementary file (Supplementary Table 2).[14]

RESULTS

Study Population and Baseline Characteristics

A total of 387 patients were included in the study. Atrioventricular nodal reentrant tachycardia was successfully induced in 281 patients (72.6%), while 106 patients (27.4%) remained non-inducible despite routine stimulation maneuvers and pharmacological provocation when applied. Crucially, all 106 non-inducible patients (100%) had previously documented clinical SVT and exhibited at least 1 electrophysiological surrogate marker of dual AV nodal physiology (AH jump or echo beats) during the procedure (Figure 1). There were no significant differences between inducible and non-inducible groups regarding age (51.0 vs. 49.5 years, $P = .381$), gender ($P = .955$), BCL ($P = .262$), or HV interval ($P = .167$). However, non-inducible patients demonstrated a significantly prolonged WBCL during induction (340 ms vs. 320 ms, $P = .042$) and a trend toward longer baseline AH intervals ($P = .079$). Baseline demographic and electrophysiological characteristics of inducible and non-inducible AVNRT patients are summarized in Table 1.

The Total Antegrade Nodal Delay Index and Multivariable Analysis

In the complete-case TAND cohort (n = 329), the composite TAND index was higher among non-inducible patients than among inducible patients. In univariable logistic regression, each 50-ms increase in TAND was associated with higher odds of non-inducibility (OR: 1.26, 95% CI: 1.02-1.56, $P = .032$). This association remained present after adjustment for age and sex (adjusted OR: 1.31, 95% CI: 1.05-1.63, $P = .016$) (Table 2).

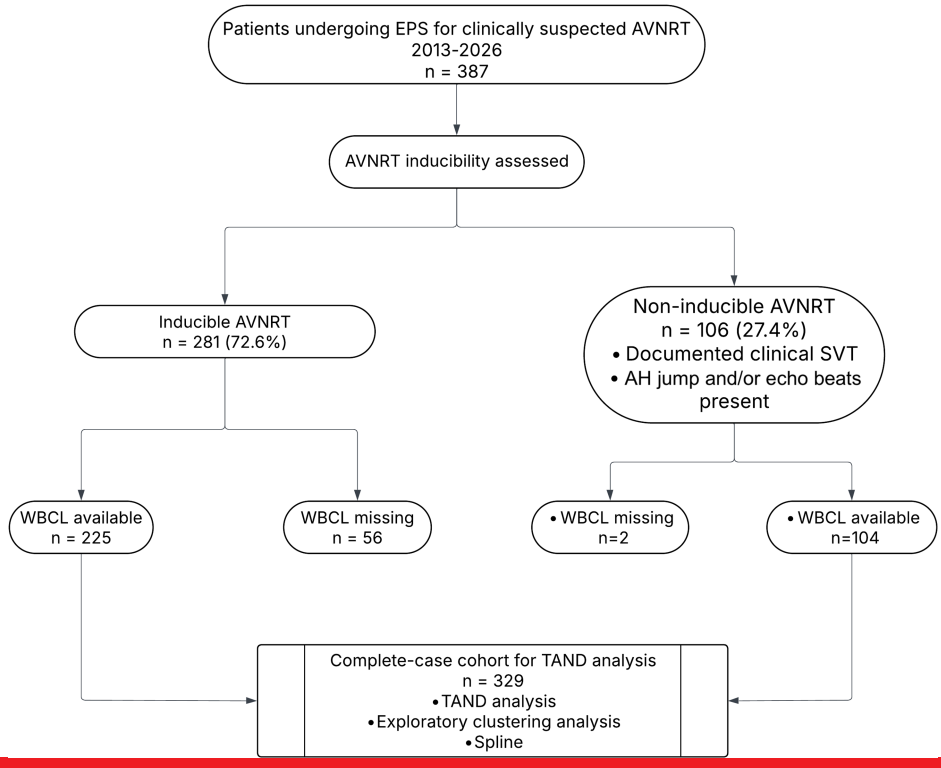

Figure 1. Study flow diagram. Flow diagram illustrating patient inclusion, inducibility classification, and availability of induction WBCL and TAND data. Among 387 consecutive patients undergoing EPS for clinically suspected AVNRT, 281 had inducible tachycardia, and 106 were non-inducible. The induction WBCL measurement required for TAND calculation was unavailable in 58 patients, resulting in a complete-case TAND cohort of 329 patients. Missing induction WBCL values occurred predominantly in inducible patients, largely reflecting early tachycardia induction before Wenckebach periodicity could be reached. Additional multiple-imputation and deterministic sensitivity analyses were conducted to evaluate the impact of missing induction WBCL values. ANNRT, atrioventricular nodal reentrant tachycardia; EPS, electrophysiological study; TAND, total antegrade nodal delay; WBCL, Wenckebach cycle length.

Table 1. Baseline Demographic and Electrophysiological Characteristics of the Study Cohort Stratified by AVNRT Inducibility

Variables	Total Cohort (n = 387)	Inducible AVNRT (n = 281)	Non-inducible AVNRT (n = 106)	*P*
Demographics				
Age (years), median [IQR]	51.0 [39.0-59.0]	51.0 [39.0-60.0]	49.5 [38.5-57.7]	.381
Female sex, n (%)	240 (62.0)	175 (62.2)	65 (61.3)	.955
Baseline Electrophysiology				
BCL (ms), median [IQR]	760 [680-870]	750 [680-864]	781 [694-890]	.262
AH interval (ms), median [IQR]	78 [68-92]	78 [68-90]	80 [70-100]	.079
HV interval (ms), median [IQR]	44 [40-48]	44 [40-48]	42 [40-47]	.167
WBCL during induction‡ (ms), median [IQR]	320 [290-350]	320 [290-350]	340 [300-360]	.042
Novel Composite Parameter				
TAND index‡ (ms), median [IQR]	406 [364-442]	402 [360-438]	420 [380-460]	.007
Exploratory AH–WBCL clustering pattern	(n = 329)	(n = 225)	(n = 104)	<.001
Lower-delay/lower-threshold pattern, n (%)	223 (67.8)	166 (73.8)	57 (54.8)	
Higher-delay/higher-threshold pattern, n (%)	106 (32.2)	59 (26.2)	47 (45.2)	

Continuous variables are expressed as median [interquartile range], and categorical variables as count (percentage).
AH, atrio-His; AVNRT, atrioventricular nodal reentrant tachycardia; BCL, basic cycle length; HV, His-ventricular; IQR, interquartile range; TAND, total antegrade nodal delay; WBCL, Wenckebach cycle length.
‡Wenckebach cycle length during induction and TAND values are reported for patients with complete induction WBCL data required for TAND calculation (n = 329; inducible n = 225, non-inducible n = 104).

Because WBCL values were missing predominantly in inducible patients, additional sensitivity analyses were performed. After multiple imputation of missing WBCL values and recalculation of TAND, the association remained directionally consistent but was attenuated (adjusted OR per 50-ms increase: 1.21, 95% CI: 0.99-1.46, *P* = .056). Deterministic sensitivity analyses showed that the association persisted when missing WBCL values were assigned to the observed first quartile or median values, but was attenuated when assigned to the third quartile. These findings indicate that the TAND association is sensitive to missing WBCL assumptions and should be interpreted cautiously. The complete-case, multiple-imputation, and deterministic sensitivity analyses are summarized in Supplementary Table 3.

Receiver operating characteristic analysis demonstrated modest discrimination for TAND in characterizing non-inducibility (AUC: 0.592, 95% CI: 0.525-0.659) (Supplementary Figure 1). The AUC of TAND was numerically higher than AH alone (AUC: 0.560, 95% CI: 0.492-0.628; DeLong *P* = .340) and significantly higher than WBCL alone (AUC: 0.552, 95% CI: 0.486-0.619; DeLong *P* = .031). These findings support the interpretation of TAND as a modest group-level descriptor rather than an individual-level prediction tool.

Atrioventricular Nodal Quadrant Analysis

Patients were mapped onto an AV nodal conduction quadrant according to AH and WBCL strata. Quadrant analysis demonstrated a graded increase in the frequency of non-inducibility across AH–WBCL combinations (Figure 2). Non-inducibility was observed in 25.0% of patients in Q1 (low AH/low WBCL), 27.3% in Q2 (high AH/low WBCL), 35.6% in Q3 (low AH/high WBCL), and 42.3% in Q4 (high AH/high WBCL). Compared with Q1, Q4 was associated with higher odds of non-inducibility (OR: 2.20, 95% CI: 1.17-4.17, *P* = .014). An ordered trend analysis also supported a graded continuum across quadrants (OR per quadrant: 1.32, 95% CI: 1.07-1.61, *P* = .008). Detailed quadrant-based results are presented in Supplementary Table 4. The overall chi-square comparison across quadrants was borderline and did not reach conventional statistical significance ($\chi^2 = 7.43$, df = 3, *P* = .059).

Discrimination and Internal Validation

Bootstrap internal validation demonstrated limited optimism in apparent discrimination; however, the optimism-corrected AUC remained modest. These findings support the stability of the observed association while reinforcing that TAND should be interpreted as an exploratory descriptor rather than a clinically predictive model.

Nonlinear Analysis

Restricted cubic spline analysis demonstrated a significant overall association between TAND and non-inducibility

Table 2. Complete-Case Logistic Regression Analysis Evaluating the Association Between TAND and Non-Inducible AVNRT

Analysis	Variables	Odds Ratio (OR)	95% (CI)	*P*
Unadjusted model	TAND index, per 50-ms increase	1.26	1.02-1.56	.032
Age/sex-adjusted model	TAND index, per 50-ms increase	1.31	1.05-1.63	.016
Age/sex-adjusted model	Age, per 1-year increase	0.988	0.971-1.004	.150
Age/sex-adjusted model	Female sex	1.05	0.65-1.72	.840

OR, odds ratio; TAND, Total Antegrade Nodal Delay.
Analyses were performed in the complete-case TAND cohort (n = 329). The age/sex-adjusted model included TAND index, age, and female sex. Total Antegrade Nodal Delay was modeled per 50-ms increase for clinical interpretability.

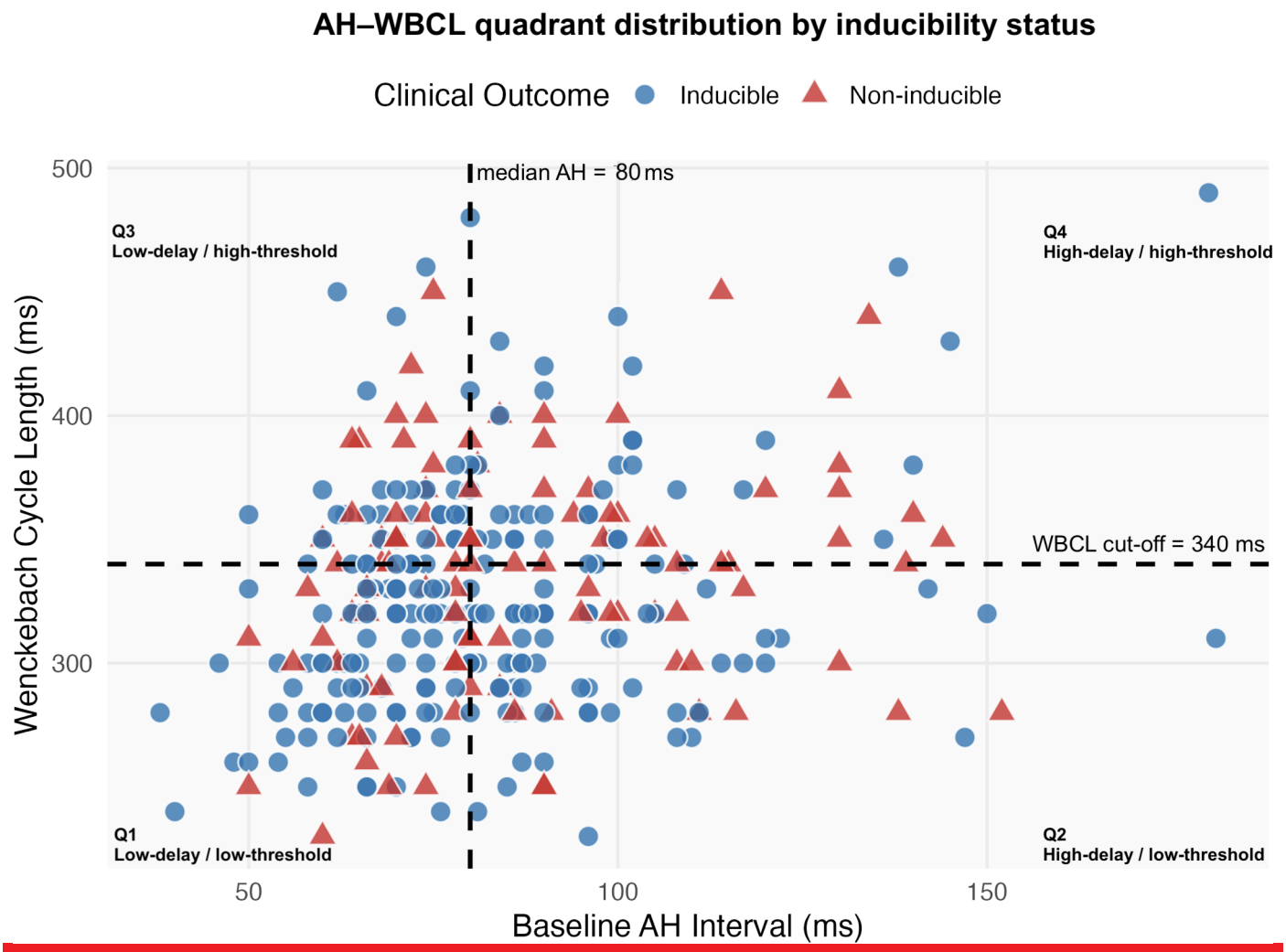

Figure 2. AH–WBCL quadrant distribution illustrates a graded continuum of non-inducibility across antegrade nodal conduction strata. Patients were mapped according to AH interval and WBCL strata. Non-inducibility increased progressively from Q1 to Q4: 25.0% in Q1, 27.3% in Q2, 35.6% in Q3, and 42.3% in Q4. Compared with Q1, Q4 was associated with higher odds of non-inducibility, and ordered trend analysis supported a graded AH–WBCL continuum. Quadrants were defined by AH and WBCL strata: Q1, low AH/low WBCL; Q2, high AH/low WBCL; Q3, low AH/high WBCL; and Q4, high AH/high WBCL. The AH threshold corresponds to the complete-case AH distribution used for quadrant construction. AH, atrio–His; WBCL, Wenckebach cycle length.

($\chi^2 = 9.87$, $P = .019$), while the nonlinear component did not reach conventional statistical significance ($P = .076$). Although this finding does not provide definitive statistical evidence of nonlinearity, the spline curve should be interpreted cautiously because uncertainty was greater at the extremes of the TAND distribution (Figure 3).

Exploratory Clustering Analysis

K-means clustering of the cohort based strictly on AH and WBCL measurements (blinded to clinical outcome) identified 2 distinct electrophysiological patterns (Supplementary Figure 2):

1. Lower-delay/Lower-threshold pattern: Characterized by rapid nodal conduction (Mean AH: 74 ms, Mean WBCL: 310 ms).
2. Higher-delay/Higher-threshold pattern: Characterized by pronounced nodal delay (Mean AH: 104 ms, Mean WBCL: 366 ms).

Non-inducible AVNRT cases were more frequently observed within the cluster characterized by longer AH and WBCL values, supporting a descriptive association between non-inducibility and a higher-delay/higher-threshold AH–WBCL pattern ($P < .001$).

DISCUSSION

In this retrospective electrophysiological cohort, TAND, a pragmatic composite descriptor of AH interval and antegrade WBCL, was modestly associated with non-inducible AVNRT at the group level. Importantly, the observed association should not be interpreted as evidence that longer AH interval or higher WBCL is required for AVNRT inducibility, nor should TAND be considered a diagnostic or clinical prediction tool. Rather, TAND summarizes routinely measured antegrade AV nodal parameters that may help describe an electrophysiological pattern associated with non-inducibility under routine EPS conditions.

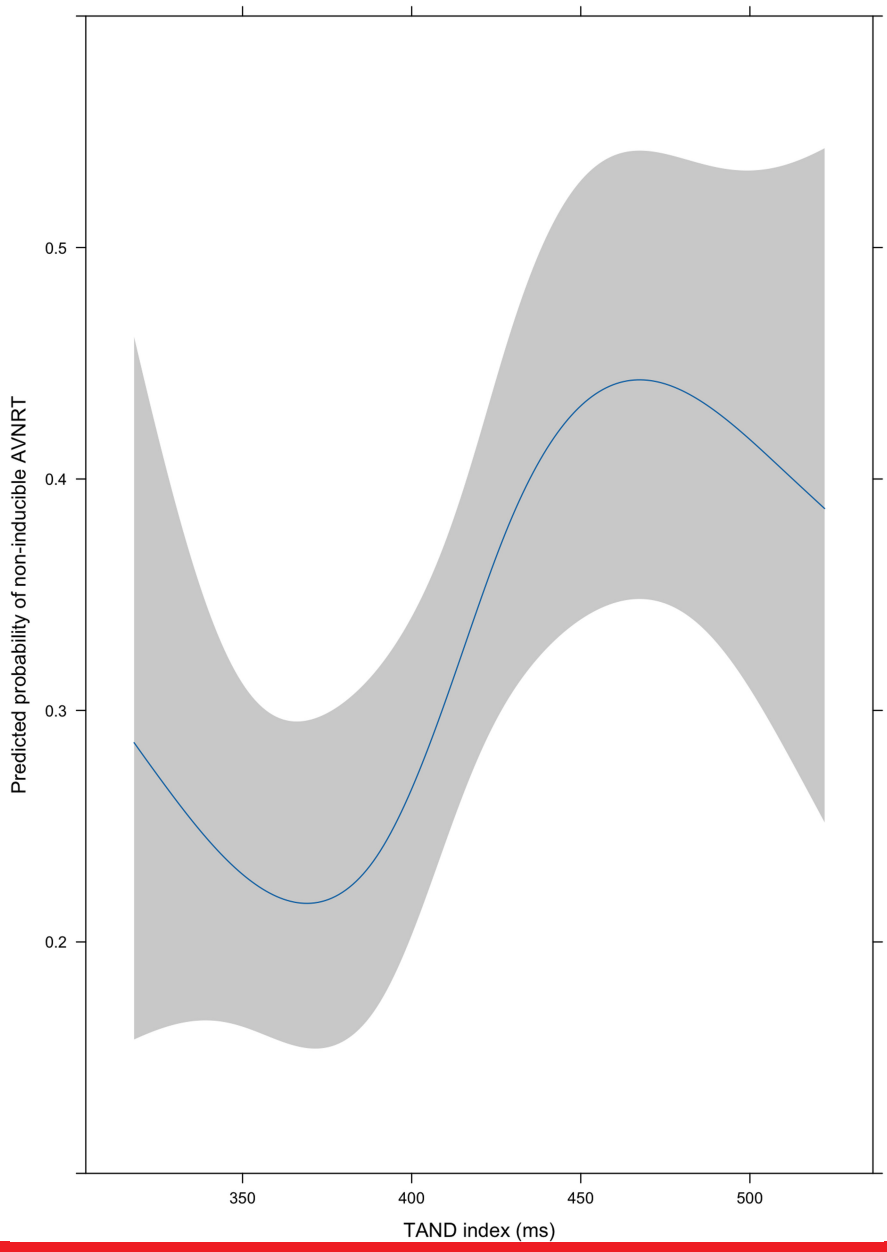

Figure 3. Restricted cubic spline analysis of the association between TAND and non-inducible AVNRT. Restricted cubic spline analysis showing the association between TAND and non-inducibility. The overall association was significant, whereas the nonlinear component did not reach conventional statistical significance. The shaded area indicates the 95% CI; uncertainty widens at the extremes because of fewer observations. This analysis should be interpreted as exploratory. AVNRT, atrioventricular nodal reentrant tachycardia; TAND, Total Antegrade Nodal Delay.

Autonomic state during electrophysiological study may differ substantially from that during spontaneous clinical episodes. Therefore, non-inducibility may reflect not only substrate-related factors but also laboratory-specific autonomic and procedural conditions.

The physiological interpretation of TAND requires caution. AVNRT inducibility depends on multiple dynamic factors, including dual AV nodal physiology, conduction delay, refractory recovery, autonomic tone, pacing protocol, and pharmacological provocation.[8,15,16] Atrio–His interval and WBCL reflect routinely available aspects of antegrade AV nodal behavior, but they are not direct one-to-one surrogates of local circuit conduction velocity or AVNRT circuit refractoriness. Therefore, TAND should be interpreted as an exploratory summary of antegrade nodal behavior rather than a mechanistic measure of the reentrant circuit.[17]

Historically, non-inducible cases have been less systematically characterized in the ablation literature, which has limited focused characterization of this subgroup.[4,6] However, the exploratory clustering analysis suggests that non-inducibility may be more frequently observed within a higher-delay/higher-threshold AH–WBCL pattern. Importantly, these observations should be viewed as descriptive and

hypothesis-generating rather than as evidence of a distinct electrophysiological phenotype.

The rationale for combining AH interval and WBCL was to summarize 2 complementary but imperfect descriptors of antegrade AV nodal conduction and functional conduction threshold. From a physiological perspective, reproducible AVNRT induction requires a favorable temporal relationship between antegrade conduction and recovery of the reentrant substrate. Therefore, longer AH intervals together with higher antegrade WBCL values may reflect a conduction profile in which sustained reentry is less readily reproducible under routine laboratory conditions. The complete-case analysis suggested that higher TAND values were associated with non-inducibility, and quadrant analysis supported a graded AH–WBCL continuum. However, sensitivity analyses demonstrated that the estimated association was influenced by missing WBCL assumptions. Multiple imputation attenuated the association, although the direction of effect remained consistent. These findings support a cautious interpretation: TAND may describe a group-level electrophysiological pattern, but it does not provide definitive individual-level prediction.

The modest AUC values observed in this study are clinically important. They indicate substantial overlap between inducible and non-inducible patients and argue against using TAND as a standalone decision tool. Nevertheless, the directionally consistent association across complete-case and sensitivity analyses suggests that TAND may capture a reproducible, although limited, electrophysiological signal.

In this context, the modest AUC likely reflects overlapping distributions between inducible and non-inducible groups rather than absence of a meaningful group-level electrophysiological association.

The modest optimism observed during bootstrap internal validation supports the stability of the association but does not alter the limited discriminatory capacity of TAND.

Non-inducibility during EPS should be interpreted as a multifactorial phenomenon. In some patients, it may reflect procedural or autonomic conditions that prevent tachycardia induction despite an underlying AVNRT substrate.[4] In others, it may reflect electrophysiological properties that make sustained reentry less reproducible under laboratory conditions.[18,19] The present findings do not distinguish these mechanisms definitively, but they suggest that longer antegrade conduction delay and higher functional conduction thresholds may be more frequently observed among non-inducible patients.

Crucially, variables such as patient age and the HV interval showed no significant association with non-inducibility. The observed pattern appears predominantly related to antegrade AV nodal electrophysiological behavior, although contributions from broader circuit properties cannot be excluded.

Clinical Implications

The present findings should not change procedural decision-making by themselves. Empirical slow pathway modification should continue to rely on a convincing clinical history, ECG documentation of SVT, and supportive electrophysiological findings such as dual AV nodal physiology or echo beats.[10] Within this context, TAND may provide a descriptive framework for understanding why some clinically suspected AVNRT cases remain non-inducible during EPS. However, because discrimination was modest and missing-data sensitivity analyses attenuated the association, TAND should not be used as a standalone criterion for diagnosis, ablation, or patient selection.

Study Limitations

This study has several important limitations. First, its retrospective single-center design may introduce selection, referral, and information bias, limiting generalizability. Although the study included consecutive patients evaluated under routine electrophysiology laboratory conditions, the induction protocol, pacing sequence, stimulation intensity, and use of pharmacological provocation were not prospectively standardized. Therefore, non-inducibility cannot be interpreted as a purely intrinsic substrate-related phenomenon.

Second, the discriminative performance of TAND was modest. The observed AUC of approximately 0.59 indicates substantial overlap between inducible and non-inducible patients. Accordingly, TAND should not be used as a standalone diagnostic threshold, procedural decision tool, or individual-level prediction model. The present findings should be interpreted as exploratory and hypothesis-generating.

Third, missing WBCL values represent a major limitation. WBCL was missing predominantly in inducible patients, most likely because tachycardia was induced before Wenckebach periodicity could be reached. Sensitivity analyses showed that the association between TAND and non-inducibility was directionally consistent after multiple imputation but attenuated and no longer conventionally significant. Deterministic sensitivity analyses further demonstrated that the estimated effect depended on assumptions regarding missing WBCL values. These findings reinforce the need for cautious interpretation.

Fourth, although all non-inducible patients had documented clinical SVT and supportive electrophysiological findings consistent with dual AV nodal physiology, diagnostic misclassification remains possible. AH jump and echo beats are supportive surrogate markers but do not provide the same diagnostic certainty as reproducible tachycardia induction. Previous registry data suggest that approximately 5%-10% of patients referred for paroxysmal SVT evaluation may ultimately have non-AVNRT mechanisms, underscoring the potential for misclassification in non-inducible cases.[18] Therefore, a proportion of non-inducible cases may have represented alternative SVT mechanisms or nonsustained AV nodal physiology rather than true clinical AVNRT.

Finally, AH interval and WBCL are dynamic measurements influenced by autonomic tone, catheter position, pacing protocol, and pharmacological state. Because these factors were not fully standardized or repeatedly assessed, the

reproducibility of TAND across different procedural conditions remains uncertain.

In addition, because WBCL values are numerically larger than AH interval values, the unweighted TAND calculation is influenced predominantly by the WBCL component. Therefore, TAND should be interpreted as a pragmatic descriptive composite rather than as a balanced representation of all aspects of AV nodal physiology.

CONCLUSIONS

In this retrospective electrophysiological cohort, TAND was modestly associated with non-inducible AVNRT at the group level and quadrant analysis supported a graded AH–WBCL continuum. The observed association may reflect a broader pattern of slower antegrade nodal conduction and higher functional conduction thresholds among patients in whom AVNRT is less readily inducible under routine electrophysiological study conditions. However, the association was attenuated after multiple imputation and was sensitive to assumptions regarding missing WBCL values. Total Antegrade Nodal Delay should therefore be interpreted as an exploratory electrophysiological descriptor rather than a mechanistic requirement, diagnostic threshold, or individual-level prediction tool. Prospective studies using standardized induction protocols are needed to validate these findings.

Data Availability Statement: All relevant data is included in the manuscript or is available from the corresponding author upon reasonable request.

Ethics Committee Approval: The study protocol was approved by İzmir Katip Çelebi University Atatürk Training and Research Hospital Ethics Committee (Approval No.: 0024; Date: January 15, 2026).

Informed Consent: The authors confirm that patient consent was not applicable to this article. This retrospective study was conducted using de-identified data. Therefore, informed consent was waived by the institutional review board.

Author Contributions: Concept – A.Ç.; design – A.Ç.; supervision – U.K., M.K.; resources and materials – A.Ç., E.N.U., A.E.A.; data collection and processing – A.Ç., E.N.U., A.E.A., T.K.; analysis and interpretation – A.Ç., A.E.A., T.K.; literature search – A.Ç., E.N.U., A.E.A., U.K., M.K.; writing – A.Ç., U.K.; critical review – U.K., M.K.

Statement on the Use of Artificial Intelligence: During the preparation of this work, the authors used ChatGPT-5.4 (OpenAI, San Francisco, CA, USA) to check for grammar and spelling to improve readability. After using this tool, the authors reviewed and edited the content as needed and took full responsibility for the content of the publication.

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Supplementary Table 1. Comparison of patients with complete versus missing Wenckebach cycle length (WBCL) data.

Variables	Complete WBCL Data (n = 329)	Missing WBCL Data (n = 58)	*P*
Age (years), median [IQR]	51.0 [40.0 – 59.0]	51.0 [37.0 – 62.0]	0.698
Female sex, n (%)	202 (61.4%)	38 (65.5%)	0.653
BCL (ms), median [IQR]	761 [682 – 877]	760 [690 – 900]	0.609
AH interval (ms), median [IQR]	80 [69 – 96]	76 [70 – 90]	0.660
HV interval (ms), median [IQR]	44 [40 – 48]	44 [42 – 48]	0.142
Inducibility status, n (%)			
- Inducible AVNRT	225 (68.4%)	56 (96.5%)	< 0.001
- Non-inducible AVNRT	104 (31.6%)	2 (3.5%)	< 0.001

Abbreviations: BCL, basic cycle length; AH, atrio-His; HV, His-ventricular; IQR, interquartile range.
Continuous variables are expressed as median [interquartile range] and compared using the Mann-Whitney U test. Categorical variables are expressed as counts (percentages) and compared using the Chi-square test. No significant differences were observed in baseline demographic or electrophysiological variables (age, sex, basic cycle length, AH, or HV intervals) between the two groups (all $p > 0.05$). However, missing WBCL data was almost exclusively observed in the inducible AVNRT cohort (96.5%, $p < 0.001$), clinically reflecting cases of rapid early tachycardia induction prior to reaching Wenckebach periodicity during programmed stimulation.

Supplementary Table 2. STROBE checklist

	Item Description	Location (or reason for not reporting)
Title and abstract		
1a. Indicate the study's design	Indicate the study's design with a commonly used term in the title or the abstract.	Title (implied via cohort description); Abstract, Methods ("We retrospectively analyzed...")
1b. Abstract	Provide in the abstract an informative and balanced summary of what was done and what was found.	Abstract (Background, Objective, Methods, Results, and Conclusions sections)
Introduction		
2. Background / rationale	Explain the scientific background and rationale for the investigation being reported.	Introduction, paragraphs 1–3
3. Objectives	State specific objectives, including any prespecified hypotheses.	Introduction, paragraph 4 ("We therefore hypothesized...")
Methods		
4. Study design	Present key elements of study design early in the paper.	Methods, Study Design and Population
5. Setting	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection.	Methods, Study Design and Population (tertiary referral center, between 2013 and 2026)
6a. Eligibility criteria	**Cohort study:** Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up. **Case-control study:** Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls. **Cross-sectional study:** Give the eligibility criteria, and the sources and methods of selection of participants.	Methods, Study Design and Population (Consecutive patients, inclusion/exclusion criteria detailed)

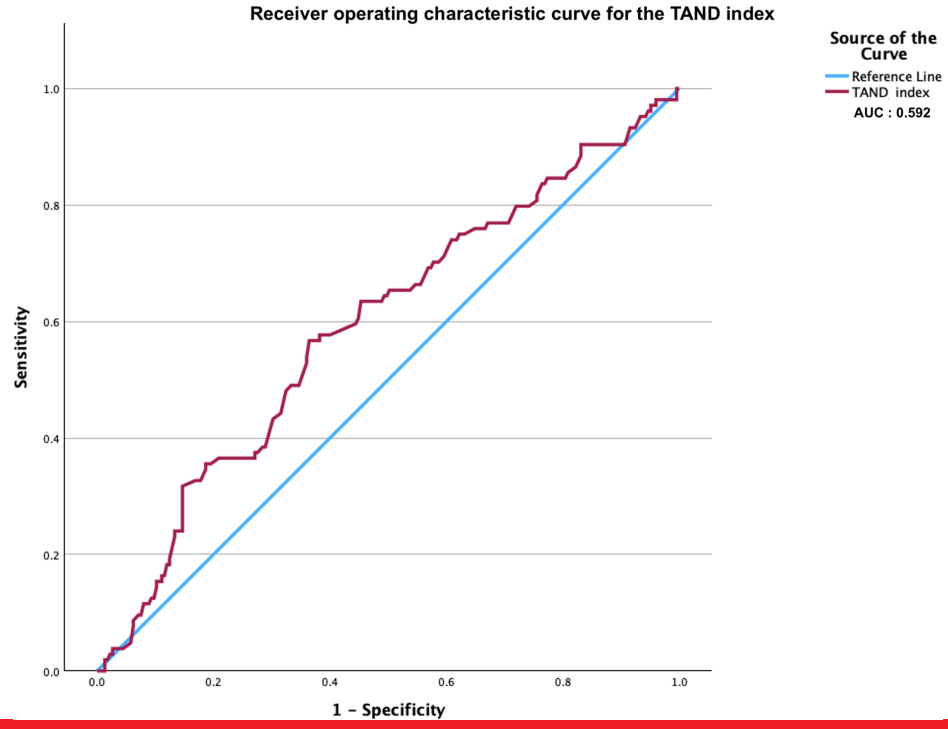
	Item Description	Location (or reason for not reporting)
6b. Matching criteria	**Cohort study:** For matched studies, give matching criteria and number of exposed and unexposed. **Case-control study:** For matched studies, give matching criteria and the number of controls per case.	Not applicable (Not a matched study design)
7. Variables	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	Methods, Electrophysiological Study & Novel Electrophysiological Parameters and Exploratory Clustering Analysis
8. Data sources / measurement	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group.	Methods, Electrophysiological Study
9. Bias	Describe any efforts to address potential sources of bias.	Methods, Statistical Analysis; Results, Missing Data Analysis; Supplementary Table 1 and Supplementary Table 2 (complete-case, multiple-imputation, and deterministic sensitivity analyses performed to assess potential selection bias related to missing WBCL values)
10. Study size	Explain how the study size was arrived at.	Methods, Study Design and Population (All consecutive eligible patients within the specified timeframe) 106 events, 4 variables model. EPV = 26
11. Quantitative variables	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why.	Methods, Statistical Analysis & Results, AV Nodal Quadrant Analysis (Cut-offs: AH ≥80 ms, WBCL ≥340 ms)
12a. Statistical methods	Describe all statistical methods, including those used to control for confounding.	Methods, Statistical Analysis (Multivariable logistic regression)
12b. Statistical methods – subgroups and interactions	Describe any methods used to examine subgroups and interactions.	Methods, Novel Electrophysiological Parameters and Exploratory Clustering Analysis (exploratory K-means clustering using standardized AH and WBCL values); Results, Exploratory Clustering Analysis and AV Nodal Quadrant Analysis
12c. Statistical methods – missing data	Explain how missing data were addressed.	Methods, Statistical Analysis; Results, Missing Data Analysis; Supplementary Table 1 and Supplementary Table 2 (complete-case analysis, multiple imputation, and deterministic sensitivity analyses)
12di. Statistical methods – loss to follow-up	**Cohort study:** If applicable, describe how loss to follow-up was addressed.	Not applicable (Cross-sectional EPS data, no long-term follow-up)
12dii. Statistical methods – matching cases and controls	**Case-control study:** If applicable, explain how matching of cases and controls was addressed.	
12diii. Statistical methods – sampling strategy	**Cross-sectional study:** If applicable, describe analytical methods taking account of sampling strategy.	
12e. Statistical methods – sensitivity analyses	Describe any sensitivity analyses.	Methods, Statistical Analysis; Results, Missing Data Analysis; Supplementary Table 2 (multiple-imputation and deterministic WBCL sensitivity analyses), bootstrap internal validation, and restricted cubic spline analysis
Results		
13a. Participant numbers	Report the numbers of individuals at each stage of the study—e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed; Consider use of a flow diagram.	Results, Baseline Characteristics (Total n=387; Inducible n=281; Non-inducible n=106)
13b. Participants – non-participation	Give reasons for non-participation at each stage.	Not applicable (Consecutive retrospective inclusion)
13c. Participants – flow diagram	Consider use of a flow diagram.	Figure 1 (study flow diagram)

	Item Description	Location (or reason for not reporting)
14a. Descriptive data – participant characteristics	Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders. Present the information in a table.	Results, Baseline Characteristics & Table 1
14b. Descriptive data – missing data	Indicate the number of participants with missing data for each variable of interest.	Results, Missing Data Analysis; Supplementary Table 1; Figure 1 (n=58 missing induction WBCL values required for TAND calculation)
14c. Descriptive data – follow-up time	**Cohort study:** Summarise follow-up time—e.g., average and total amount.	Not applicable (Procedure-based cross-sectional outcomes)
15. Outcome data	**Cohort study:** Report numbers of outcome events or summary measures over time. **Case-control study:** Report numbers in each exposure category, or summary measures of exposure. **Cross-sectional study:** Report numbers of outcome events or summary measures.	Results, Baseline Characteristics (Outcome: inducibility status)
16a. Main results	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence intervals). Make clear which confounders were adjusted for and why they were included.	Results, The TAND Index and Multivariable Analysis & Table 2
16b. Main results – category boundaries	Report category boundaries when continuous variables were categorised.	Results, AV Nodal Quadrant Analysis (AH ≥80 ms, WBCL ≥340 ms)
16c. Main results – risk	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period.	Not applicable
17. Other analyses	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses.	Results, Exploratory Clustering Analysis; AV Nodal Quadrant Analysis; ROC Curve Analysis; Missing Data Sensitivity Analyses; Supplementary Tables 2 and 3
Discussion		
18. Key results	Summarise key results with reference to study objectives.	Discussion, paragraph 1
19. Limitations	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	Discussion, Limitations
20. Interpretation	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	Discussion, paragraphs 2-4
21. Generalisability	Discuss the generalisability (external validity) of the study results.	**Discussion, Limitations** (Single-center nature noted, multicenter validation suggested)
Other information		
22. Funding	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based.	Funding section (end of manuscript)

Supplementary Table 3. Complete-case, multiple-imputation, and deterministic sensitivity analyses evaluating the association between TAND and non-inducible AVNRT.

Analysis	Model	OR per 50-ms increase	95% CI	*P*
Complete-case	Unadjusted	1.26	1.02–1.56	0.032
Complete-case	Age/sex-adjusted	1.31	1.05–1.63	0.016
Multiple imputation	Unadjusted	1.17	0.98–1.41	0.086
Multiple imputation	Age/sex-adjusted	1.21	0.99–1.46	0.056
Q1 deterministic imputation (WBCL=300 ms)	Age/sex-adjusted	1.33	1.09–1.62	0.004
Median deterministic imputation (WBCL=330 ms)	Age/sex-adjusted	1.23	1.01–1.51	0.039
Q3 deterministic imputation (WBCL=360 ms)	Age/sex-adjusted	1.12	0.92–1.37	0.247

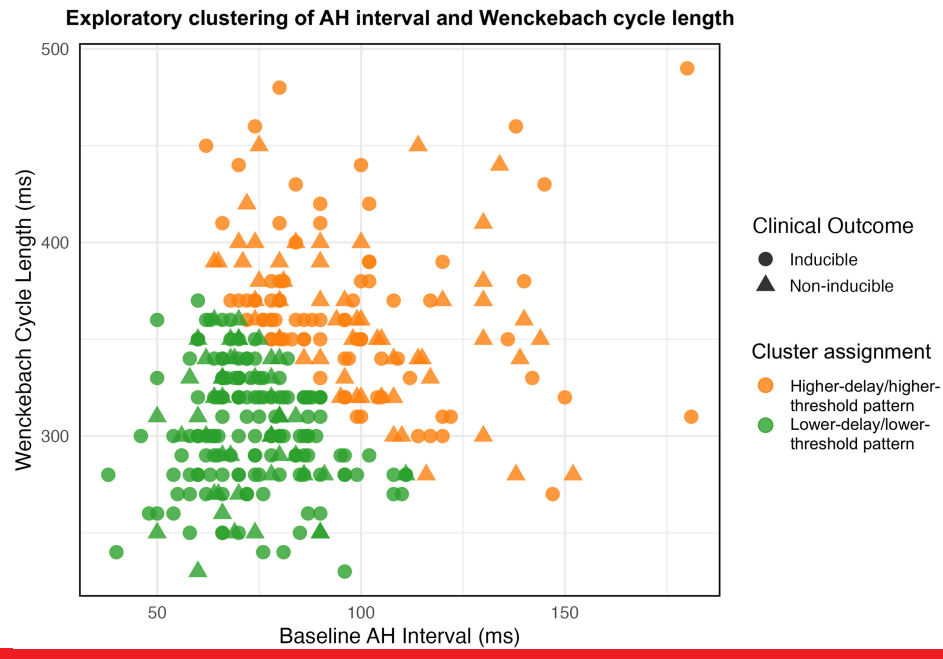
Abbreviations: TAND, Total Antegrade Nodal Delay; WBCL, Wenckebach cycle length; OR, odds ratio; CI, confidence interval.



Supplementary Figure 1. Receiver operating characteristic curve for the TAND index. Receiver operating characteristic curve demonstrating the modest discriminatory capacity of TAND for characterizing non-inducibility. TAND showed an AUC of 0.592, supporting its interpretation as a group-level electrophysiological descriptor rather than an individual-level prediction tool.

Supplementary Table 4. AH–WBCL quadrant-based continuum analysis of non-inducibility.

Quadrant	n	Non-inducible, n (%)	Median AH (ms)	Median WBCL (ms)	Median TAND (ms)
Q1: Low AH / Low WBCL	104	26 (25.0)	66	300	362
Q2: High AH / Low WBCL	88	24 (27.3)	90	300	396
Q3: Low AH / High WBCL	59	21 (35.6)	70	360	428
Q4: High AH / High WBCL	78	33 (42.3)	97.5	370	460
Additional analyses					
*Pearson $\chi^2 = 7.43$, df = 3, $P = 0.059$					
*Ordered trend analysis: OR per quadrant increase = 1.32 (95% CI: 1.07–1.61), $P = 0.008$					
*Q4 vs Q1: OR = 2.20 (95% CI: 1.17–4.17), $P = 0.014$					
Abbreviations: AH, atrio-His interval; WBCL, Wenckebach cycle length; TAND, Total Antegrade Nodal Delay.					



Supplementary Figure 2. Exploratory clustering of AH interval and Wenckebach cycle length. Scatter plot of standardized baseline AH interval and antegrade Wenckebach cycle length (WBCL). Exploratory clustering analysis identified two distinct electrophysiological patterns: a lower-delay/lower-threshold pattern and a higher-delay/higher-threshold electrophysiological pattern. Importantly, clustering was performed independent of inducibility status, showing that AH and WBCL values cluster into distinct group-level electrophysiological patterns.