# Head-Up Tilt Test in the Diagnosis of Vasovagal Syncope: A Cross-Sectional Study Evaluating Hemodynamic Profiles, Arrhythmic Patterns, and Predictive Factors

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## ABSTRACT

### BACKGROUND
Vasovagal syncope (VVS) is the most common cause of transient loss of consciousness, accounting for up to half of all syncope cases. The head-up tilt test (HUTT) remains a cornerstone diagnostic tool endorsed by international guidelines, yet hemodynamic profiles and arrhythmic subtypes in Southeast Asian populations remain incompletely characterized.

### OBJECTIVES
To evaluate HUTT outcomes in a cross-sectional sample, characterize hemodynamic and arrhythmic response profiles, and identify independent predictors of test positivity at Vinmec Times City International Hospital.

### METHODS
We enrolled 92 consecutive patients (mean age 43.2 ± 16.8 years; 58.7% female; range 14-81 years) undergoing HUTT between January 2022 and June 2024. Protocol comprised passive Phase 1 (70 degrees, 20 min), pharmacological Phase 2 (sublingual NTG 0.4 mg), and recovery Phase 3. Endpoints: SBP drop, HR change, arrhythmic events (asystole ≥ 3s, AV block, junctional rhythm), and syncope/presyncope. VASIS classification was applied.

### RESULTS
Out of 92 patients, 68 (73.9%) had a positive HUTT. Vasovagal syncope (VVS) was the predominant etiology (94.1%), while orthostatic hypotension (OH) was identified in 4.4%. Mean SBP at the syncopal event dropped significantly to 63.1 ± 19.2 mmHg. Notably, severe arrhythmic events occurred in 20.6% of positive cases, including asystole ≥ 3s (8.8%), junctional rhythm (7.4%), and high-degree AV block (4.4%). Patients testing positive during the passive Phase 1 (unprovoked) exhibited a 3.4-fold higher risk of cardioinhibitory responses compared to those in Phase 2 (aOR = 3.41; 95%CI: 1.08–10.77; p=0.037). Multivariate analysis identified younger age and the absence of hypertension as independent predictors of HUTT positivity.

### CONCLUSION
HUTT demonstrates a high diagnostic yield across the 14–81 age spectrum. The significant prevalence of cardioinhibitory phenotypes (20.6%), particularly among passive-phase responders, identifies a high-risk subset requiring systematic risk stratification. These findings highlight the need for individualized risk assessment, with further studies warranted to clarify the role of pacemaker therapy in Southeast Asian patients presenting with malignant reflex syncope.

**Keywords**
head-up tilt test | vasovagal syncope | asystole | AV block | hemodynamics | Vinmec | Vietnam | Southeast Asia

## 1. INTRODUCTION

Syncope affects an estimated 15–39% of the general population over a lifetime; vasovagal syncope (VVS) is the leading etiology.[1, 2] Recurrent episodes impose physical injury, impaired quality of life, and substantial healthcare costs.[3] The HUTT is endorsed by ESC and ACC/AHA/HRS guidelines as a key diagnostic modality for unexplained syncope suspected to be reflex or orthostatic in origin,[4] exploiting orthostatic stress to unmask pathological neuroautonomic reflexes.[5] Arrhythmic subtypes — asystole, high-degree AV block, junctional escape — carry direct pacing-therapy implications[6, 7] but remain underreported in Southeast Asia. This study from Vinmec Times City International Hospital presents the first cross-sectional characterization in a Vietnamese cohort spanning ages 14–81 years.

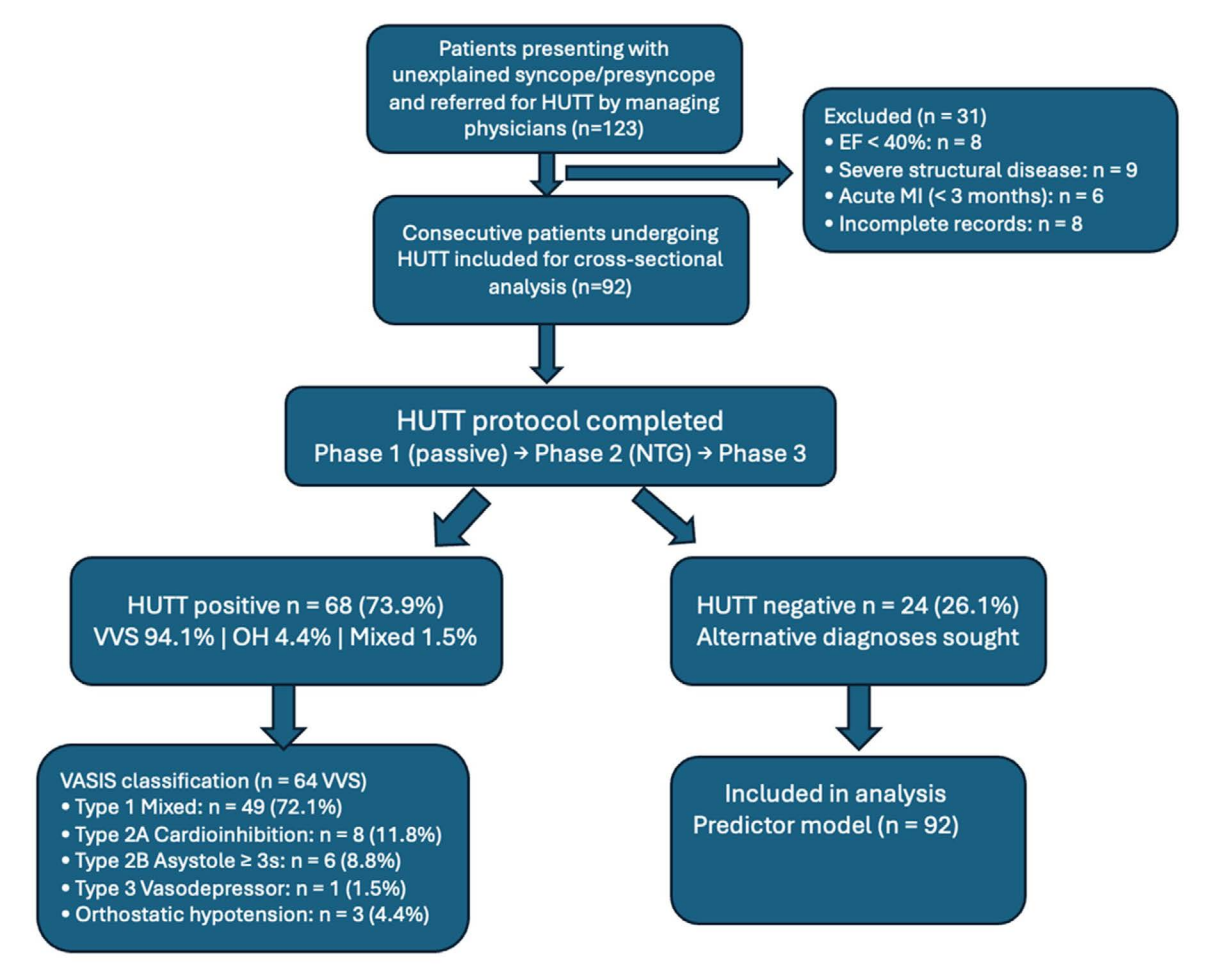
## 2. METHODS

### 2.1 Study Design and Setting

Descriptive cross-sectional study. Consecutive patients referred for HUTT at the Cardiology Department, Vinmec Times City International Hospital, January 2022 - June 2024 (Figure 1). Referral for HUTT was determined by the requesting physician based on clinical indication; the study authors did not select or screen patients prospectively, but enrolled and described, at a single time point, all consecutive patients who underwent the test during the study period.

Inclusion: age ≥ 14 years; ≥ 1 unexplained syncope or orthostatic presyncope; non-diagnostic initial workup (ECG, 24h Holter, echocardiography), all of whom had already been referred for HUTT by their treating physician. Exclusion: EF <40%, severe structural disease, acute MI within 3 months. Ethics: Vinmec IRB Protocol Vinmec Times City number: 16/2026/CN/HDDD, Declaration of Helsinki. Written informed consent from all participants; parental consent for minors.

**Figure 1:** Patient enrollment and HUTT outcome classification flow. All 123 patients assessed had been referred for HUTT by their treating physician based on clinical indication; the authors had no role in selecting or screening which patients underwent the test. Of these, 92 were enrolled and completed the HUTT protocol after exclusion of 31 patients per the criteria shown. VVS = vasovagal syncope; OH = orthostatic hypotension; NTG = nitroglycerin; VASIS = Vasovagal Syncope International Study.




### 2.2 HUTT Protocol

After 20-min supine rest, patients were tilted to 70 degrees for passive Phase 1 (20 min) with continuous beat-to-beat BP monitoring (Finapres, Ohmeda) and 12-lead ECG. If Phase 1 was negative, sublingual NTG 0.4 mg was administered (Phase 2, 20 min), followed by supine recovery (Phase 3). Positive test criteria were defined according to the 2018 ESC Guidelines for the diagnosis and management of syncope. VASIS classification was applied.

### 2.3 Statistical Analysis

Continuous variables as mean ± SD or median (IQR); categorical as n (%). Between-group comparisons: Student's t-test or Mann-Whitney U; chi-square or Fisher's exact. Univariate and multivariate logistic regression for HUTT positivity predictors; results as OR (95%CI). Two-tailed p<0.05 significant. SPSS v27.0 (IBM, USA).

## 3. RESULTS

### 3.1 Baseline Characteristics

**Table 1. Baseline clinical characteristics (N=92)**

| Variable | All (n=92) | HUTT positive (n=68) | HUTT negative (n=24) | P |
|---|---|---|---|---|
| Age, mean ± SD (years) | 43.2 ± 16.8 | 40.1 ± 15.5 | 51.8 ± 18.2 | **0.004** |
| Age range (years) | 14-81 | 14-76 | 19-81 | - |
| Female sex, n (%) | 54 (58.7) | 42 (61.8) | 12 (50.0) | 0.311 |
| Hypertension, n (%) | 21 (22.8) | 12 (17.6) | 9 (37.5) | **0.041** |
| Diabetes mellitus, n (%) | 9 (9.8) | 6 (8.8) | 3 (12.5) | 0.584 |
| Unexplained syncope, n (%) | 73 (79.3) | 58 (85.3) | 15 (62.5) | **0.020** |
| Orthostatic presyncope, n (%) | 19 (20.7) | 10 (14.7) | 9 (37.5) | **0.020** |
| Baseline SBP (mmHg) | 107.5 ± 15.4 | 105.9 ± 14.9 | 112.3 ± 16.8 | 0.076 |
| Baseline HR (bpm) | 68.4 ± 16.5 | 69.1 ± 16.8 | 66.2 ± 15.8 | 0.441 |
| Bundle branch block, n (%) | 7 (7.6) | 4 (5.9) | 3 (12.5) | 0.265 |

*SBP: systolic blood pressure; HR: heart rate. *p<0.05.*

Our research contains 92 patients, included 68 cases (73.9%) that has positive HUTT and 24 cases (26.1%) are negative (Figure 2). Median overall age is 43.2 ± 16.8, HUTT (+) is significant younger than the HUTT (-) (40.1 vs 51.8, p = 0.004) (Figure 3). Female occupied the most (58.7%) but no significant stasistically between two groups (p = 0.311). Hypertension is appeared more than group of negatively HUTT (37.5% vs 17.6%, p = 0.041), meanwhile the rate of Diabetes type 2 is equal for two groups (p = 0.584). Unknown cause of syncope is the major indication, that occupied 79.3% all the sample, and more commonly meaning in the positive group (85.3% vs 62.5%, p = 0.020). In constrast, pre VVS occurred more than usual in negative group (37.5% vs 14.7%, p = 0.020). Systolic blood pressure and baseline heart rate is no significant statisticallly between two group (p = 0.076 và 0.441). Block His bundle is no difference (p = 0.265).

**Figure 3: Age distribution by HUTT result (N=92, range 14-81 years).** Positive cases predminate in 20-49 year group; negative cases shift older, reflecting progressive autonomic blunting with aging.

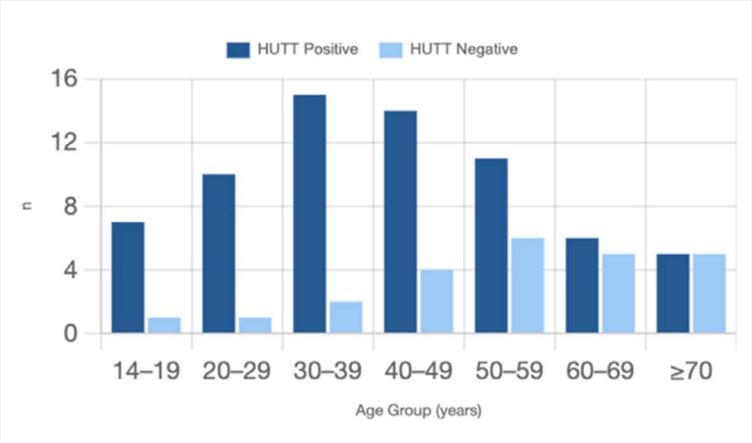
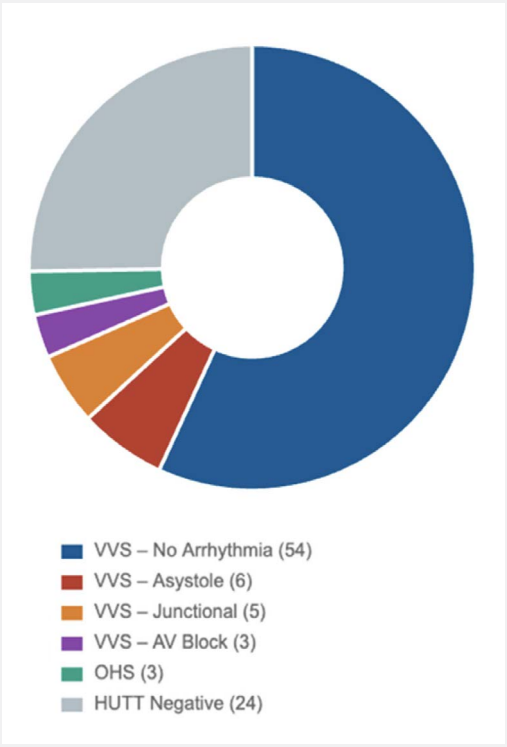



**Figure 2: HUTT outcome distribution (N=92).** VVS = vasovagal syncope; OH = orthostatic hypotension; HUTT− = negative.
Segments within the positive group reflect arrhythmic subtypes. All 92 patients shown had already been referred for and underwent HUTT by their treating physician; the authors had no role in selecting or screening patients for the test.




### 3.2 HUTT Outcomes and Hemodynamics

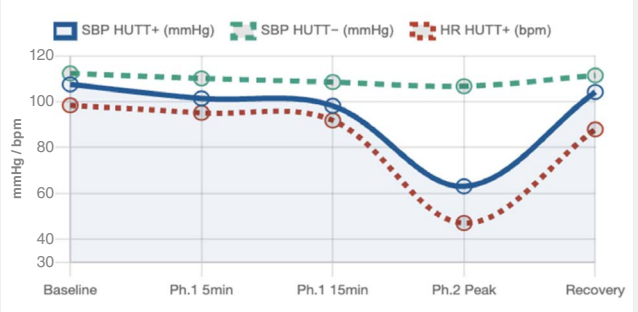
**Table 2. HUTT outcomes and hemodynamic parameters**

| Parameter | n (%) | Mean ± SD |
|---|---|---|
| HUTT positive (overall) | 68 (73.9) | - |
| - Vasovagal syncope (VVS) | 64 (94.1) | - |
| - Orthostatic hypotension (OH) | 3 (4.4) | - |
| - Mixed / other | 1 (1.5) | - |
| Phase 1 positive (passive tilt) | 6 (8.8) | - |
| Phase 2 positive (NTG-provoked) | 62 (91.2) | - |
| SBP at syncopal event (mmHg) | - | 63.1 ± 19.2 |
| HR at syncopal event (bpm) | | 58.8 ± 26.9 |
| Delta-SBP from baseline (mmHg) | - | -44.4 ± 17.1 |
| Delta-HR from baseline (bpm) | - | -51.3 ± 22.4 |
| Time-to-event Phase 1 (min) | - | 7.6 ± 2.1 |
| Time-to-event Phase 2 (min) | - | 3.5 ± 1.8 |
| Full syncope (LOC) | 53 (77.9) | - |
| Presyncope only | 15 (22.1) | - |

*NTG: nitroglycerin; LOC: loss of consciousness; OH: orthostatic hypotension.*

Among the 68 HUTT-positive patients (73.9% of the total cohort), vasovagal syncope was the predominant diagnosis, accounting for 94.1% of cases, while orthostatic hypotension and mixed/other responses were rare (4.4% and 1.5%, respectively). The vast majority of positive responses occurred during Phase 2 with nitroglycerin provocation (91.2%), whereas only 8.8% were positive during the passive tilt phase. At the time of the syncopal event, mean SBP dropped to 63.1 ± 19.2 mmHg and mean HR to 58.8 ± 26.9 bpm (Figure 4), corresponding to substantial decreases from baseline (delta-SBP −44.4 ± 17.1 mmHg; delta-HR −51.3 ± 22.4 bpm). Time-to-event was notably shorter in Phase 2 (3.5 ± 1.8 min) compared to Phase 1 (7.6 ± 2.1 min), reflecting the pharmacological provocation effect of nitroglycerin. Full syncope with loss of consciousness occurred in 77.9% of positive cases, while the remaining 22.1% experienced presyncope only.

**Figure 4: Hemodynamic trajectories.** SBP nadir 63.1 mmHg and HR nadir 47.1 bpm in HUTT-positive cases; near-stable profiles in HUTT-negative patients throughout all phases.



### 3.3 VASIS Classification

**Table 3. VASIS Classification in Patients with Positive Head-Up Tilt Test (n=68)**

| Classification | All (n) | Positive HUTT (n=68) | Total (N=92) |
|---|---|---|---|
| Vasovagal syncope (VVS) – Total | 64 | 94.1 % | 69.6% |
| Type 1 (Mixed) | 49 | 72.1% | 53.3% |
| Type 2A (Cardioinhibition without asystole) | 8 | 11.8% | 8.7% |
| Type 2B (Cardioinhibition with asystole ≥ 3s) | 6 | 8.8% | 6.5% |
| Type 3 (Pure Vasodepressor) | 1 | 1.5% | 1.1% |
| Orthostatic Hypotension (OH) | 3 | 4.4% | 3.3% |
| Mixed | 1 | 1.5% | 1.1% |
| Negative HUTT | 24 | | 26.1% |

Within the VVS subgroup (n=64): Type 1 (Mixed) was the most common form with 49 patients (72.1% of VVS), characterized by a concomitant drop in both blood pressure and heart rate. Type 2 (Cardioinhibitory) accounted for a total of 20.6% of HUTT-positive cases. Specifically, Type 2B (asystole ≥ 3 seconds) was identified in 6 patients (8.8% of VVS). This group represents the highest clinical risk due to transient cardiac arrest, which may cause physical injury and often warrants consideration for permanent pacemaker implantation. Type 3 (Pure Vasodepressor) was rare (1.5% of VVS), indicating that isolated peripheral vasodilation without significant bradycardia was not the primary mechanism in this cohort.

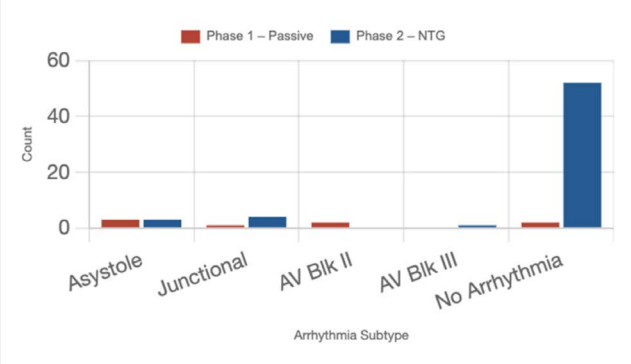
### 3.4 Arrhythmic Events

**Table 4. Arrhythmic events in HUTT-positive patients (n=68)**

| Arrhythmia Type | n | % | Phase 1 | Phase 2 | P value |
|---|---|---|---|---|---|
| None (pure vasodepressor) | 54 | 79.4 | 2 | 52 | |
| Asystole (≥ 3 seconds) | 6 | 8.8 | 3 | 3 | |
| Junctional escape rhythm | 5 | 7.4 | 1 | 4 | |
| 2nd degree AV block (Mobitz II) | 2 | 2.9 | 2 | 0 | |
| 3rd degree AV block (complete) | 1 | 1.5 | 0 | 1 | |
| Any Arrhythmia | 14 | 20.6 | 6 | 8 | 0.037 |

**Key finding:** Phase 1 passive positivity conferred a 3.4-fold higher risk of cardioinhibitory arrhythmia vs. Phase 2 (OR 3.41; 95%CI 1.08–10.77; p=0.037) (Figure 5). Among the 6 Phase 1-positive patients, 6 (75%) developed arrhythmic events including asystole ≥ 3s or high-degree AV block — independent of pharmacological provocation. Arrhythmias occurred significantly more frequently during Phase 1 passive tilt (75.0%) than during Phase 2 NTG-provoked tilt (13.3%), indicating that spontaneous vasovagal responses are more likely to involve a cardioinhibitory mechanism.

**Figure 5: Arrhythmic subtypes by HUTT phase.** Phase 1 (passive) events are predominantly cardioinhibitory; Phase 2 (NTG) shows a mixed vasodepressor-cardioinihibitory pattern.




### 3.5 Predictors of Positive HUTT

**Table 5. Logistic regression - predictors of positive HUTT**

| Variable | Univariate | | Multivariate | |
|---|---|---|---|---|
| | OR (95%CI) | p | OR (95%CI) | P |
| Age (per year increase) | 0.96 (0.93-0.99) | **0.016** | 0.97 (0.94-1.00) | **0.029** |
| Female sex | 1.62 (0.63-4.13) | 0.314 | - | NS |
| Absent hypertension | 2.82 (0.97-8.21) | 0.057 | 2.94 (1.78-8.68) | **0.008** |
| Unexplained syncope (vs presyncope) | 3.48 (1.20-10.12) | **0.022** | 2.87 (0.94-8.73) | 0.063 |
| Diabetes mellitus | 0.67 (0.16-2.76) | 0.580 | - | NS |

On univariate analysis, younger age (OR 0.96 per year, p = 0.016) and unexplained syncope as the indication (OR 3.48, p = 0.022) were significantly associated with a positive HUTT result. Absent hypertension showed a trend toward significance (OR 2.82, p = 0.057), while diabetes mellitus was not associated (p = 0.580).

After multivariate adjustment, two independent predictors of a positive HUTT remained significant: younger age (aOR 0.97 per year increase, 95%CI 0.94–1.00, p = 0.029) and absent hypertension (aOR 2.94, 95%CI 1.78–8.68, p = 0.008). Notably, absent hypertension became statistically significant in the multivariate model, suggesting a confounding effect masked in univariate analysis. Conversely, unexplained syncope lost its significance after adjustment (aOR 2.87, p = 0.063), indicating that its univariate association was partly confounded by other variables. Diabetes mellitus was excluded from the final model due to non-significance. These findings suggest that the typical profile of a patient likely to have a positive HUTT is a younger without hypertension.

## 4. DISCUSSION

This study at Vinmec Times City International Hospital provides a comprehensive characterization of hemodynamic responses during the Head-Up Tilt Test (HUTT) in a Vietnamese cohort. With an overall positivity rate of 73.9%, our findings reaffirm the diagnostic utility of HUTT in evaluating unexplained syncope and reveal clinically significant arrhythmic phenotypes that warrant further attention.

### 4.1. Positivity Rates and Population Characteristics

The 73.9% positivity rate observed in this study exceeds that of classic Western series, large meta-analyses report pooled positivity of ~34% passive, 53% with isoproterenol, and 62% with nitroglycerin in patients with suspected reflex syncope. Shortened "Fast Italian" nitroglycerin protocols achieve ~58–60% positivity, similar to traditional longer protocols.[8, 9, 10] Two factors may account for this discrepancy. The systematic use of sublingual nitroglycerin (Phase 2) likely optimized diagnostic sensitivity without substantially compromising specificity. Second, HUTT is not a routine investigation; it was performed selectively in patients already referred for evaluation of unexplained syncope or orthostatic presyncope. As the pretest probability of a reflex mechanism is inherently higher in this referred population than in the general population, a higher positivity rate than community-based estimates is expected and should not be interpreted as evidence of excessive test sensitivity.

Notably, VVS is not confined to younger age groups. Although multivariate analysis identified younger age as a significant predictor of positivity (aOR = 0.97 per year), the occurrence of asystole in both elderly patients and a 14-year-old adolescent underscores that reflex syncope remains a clinical entity spanning the entire age spectrum.

### 4.2. VASIS Classification and Clinical Significance of Cardioinhibition

The majority of our patients were classified as VASIS Type 1 (Mixed) (72.1%), characterized by a concomitant decline in blood pressure followed by progressive bradycardia culminating in syncope.

However, the most clinically relevant finding is the 20.6% prevalence of arrhythmic events. The Type 2B (asystole ≥3s) rate of 8.8% exceeds the average reported in many European cohorts.[1, 2] This observation raises an important question: whether we are observing a population with inherently heightened parasympathetic tone, or whether the beat-to-beat resolution of the Finapres monitoring system provides superior detection of transient pauses. Irrespective of the underlying mechanism, the Type 2B subgroup represents the highest-risk category due to the potential for physical injury from sudden, unpredictable loss of consciousness.

### 4.3. Prognostic Value of the Passive Phase (Phase 1)

A clinically significant observation in this study is that patients who tested positive during the passive Phase 1 (unprovoked) exhibited a 3.4-fold higher risk of cardioinhibitory events compared to those responding only during pharmacologically provoked Phase 2.

This observation has important implications for clinical management. Patients who develop syncope within the first 20 minutes of passive tilting likely possess a hypersensitive autonomic nervous system predisposed to prolonged asystole. In light of evidence from the ISSUE-3 and BioSync-CLS trials,[11] these individuals represent primary candidates for permanent cardiac pacing—particularly those over 40 years of age with recurrent episodes. We propose that a positive response during the passive phase should be considered a significant clinical indicator warranting expedited evaluation for pacing candidacy.

### 4.4. Predictors: Age, and Blood Pressure

Our multivariate model demonstrates that the absence of hypertension (aOR = 2.94) are independently associated with a positive HUTT. In normotensive subjects, greater vascular compliance may facilitate a more rapid vasodepressor response. Conversely, in hypertensive patients, increased arterial stiffness and attenuated baroreceptor sensitivity may confer relative protection against the acute hemodynamic collapse characteristic of VVS, while paradoxically increasing susceptibility to orthostatic hypotension (OH).

### 4.5. Limitations and Future Directions

Several limitations merit consideration. First, the cross-sectional design captures findings at the single time point of HUTT and does not permit assessment of clinical outcomes over time. Although this represents the first cross-sectional HUTT study at a major Vietnamese tertiary center, the sample size (N=92) limits generalizability to the broader national population. Additionally, the absence of long-term follow-up data via Implantable Loop Recorders (ILR) precludes definitive confirmation of the concordance between tilt-induced and spontaneous asystolic events in daily life.

Nevertheless, based on these results, we advocate for the systematic implementation of HUTT—not solely as a diagnostic tool, but as a means of arrhythmic risk stratification. This approach enables a truly individualized therapeutic strategy, ranging from physical counterpressure maneuvers and pharmacological interventions to the informed consideration of cardiac pacing.

## 5. CONCLUSION

This cross-sectional study of 92 patients at Vinmec Times City International Hospital demonstrates that the Head-Up Tilt Test (HUTT) yields a high positivity rate (73.9%) for unexplained syncope and orthostatic presyncope. Our findings support three principal conclusions.

Vasovagal Syncope (VVS) constitutes the predominant diagnosis (94.1%), with the mixed phenotype (VASIS Type 1) being most prevalent. However, the 20.6% incidence of severe cardioinhibitory events — including prolonged asystole and high-degree AV block — identifies a high-risk subset prone to physical injury that mandates rigorous clinical surveillance.

Patients testing positive during the unprovoked passive phase carry a 3.4-fold higher risk of cardioinhibitory responses

compared to pharmacological responders. Passive-phase positivity should be recognized as a critical prognostic marker, potentially warranting expedited evaluation for permanent pacing in accordance with ISSUE-3 and BioSync-CLS trial criteria.

Younger age, and the absence of hypertension serve as independent clinical predictors of HUTT positivity, reflecting heightened autonomic reactivity in these populations.

## DECLARATIONS

**Funding:** No external funding. Conducted as part of routine clinical care at Vinmec Times City International Hospital.

**Conflicts of interest:** All authors declare no conflicts of interest.

**Ethics:** Vinmec Times City Hospital IRB. Declaration of Helsinki. Written informed consent obtained.

**Data availability:** De-identified data available on request: ducdung.doan@vinmec.com.

**Author contributions (CRediT):** Doan Duc Dung: Conceptualization, Methodology, Formal analysis, Supervision, Writing - original draft. Vu Quoc Oai: Data collection, Validation, Writing - review & editing. Hoang Phu Quy: Investigation, Data collection, Writing - review & editing. All authors approved the final manuscript.

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