

Gender and age effects on the type of result of head-up tilt-table test: A retrospective study

Murat YALÇIN(*), Mustafa APARCI(**), Zafer IŞILAK (*), Ömer Uz (*), Murat ATALAY (***), Emrah ERDAL (*), Ejder KARDEŞOĞLU (*), Mehmet UZUN (*)

ÖZET

Eğik masa testi sonuçlarına yaş ve cinsiyetin etkisi: Retrospektif çalışma

Bu çalışmada, eğik masa testi yapılan 591 hastanın test sonuçlarını ve klinik özelliklerini geriye dönük olarak incelendik. Eğik masa testi sonuçları [normal, vasovagal senkop (mikst, vazodepresör ve kardiyoinhibitör tip 2A ve 2B)] ve asistol süreleri, yaş grupları (<25, 25-50, >50 yaş) ve cinsiyete göre karşılaştırıldı. Mikst tip ve vazodepresör tip vasovagal senkop en çok tespit edilen cevap tipleriydi [Sırasıyla 140(%23.7) ve 76(%12.9)]. Vazodepresör, kardiyoinhibitör tip 2A ve 2B vasovagal senkop daha ileri yaşlarda (>50 yaş) biraz daha fazla tespit edilirken, mikst tip vasovagal senkop en çok daha genç yaşlarda (<25 yaş) tespit edildi (p=0.652). En çok gözlenen asistol süresi olan 3-6 saniye, daha genç yaşlarda gözlenirken, bu süre daha yetişkinlerde (25-50 yaş) 7-8 saniye ve üzerine uzadığı görüldü (p=0.285). Cinsiyet açısından tek fark olarak kadınlarda vazodepresör tip vasovagal senkop hafif fazla (P=0.153), erkeklerde asistol daha sık gözlemlendi (P=0.709). Eğik masa testi tüm yaş gruplarında uygun şartlarda kolayca uygulanabilen bir testtir. Mikst tip vasovagal senkop en çok tespit edilen tanı olmasına rağmen kardiyoinhibitör tip vasovagal senkop da tüm yaş gruplarında nadir olmayan sonuçlardan biridir. 3-6 saniye süreli asistol genellikle daha gençlerde gözlenirken bu süre daha yaşlılarda komplikasyon gelişmeden 7-8 saniyeye kadar uzayabildi.

Anahtar Kelimeler: Eğimli masa testi; vasovagal senkop; asistol; aritmi,

SUMMARY

In this study we analyzed retrospectively the results of head-up tilt-table test (HUTT) and clinical features of 591 subjects. The head-up tilt-table test results [normal, vasovagal syncope (mixed, vasodepressor and cardioinhibitory type 2A and 2B)] and the asystole periods were compared by age groups (<25, 25-50, >50 years old) and gender. Mixed type and vasodepressor type vasovagal syncope were the predominant types of response [140 (23.7%) and 76 (12.9%), respectively]. Mixed type vasovagal syncope was higher in younger ages (<25 years) whereas vasodepressor and cardioinhibitory type 2A and 2B type vasovagal syncope was slightly higher in older ages (>50 years) (p=0.652). While the mostly observed asystole period was 3-6 sec and over in younger ages, it may prolong 7-8 sec and over in adults (25-50 years old) (p=0.285). The only difference with regard to gender was that the rate of vasodepressor type was slightly higher in females (P=0.153) whereas asystole period was more frequently observed in males (P=0.709). Head-up tilt-table test is a convenient and easily applicable test in proper circumstances for all age groups. Although mixed type vasovagal syncope is a predominant diagnosis in the test, cardioinhibitory type vasovagal syncope is not an infrequent one in all age groups. While asystole period of 3-6 sec was mainly observed in younger patients, it was prolonging over 7-8 sec in older ages without any complication.

Key words: Head-up tilt-table test; vasovagal syncope; asystole; arrhythmia,

Introduction

Dizziness, pre-syncope and syncope are among the most frequently encountered complaints of subjects from all ages (1). Symptoms may originate from a wide variation of causes including bradyarrhythmia, neurally mediated abnormal responses, orthostatic hypotension, cerebrovascular diseases and valvular heart diseases (2). Furthermore, symptoms may proceed to clinical events ranging from a transient loss of consciousness to death (3).

Vasovagal syncope (VVS) is one of the most frequent diagnoses of syncope in daily clinical practice. Interrogation of medical history, the clinical scene and circumstances related to syncope will usually establish the diagnosis. Undesired or noxious stimulants, medical interventions, fixed long duration standing may trigger the syncope. Although it was previously supposed to be limited mainly to younger subjects due to exaggerated responses of vagotonic activity, currently VVS is accepted to be a clinical entity of subjects of any ages, and a potential threat to both individual and public safety (4, 5). Therefore, discrimination of type and degree of responses including blood pressure and heart rate is clinically important for not only medical and legal issues but also guiding the management of VVS (6).

Head-up tilt-table test (HUTT) is an effective method for evaluating the etiology of syncope, and also for diagnosing VVS. However, it is available only in a limited number of centers because the test necessitates an arrhythmia laboratory with capability to intervene, monitor, and resuscitate immediately. In our country, these conditions were provided in the last decade so that HUTT could be set and performed.

Because there are a limited number of HUTT laboratories in our country, their workload is very high, and the waiting lists are very long. Given the fact that the type of the HUTT is important in determining the type of treatment, especially the pacemaker implantation, the prediction of the test result may be helpful in deciding which patients should be given priority in these waiting lists. In this study, we aimed to evaluate the results of HUTT performed in our arrhythmia laboratory and to describe the hemodynamic responses during syncope according to age and gender.

Patients, Material and Method

Medical recordings of consecutive 591 patients who were underwent HUTT in arrhythmia laboratory due to complaints of pre-syncope and syncope between 2010 and 2013 were analyzed retrospectively. The subjects with sick sinus syndrome, coronary artery disease, congestive heart failure, beta

*Gülhane Askeri Tıp Akademisi, Haydarpaşa Eğitim Hastanesi, Kardiyoloji Servisi İstanbul, TÜRKİYE.

**Kasımpaşa Asker Hastanesi, Yeşilyurt Polikliniği, İstanbul, TÜRKİYE.

***İzmir Asker Hastanesi, Kardiyoloji Servisi, İzmir, TÜRKİYE.

Reprint request: Murat YALÇIN

Adres: GATA Haydarpaşa Eğitim Hastanesi Kardiyoloji servisi Kadıköy, İstanbul, TÜRKİYE

E-mail: med_murat@yahoo.com

blocking treatment and anemia were excluded from the study.

Head-up tilt-table test protocol

The test was performed under the supervision of a team including a nurse and a cardiologist in a laboratory with the capability of cardiopulmonary resuscitation, equipments and bedside monitoring. Environmental condition was strictly silent, lightly dimmed with a room temperature of 24-25°C. All the patients were informed about the test and signed an informed consent.

Patients underwent the test following a 2-3 hour fasting state and a resting period of 20-25 minutes at supine position. Continuous electrocardiographic monitorization and automated blood pressure measurement at least every 2 minutes were performed during the test period. Patients lay at a supine position and were tied with comfortable secures on a foot-board support. Thereafter, the table was given an upright position with an incline of 70° within 10-15 seconds for the passive phase of the tilt test. Patients were pharmacologically provoked if the passive phase was negative. Drug provocation phase consisted of additional 20 minutes at the same position preceded by a sublingual 0.4 mg nitroglycerin. Positive test criteria for ending the HUTT were defined as (7);

Mixed type VVS; heart rate lower than 40 beat per minute for a period of less than 10 sec and/or asystole period less than 3 sec accompanied by hypotension (lower than <40 mmHg),

Cardioinhibitory type 2A VVS; heart rate lower than 40 bpm for a period of longer than 10 sec with an asystole period less than 3 sec, blood pressure falls before the heart rate falls,

Cardioinhibitory type 2B VVS; heart rate lower than 40 bpm for a period of longer than 10 sec and/or asystole period longer than 3 sec, heart rate fall coincides with or precedes blood pressure fall.

Vasodepressor type-VVS (type 3); hypotension lower than <40 mmHg without heart rate fall less than 10% from its peak,

Symptomatic without objective finding; symptoms associated with pre-syncope not accompanied by bradycardia or hypotension,

Asystole; absence of QRS wave lasting more than 3 sec,

Postural orthostatic tachycardia syndrome (POTS); increase in heart rate >30% or to >120 bpm, not syncope, instability of blood pressure.

Statistical Analysis

Statistical analysis was performed by using SPSS 11.0 for Windows. Numerical variables with normal distribution were analyzed by parametric tests. Categorized variables were analyzed by Chi-Square test. Correlation analyses of parametric and nonparametric data was performed by Pearson and Spearman's correlation test, respectively. P <0.05 was accepted as statistically significant.

Results

The results of 476 males (age 26.3±11.5) and 115 females (33.2±15.9) were analyzed. Normal or negative test results were observed in 263 (44.5%) subjects. Positive test results [n=328 (55.5%)] were illustrated as a pie-chart graphic. The distribution of responses as VVS were as mixed type VVS (n=140, 24%), vasodepressor type VVS (n=76, 13%), cardioinhibitory type 2A VVS (n=41, 7%), cardioinhibitory type 2B VVS (n=52, 9%), and others (Figure 1). Study groups designed according to age <25 (20.8±2.1), 25-50 (34.8±7.2), and

>50 (61.9±7.6) are composed of 401, 140, and 50 subjects, respectively. The distribution of positive and negative test results and also diagnosis was not statistically significant according to age groups (p=0.652) (Table I) and also genders (p=0.153) (Table II). Mixed type and vasodepressor type VVS were the predominant types of response [140(23.7%) and 76 (12.9%), respectively]. Mixed type VVS was higher in younger ages (<25 years old) whereas vasodepressor and cardioinhibitory type 2A and 2B type VVS were slightly higher in older ages (>50 years old) (Table I). While mostly observed asystole period was 3-6 sec in younger ages (<25 years old), it was 7-8 sec or more in adults (25-50 years old) (p=0.285) (Table I). The distribution of test results and diagnosis was not statistically significant between genders except for the finding that vasodepressor type VVS was slightly higher in females (Table II). Asystole period was more frequently observed among males and was cumulated around 3-5 sec with a few cases reaching at 10-25 sec (p=0.709) (Table II). No statistically significant relation was found between the HUTT results and clinical features (gender and age).

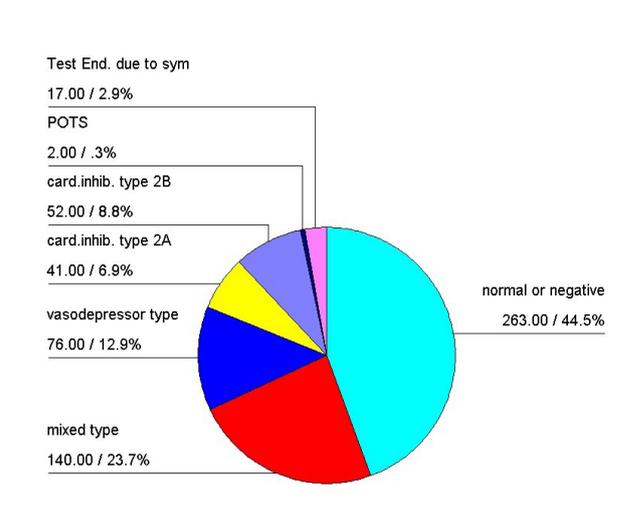


Figure 1: Description of positive and negative test results by a pie-chart graphic.

Discussion

In the differential diagnosis of syncope or related symptoms, evaluation of prodromal symptoms preceding the syncope is clinically essential in guidance for further tests. Medical history of subjects may also provide critical clues for the etiology of syncope such as ventricular arrhythmia in patients with left ventricular systolic dysfunction. Head-up tilt-table test can conveniently be performed to all age groups under proper laboratory circumstances including blood pressure and rhythm monitorization. Provocative administration of sublingually nitroglycerine was preferred due to moderate sensitivity and higher specificity with a less potential to complications. We also observed no complication related to the test and during the syncope period. The study population was composed of subjects from all age groups, excluding children. The percentages of negative and positive test results were similar at all age groups. However, there was a slight difference with regard to the type of response such that the number of positive results was higher in diagnosis among age groups (Table I). The HUTT is mostly preferred for young subjects in daily clinical practice in

Table 1: Distribution of diagnosis and asystole duration according to the age groups (<25, 25-50; >50 years old)

	Age groups			Total
	<25	25-50	>50	
Age (years old)	20.8±2.1	34.8±7.2	61.9±7.6	
Diagnosis				p=0.652*
Normal or negative (n,%)	178 (44.4)	64 (45.7)	21 (42.0)	263 (44.5)
Positive test results (n,%)	223 (55.6)	76 (54.3)	29 (58)	328 (55.5)
mixed type (n,%)	103 (25.7)	29 (20.7)	8 (16.0)	140 (23.7)
vasodepressor type (n,%)	50 (12.5)	19 (13.6)	7 (14.0)	76 (12.9)
type 2A (n,%)	26 (6.5)	10 (7.1)	5 (10.0)	41 (6.9)
type 2B (n,%)	33 (8.2)	13 (9.3)	6 (12.0)	52 (8.8)
POTS (n,%)	1 (0.2)	-	1 (2.0)	2 (0.3)
test ending to symptom (n,%)	10 (2.5)	5 (3.6)	2 (4.0)	17 (2.9)
Total	401 (100.0 %)	140(100.0%)	50(100.0%)	591 (100%)
Asystole Duration				p=0.285*
3-6 sec (n,%)	20 (%76.9)	4(%30.8)	4 (%100)	28 (%65.1)
7-8 sec (n,%)	2 (%7.6)	6 (%46.2)	-	8(%18.6)
9-10 sec (n,%)	3 (%11.5)	-	-	3(%7)
12-14 sec (n,%)	-	2 (%15.4)	-	2(%4.6)
20-25 sec (n,%)	1 (3.8%)	1(7.7%)	-	2(4.6)
Total	26 (100.0%)	13 (100.0%)	4 (100.0%)	43

*Chi-Square test

order to evaluate the etiology of syncope as it was the case in our study in which there were a predominance of the group of age <25 years. However, the number of adult and older subjects with syncope who were performed HUTT is also high enough to generalize the results. Thus we suggest that HUTT could be conveniently preferred and efficiently performed at all age groups unless the subject has co-existing diseases that could potentially be complicated by the test procedure. Additionally, HUTT was highly discriminative with both positive and negative results for the etiology of syncope within the whole study population except for only a small group without any objective finding and thus equivocal results (n=17, 2.9%). Moreover, HUTT was almost explanative for identification of POTS in a very small group by documenting the responses of blood pressure and heart rate during the test procedure (n=2, 0.3%). Postural orthostatic tachycardia syndrome is a common clinical condition which may not be easily differentiated from VVS and is generally overlooked (8). However, HUTT may allow documenting the physiological responses to the positional or physical changes and longstanding upright posture.

Recently, it was reported that HUTT is a cost-effective method of guiding pace-maker therapy in the management of patients with VVS (9). Cardioinhibitory response of subjects with VVS could exactly be revealed and identified during the test procedure. Also the test may overtly reproduce the clinical scene and the spontaneous recovery period which the subject could suffer. For example, we observed that asystole period during the cardioinhibitory response could reach 14 sec and extremely over up to 25 sec especially in adult subjects with age among 25-50. Guaraldi et al. recently reported that asystole period developed during the HUTT did not lead a poor prognosis in a study population other than frequent syncope

episodes in a limited number of subjects (10). Although those long asystole periods did not precede or degenerated to any undesired events in our study, we already recommended the implantation of a pacemaker with the feature of heart rate acceleration to our patients with asystole period longer than 5 sec.

Besides we observed that prolonged asystole periods reaching 10 sec were cumulatively higher in younger subjects whereas extremely prolonged durations were developed in adults, too. It may indicate an inability of sinus node to produce an electrical stimulus or to have a prolonged recovery time as an attributed mechanism underlying the syncope with cardio-inhibitory response. So it may probably indicate the development of sinus node dysfunction in further ages, e.g. sick sinus syndrome. Basal sinus node rate might have been tested and measured by parenterally administration of atropine and beta blocker agent in order to evaluate sinus node functions following the recovery from HUTT. This may be a limitation of our study.

Hypotensive and bradycardic component of hemodynamic responses within VVS are determined by withdrawal of sympathetic activity and over-activity of parasympathetic system, respectively. We observed that mixed typed VVS was higher in younger ages whereas vasodepressor and cardio-inhibitory typed VVS were higher in older ones in our study. Galetta et al. reported that vasodepressive response was the most frequently observed response in older subjects rather than mixed type (11). They also reported that mixed type response was similarly higher in young subjects as is the case in our study. Sympathetic autonomic system was documented to be predominated in adults and older ones (12, 13). Thus withdrawal of sympathetic activity in older ones could be

blunted and represented with less or absence of hypotensive response but a cardioinhibitory typed VVS with a prolonged bradycardia as in our study. We may hypothetically claim that the severity and level of bradycardic and vasodepressor responses could be changed or alternated according to aging in patients with VVS.

Sheldon et al reported that beta blocker therapy may suppress the development of VVS syncope in an age dependent fashion especially in middle aged patients over 40 years old (14). Since HUTT is a conveniently applicable and reproducible test, effectiveness of beta blocker therapy for the prevention of development of VVS may be tested in those adult subjects via HUTT. Additionally novel preventive measures such as moderate exercise including comprehensive tilt training program are being proposed in order to reduce the frequency of fainting (15). So influence of those preventive measures could objectively be qualified by means of HUTT.

When we evaluated the impact of gender on the distribution of diagnosis and also asystole duration periods, we could not find any statistically significant difference. However, we observed that vasodepressor type VVS was slightly higher among females and also moderately and extremely long period of asystole was cumulated among males. Our findings are consistent with the results reported by Zysko et al. They reported that loss of conscious due sinus arrest was significantly correlated with young age and male gender (16). Although the sinus arrest was mostly present among younger subjects, it was observed among middle aged subjects with a rate at least half of those young ones.

Conclusion

Head-up tilt-table test is a convenient method for evaluation of etiology of syncope among subjects from all age groups. Mi-

xed type VVS is the most frequently observed type of syncope among all age groups, but especially in young patients. Although the total number of vasodepressor and cardioinhibitory typed VVS was cumulatively higher among young subjects, probability of them tends to increase with aging. Probability of development of asystole period even with an extreme duration was high among young males.

In this study we aimed to evaluate the HUTT results of our laboratory according to the diagnosis, age, and any other clinical features.

References

1. Linzer M, Yang EH, Estes NA 3rd, Wang P, Vorperian VR, Kapoor WN. Diagnosing syncope. Part 1: Value of history, physical examination, and electrocardiography. Clinical Efficacy Assessment Project of the American College of Physicians. *Ann Intern Med.* 1997;126:989-96.
2. Arthur W, Kaye GC. The pathophysiology of common causes of syncope. *Postgrad Med J.* 2000;76:750-3.
3. Arthur W, Kaye GC. Important points in the clinical evaluation of patients with syncope. *Postgrad Med J.* 2001;77:99-102.
4. Boehm KE, Morris EJ, Kip KT, Karas B, Grubb BP. Diagnosis and management of neurally mediated syncope and related conditions in adolescents. *J Adolesc Health.* 2001;28:2-9.
5. Parry SW, Kenny RA. The role of tilt table testing in neurocardiac instability in older adults. *Eur Heart J.* 2001;22:370-2.
6. Getchell WS, Larsen GC, Morris CD, McAnulty JH. A comparison of Medicare fee-for-service and a group-model HMO in the inpatient management and long-term survi-

Table 2: Distribution of diagnosis and asystole duration according to gender; male and female

Diagnosis	Gender		Total
	Male	Female	
			P=0.153*
normal or negative (n,%)	219 (46.0)	44 (38.3)	263 (44.5)
Positive results (n,%)	257 (54.0)	71 (61.7)	328 (55.5)
mixed type (n,%)	113 (23.7)	27 (23.5)	140 (23.7)
vasodepressor type (n,%)	53 (11.1)	23 (20.0)	76 (12.9)
Cardioinhibitory type 2A (n,%)	36 (7.6)	5 (4.3)	41 (6.9)
Cardioinhibitory type 2B (n,%)	40 (8.4)	12 (10.4)	52 (8.8)
POTS (n,%)	2 (0.4)	-	2 (0.3)
Test ending to symptom (n,%)	13 (2.7)	4 (3.5)	17 (2.9)
Total	476 (100)	115 (100)	591 (100)
Asystole Duration			P=0.709*
3-5 sec (n,%)	18 (52.9)	3(33.3)	21
6-10 sec (n,%)	11(32.3))	6(66.6)	17
10-25 sec (n,%)	5 (14.5)	-	5
Total	34 (100.0)	9 (100.0)	43

*Chi-Square test

- val of elderly individuals with syncope. *Am J Manag Care*. 2000;6:1089-98.
7. Brignole M1, Menozzi C, Del Rosso A, et al. New classification of haemodynamics of vasovagal syncope: beyond the VASIS classification. Analysis of the pre-syncopal phase of the tilt test without and with nitroglycerin challenge. *Vasovagal Syncope International Study*. *Europace*. 2000 Jan;2(1):66-76.
 8. Stewart JM. Postural Tachycardia Syndrome and Reflex Syncope: Similarities and Differences. *The Journal of Pediatrics*. 2009;154:481-5.
 9. Davis S, Westby M, Petkar S, Pitcher D. Tilt testing is more cost-effective than implantable loop recorder monitoring as a means of directing pacing therapy in people with recurrent episodes of suspected vasovagal syncope that affect their quality of life or present a high risk of injury. *Heart*. 2013;99:805-10.
 10. Guaraldi P, Calandra-Buonaura G, Terlizzi R, et al. Tilt-induced cardioinhibitory syncope: a follow-up study in 16 patients. *Clin Auton Res*. 2012;22:155-60.
 11. Galeta F, Franzoni F, Femia FR, et al. Responses to Tilt test in young and elderly patients with syncope of unknown origin *Biomed Pharmacother* 2004;58:443-6.
 12. Seals DR, Monahan KD, Bell C, Tanaka H, Jones PP. The aging cardiovascular system: changes in autonomic function at rest and in response to exercise. *Int J Sport Nutr Exerc Metab*. 2001;11:189-95.
 13. Abhishekh HA, Nisarga P, Kisan R, et al. Influence of age and gender on autonomic regulation of heart. *J Clin Monit Comput*. 2013;27:259-64.
 14. Sheldon RS, Morillo CA, Klingenheben T, Krahn AD, Sheldon A, Rose MS. Age-dependent effect of blockers in preventing vasovagal syncope. *Circ Arrhythm Electrophysiol*. 2012 Oct;5(5):920-6.
 15. Gardenghi G, Rondon MU, Braga AM, et al. The effects of exercise training on arterial baroreflex sensitivity in neurally mediated syncope patients. *Eur Heart J*. 2007; 28: 2749-55.
 16. Zysko D, Gajek J, Aqrawal AK, Rudnicki J. The relevance of junctional rhythm during neurocardiogenic reaction provoked by tilt testing. *Kardio Pol*. 2012;70:148-55.