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Original Article

Evaluation of syncope in patients referred to afshar heart clinic, yazd, iran from september 2016 to march 2017

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Abstract

Objectives: Syncope is defined as a sudden and transient loss of consciousness followed by complete spontaneous recovery. This study describes the syncope evaluation in patients referred to the Heart Clinic.

Methods: This descriptive cross-sectional study was conducted on 60 syncope patients referred to Afshar Heart Clinic of Yazd, Iran, from September 2016 to March 2017. After performing clinical workups, the etiology of syncope was diagnosed in each patient. Electrocardiography and blood pressure measurements were done for all patients. Additional clinical tests, including echocardiography, Holter Monitoring, Head-Up tilt table test (HUTT), electroencephalography, and Magnetic Resonance Imaging, were performed for some patients based on the cardiologist's opinion. The distribution of patient's clinical records, such as age, sex, diabetes, hypertension, history of ischemic heart disease (IHD), duration of syncope, postdrome, prodromal symptoms, and clinical test results according to causes of syncope in patients, were reported.

Results: Sixty patients with a mean age of 50.7 ± 20.4 years were evaluated (55% male). Thirty-five patients (58.3%) had Neurally Mediated Syncope, 18 patients (30%) had arterioventricular (AV) Block induced syncope, and 7 (11.7%) patients had Sick Sinus Syndrome (SSS) induced syncope. Age, hypertension, prodromal symptoms, history of IHD, ECG, Holter monitoring, and HUTT results were associated with the cause of the syncope.

Conclusions: Cardiac syncopes (AV-Block induced and SSS induced) were related to older age, hypertension, abnormal electrocardiogram, and abnormal Holter monitoring results. Neurally mediated syncope was associated with younger age, prodromal symptoms, and abnormal HUTT results.

Keywords: Syncope, Neurally mediated, Arterioventricular block, Sick Sinus Syndrome

Introduction

Syncope is defined as a sudden, transient loss of consciousness due to temporary reduced cerebral perfusion followed by complete spontaneous recovery. Syncope may occur with or without pre-syncopal prodromes, including nausea, sweating, pallor, and light-headedness {Brignole, 2018 #1; Brignole, 2018 #1}. As a public health problem, the prevalence of syncope in the general population is 3% in men and 3.5% in women {Savage, 1985 #2}. It

comprises 0.6% to 1.7% of emergency department visits {Sandhu, 2019 #3}, and 0.6% to 1.5% of all hospitalizations {Alshekhlee, 2009 #4; Joy, 2017 #5}. Syncope imposes annually about 2.4 billion dollars burden on the federal government in the United States {Sun, 2005 #6}.

According to the underlying cause, syncope is classified into three main groups: syncope due to orthostatic hypotension (OH), cardiac, and reflex (neurally mediated) syncope Figure 1.{Brignole, 2018 #1}.

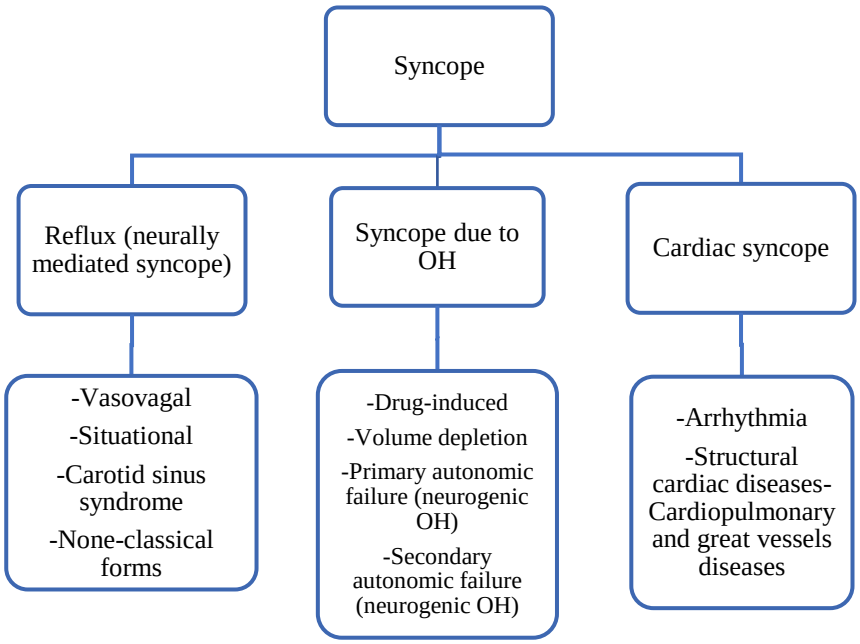

Figure 1.Classification of syncope according to underlying causes

While vasovagal syncope is regarded as a benign condition, cardiac syncope increases the risk of premature mortality due to cardiovascular events {Soteriades, 2002 #12}. Moreover, syncope increases the risk of sudden cardiac arrest in patients with hypertrophic cardiomyopathy, coronary artery disease, prolonged QT interval, and Brugada syndrome {Adler, 2016 #13; Spirito, 2009 #14; Aro, 2017 #15; Wehrens, 2002 #16}.

Diagnostic assessment of syncopal patients is complex due to its variety of causes and transient nature {Manolis, 1990 #17}. Although the utilization of appropriate diagnostic and therapeutic approaches improves the quality of life, conventional methods are characterized by high diversity, low diagnostic efficiency, and high cost {Sun, 2013 #9}, and syncope management challenges lead to the overuse of clinical diagnostic tests{Kachalia, 2015 #18}.

Recognizing these complications and the risks, causes, and results of clinical practices in syncopal patients helps us improve our insight into upcoming confrontations. Thus, we investigated the prevalence of causes and possible risk factors of syncope in syncopal patients referred to our heart center.

Materials and Methods

Study design and participants

In this descriptive cross-sectional study, medical records of patients with a primary diagnosis of syncope who, from September 2016 to March 2017, referred to Afshar Heart Clinic of Yazd, were reviewed and validated for the occurrence of definite syncope based on a diagnosis of cardiology specialist. Exclusion criteria included near-syncope, seizure, a previously known cause for syncope, and severe cognitive impairments. Consequently, decisive syncopal patients fulfilled the entrance criteria and entered the study.

Instruments, Assessments and data gathering

After performing initial clinical workups, consisting of a complete history and physical examination and completion of the pre-prepared questionnaire, the etiology of syncope was diagnosed in each patient. We classified patients according to the specific cause of syncope in groups. 12-lead electrocardiogram (ECG) and Blood pressure measurements were assessed for all the patients. Other non-invasive diagnostic assessments such as echocardiography (51 patients), twenty-four-hour Holter monitoring (38 patients), Head-Up tilt table test(HUTT) (27 patients), electroencephalography(EEG) (19 patients), Magnetic resonance imaging (MRI) (11 patients), and brain computed tomography (brain CT) scan (4 patients) were performed on a case by case basis according to the cardiologist's opinion. We investigated the prevalence of clinical test results and various possible risk factors such as sex, age, diabetes, hypertension, history of ischemic heart disease (IHD), duration of syncope, number of syncope attacks in the past year, prodromal symptoms, as well as postdrome symptoms in each group.

Statistical Analysis

We did data analysis using SPSS version 17.0.0 for Windows software (SPSS Inc., Chicago, IL, USA). Descriptive statistics including mean and standard deviation were provided. Variables were compared using the chi-square or Fisher exact test. The p-value of ≤ 0.05 was considered significant.

Ethical considerations

This study was approved by the local ethics committee and performed according to the Declaration of Helsinki. Before starting the study, written informed consent was obtained from all the patients and all ethical considerations have been followed.

Results

This study was conducted on 60 patients diagnosed with definite syncope who met inclusion and exclusion criteria. The study population consisted of 33(55%) men and 27(45%) women, and the mean age of participants was 50.7 ± 20.4 (range 11-85). Patients aged 50 years or older were defined as the elderly group, and patients under 50 were defined as the young group.

After assessing clinical workups, etiologies of syncope were as follows:

- 35 cases (58.3٪) of neurally mediated syncope
- 18 cases (30%) of arterioventricular (AV) Block induced syncope
- 7 cases (11.7%) due to Sick Sinus Syndrome (SSS) induced syncope

According to the patient's medical records, nine people (15%) had diabetes, 18 (30%) had hypertension, and 9 (15٪) had a history of IHD. Syncopes, in terms of duration, were divided into two groups: short syncope (≤ 6 seconds) and long syncope (> 6 seconds).

Twenty-two patients (36.7%) experienced long syncope, and 38 (63.3%) experienced short syncope. The prodromal symptoms included: 36 cases (60%) of dizziness, 5 cases (8.3%) of nausea, 7 cases (11.7%) of sweating, and one case (1.7%) of vomiting. Nineteen cases (31.7%) did not have any prodromal symptoms. Postdrome symptoms included: 7 cases (11.7%) of fatigue, 10 cases (16.7%) of light-headedness, and 1 case (1.7%) of vomiting. Forty-five patients (75%) did not report any postdrome symptoms. The distribution of syncope causes according to the clinical characteristics of patients has shown in Table 1.

Table 1. Distribution of syncope etiologies according to medical records of patients

Variables	Cases (%) Neutrally Mediated Syncope	AV-block induced syncope	SSS induced syncope	p-value
sex				
male	22 (66.6)	10 (30.03)	1 (3.03)	0.68
female	13 (48.1)	8 (29.6)	6 (22.2)	
age				
11-49 years	25 (86.4)	2 (6.8)	2 (6.8)	0.00
50-85 years	10 (32.2)	16 (51.6)	5 (16.1)	
diabetes				
yes	3 (33.3)	5 (55.5)	1 (11.1)	0.19
no	32 (62.7)	13 (25.4)	6 (11.7)	
hypertension				
yes	5 (27.7)	10 (55.5)	3 (16.6)	0.05
no	30 (71.4)	8 (19.04)	4 (9.5)	
Syncope duration				
short syncope	20 (52.6)	13 (34.2)	5 (13.1)	0.58
long syncope	15 (68.1)	5 (22.7)	2 (9.09)	
History of cardiac ischemia				
yes	1 (11.1)	5 (55.5)	3 (33.3)	0.01
no	34 (66.6)	13 (25.4)	4 (7.8)	
Prodrome				
no	6 (31.5)	7 (36.8)	6 (31.5)	0.01
yes	29 (70.7)	11 (26.6)	1 (2.4)	
Postdrome				
no	26 (57.7)	13 (28.8)	6 (13.3)	0.83
yes	9 (60.0)	5 (33.3)	1 (6.6)	

The distribution of syncope causes according to the number of syncope episodes in the past year has shown in Table 2. (p value=0.01).

Table2. Distribution of number of syncope episodes within the past year according to the syncope etiologies

Cause of Syncope / Syncope number episodes within the past year	Neutrally Mediated Syncope	AV-Block induced syncope	SSS induced syncope
1	19	5	0
2	9	5	2
3	2	2	4
4	1	1	0
5	0	3	1
≥6	4	2	0

Age, hypertension, number of recurrent syncope attacks over the past year, prodromal symptoms, and history of IHD were significantly (i.e., p value<0.05) associated with the cause of syncope. ECG was taken from all patients, and 33 patients (55%) had abnormal ECGs. Among 51 people who underwent echocardiography, 7 cases (13.7%) reported abnormal results. We performed 24-hour Holter Monitoring for 38 patients, and the results of 16 patients (42.1%) were reported abnormal. The HUTT test was performed for 27 cases, and 24 (88.8%) were reported as abnormal. The distribution of syncope causes according to the clinical test results has shown in Table 3.

Table3. Distribution of syncope etiologies according to clinical tests result

Variables	Cases (%) Neutrally Mediated Syncope	AV-Block induced syncope	SSS induced syncope	p-value
ECG				
Normal	29 (87.8)	3 (9.09)	1 (3.03)	0.00
abnormal	6 (22.2)	15 (55.5)	6 (22.2)	
Echocardiography				
normal	30 (68.1)	11 (25.0)	3 (6.8)	0.15
abnormal	2 (26.5)	4 (57.1)	1 (14.2)	
Holter Monitoring				
normal	19 (86.4)	3 (13.6)	0 (0)	0.00
abnormal	2 (12.5)	10 (62.5)	4 (25)	
HUTT				
normal	2 (66.7)	0 (0)	1 (33.3)	0.01
abnormal	21 (87.5)	2 (8.3)	1 (4.1)	

Among 19 cases who had done EEG, only 1 (5.2%) had an abnormal EEG. The results of all 11 (100%) patients who had done MRI and four (100%) patients who had done CT scans were normal. Among clinical tests, ECG, Holter Monitoring, and HUTT were significantly (i.e., p value<0.05) associated with the syncope etiology.

Discussion

The current study was carried out to determine the risk factors of syncope according to its etiology in patients referred to Afshar heart clinic in Yazd, Iran. We found that age, hypertension, number of recurrent syncope attacks over the past year, prodromal symptoms, and history of IHD, as well as results of ECG, Holter Monitoring, and HUTT, were significantly associated with the etiology of syncope.

While neurally mediated syncope was significantly more common in the young group (11-49 years), syncope of cardiac origin (AV block-induced and SSS-induced) was more common in the older group (50-85 years), consistent with previous studies showing that cardiac syncope was more common in older people and neurally mediated syncope was more common in young people. This may be due to the higher prevalence of cardiovascular disease in the elderly In our study, hypertension was more common in patients with cardiogenic syncope. In contrast, 71% of patients with neurally mediated syncope did not have hypertension. Jorge JG et al. found that injury risk from vasovagal syncope was associated with age but not with gender or hypertension, consistent with our results {Jorge, 2021 #26}.The highest number of recurrences of neurally mediated syncope, AV block-induced syncope, and SSS-induced syncope in the past year were reported once, once, and/or twice, and three times, respectively. In our results, syncope episodes with only one episode in the past year were mostly neurally mediated. However, Kapoor et al. reported that recurrent syncope with more than four episodes per year could predict mental disorders {Kapoor, 1995 #27}. In addition, Karol's study showed that the increase in syncope episodes was significantly related to negative electrophysiology test results, since all individuals who had more than six episodes of syncope had negative cardiac electrophysiology results {Krol, 1987 #28}. Our results challenge these findings.

Prodromal symptoms were more common in neurally mediated syncope than cardiac syncope. Hurst et al. reported that pre-exercise syncope, palpitations, and non-prodrome chest pain were 100% sensitive to cardiac causes {Hurst, 2015 #29}. Delrosso et al. asserted that the absence of a prodrome, abnormal ECG, palpitations prior to syncope are predictors of cardiac syncope {Del Rosso, 2008 #30}.Prodromal symptoms (e.g., nausea, vomiting, warmth) are also associated with non-cardiac syncope {Shen, 2017 #31}, which is in agreement with our findings.

IHD was more frequent in patients with cardiac syncope than patients with neurally mediated syncope. Other studies have shown that among syncope patients, those with a history of ischemic abnormalities of ECG, even in the absence of chest pain, were more likely to experience acute cardiac ischemia than those who had normal ECGs {Georgeson, 1992 #32}. Furthermore, syncope in patients with a history of coronary artery disease can define as a risk factor for sudden cardiac arrest {Aro, 2017 #15}. These findings are consistent with our results and indicate the necessity of

follow-up in syncopal patients with a history of ischemia.

Although cardiac syncopes were related to abnormal ECGs, neurally mediated syncope patients mostly had normal ECGs. Electrocardiography, history, and physical examination are the main components of the initial clinical examination of all syncopal patients {Runser, 2017 #33}. Abnormal ECG findings can be a predictor of cardiac syncope {Del Rosso, 2008 #30; Zhang, 2013 #34}, which is in agreement with our results.

Echocardiography findings were not significantly associated with the causes of syncope. Previous studies have shown that the diagnostic yield of echocardiography in patients with normal examination and ECG is limited {Ghani, 2019 #35; Madeira, 2017 #37}. Satish et al. showed that echocardiography increased the cost of hospitalization and did not have any desirable effect on the mortality of syncope {Satish, 2019 #38}

Abnormal Holter monitoring test results were associated with AV-block induced, and SSS induced syncope. The diagnostic value of the Holter monitoring in possible arrhythmogenic syncopes has been confirmed in other studies {Giada, 2013 #39; Hadjikoutis, 2004 #40}. Holter monitoring test has been reported as a proper initial diagnostic method in evaluating high-risk cardiac patients with unexplained syncope {Sarasin, 2005 #41}. Krahn et al. demonstrated that the primary monitoring approach is more cost-effective than the conventional assessment method of recurrent unexplained syncope {Krahn, 2003 #42}.

Abnormal result of the HUTT was significantly related to neurally mediated syncope. Previous studies have found that HUTT may propose an efficient, practical, and safe method to diagnose neurally mediated syncope and prevent unnecessary diagnostic test overuse. These findings are consistent with our study {Benditt, 1996 #43; Kohno, 2018 #44;Barón-Esquivias, 2020 #45}.

Results of neurological tests such as MRI, brain CT scan, and EEG were reported normal in most cases and indicated no significant changes. The result is incompatible with former studies that showed that neuroimaging technics including EEG, brain CT scan, and MRI, are inefficient and unnecessary in assessing non-neurogenic syncope {Day, 1982 #46; Davis, 1990 #47; İdil, 2019 #48; Dantas, 2012 #49}, which may indicate the low prevalence of cerebrovascular syncope.

Limitations of our study included the limited statistical population and the lack of long-term follow-up of the patients. Due to participants' recall bias, some valuable recordings may not be adequately reported. Syncope is a clinical manifestation of a variety of diseases, so the risk factors we have introduced indicate only a dependency relationship, not a cause-and-effect relationship. Nevertheless, more extensive epidemiological studies to determine the risk factors of syncope according to their etiology are urgently needed, which can help the diagnostic algorithms to apply efficient and cost-effective practices in syncope management.

Conclusion

In the current study, neurally mediated syncope was more common in the young group (11-49 years) and syncope of cardiac origin (AV block-induced and SSS-induced) was more common in the older group (50-85 years). IHD, hypertension, abnormal ECG, and abnormal Holter monitoring results were associated with cardiogenic syncope. Prodromal symptoms and abnormal HUTT had a significant association with neurally mediated syncope. EEG, MRI, and brain CT scan results have been reported as normal in both cardiac and neurally mediated syncope, and overuse of these tests could waste time and money in syncope patients.

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References

1.Brignole M, Moya A, de Lange FJ, et al. 2018 ESC Guidelines for the diagnosis and management of syncope. *Eur Heart J*. 2018;39(21):1883-1948.

2.Savage DD, Corwin L, McGee DL, et al. Epidemiologic features of isolated syncope: the Framingham Study. *Stroke*. 1985;16(4):626-9.

3.Sandhu RK, Sheldon RS. Syncope in the Emergency Department. *Front Cardiovasc Med*. 2019;6:180.

4.Alshekhlee A, Shen WK, Mackall J, et al. Incidence and mortality rates of syncope in the United States. *Am J Med*. 2009;122(2):181-8.

5.Joy PS, Kumar G, Olshansky B. Syncope: Outcomes

and Conditions Associated with Hospitalization. *Am J Med*. 2017;130(6):699-706 e6.
6.Sun BC, Emond JA, Camargo CA Jr. Direct medical costs of syncope-related hospitalizations in the United States. *Am J Cardiol*. 2005;95(5):668-71.
7.Soteriades ES, Evans JC, Larson MG, et al. Incidence and prognosis of syncope. *N Engl J Med*. 2002;347(12):878-85.
8.Adler A, Rosso R, Chorin E, et al. Risk stratification in Brugada syndrome: Clinical characteristics, electrocardiographic parameters, and auxiliary testing. *Heart Rhythm*. 2016;13(1):299-310.
9.Spirito P, Autore C, Rapezzi C, et al. Syncope and risk of sudden death in hypertrophic cardiomyopathy. *Circulation*. 2009;119(13):1703-10.
10.Aro AL, Rusinaru C, Uy-Evanado A, et al. Syncope and risk of sudden cardiac arrest in coronary artery disease. *Int J Cardiol.* 2017;231:26-30.
11.Wehrens XH, Vos MA, Doevendans PA, et al. Novel insights in the congenital long QT syndrome. *Ann Intern Med*. 2002;137(12):981-92.
12.Manolis AS, Linzer M, Salem D, et al. Syncope: current diagnostic evaluation and management. *Ann Intern Med*. 1990;112(11):850-63.
13.Sun BC. Quality-of-life, health service use, and costs associated with syncope. *Prog Cardiovasc Dis.* 2013;55(4):370-5.
14.Kachalia A, Berg A, Fagerlin A, et al. Overuse of testing in preoperative evaluation and syncope: a survey of hospitalists. *Ann Intern Med*. 2015;162(2):100-8.
15.Jorge JG, Raj SR, Teixeira PS, et al. Likelihood of injury due to vasovagal syncope: a systematic review and meta-analysis. *Europace*. 2021;23(7):1092-1099.
16.Kapoor WN, Fortunato M, Hanusa BH, et al. Psychiatric illnesses in patients with syncope. *Am J Med*. 1995;99(5):505-12.
17.Krol RB, Morady F, Flaker GC, et al. Electrophysiologic testing in patients with unexplained syncope: clinical and noninvasive predictors of outcome. *J Am Coll Cardiol*. 1987;10(2):358-63.
18.Hurst D, Hirsh DA, Oster ME, et al. Syncope in the pediatric emergency department–can we predict cardiac disease based on history alone? *J Emerg Med.* 2015;49(1):1-7.
19.Del Rosso A, Ungar A, Maggi R, et al. Clinical predictors of cardiac syncope at initial evaluation in patients referred urgently to a general hospital: the EGSYS score. *Heart.* 2008;94(12):1620-6.
20.Shen WK, Sheldon RS, Benditt DG, et al. 2017 ACC/AHA/HRS Guideline for the Evaluation and Management of Patients With Syncope: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol*. 2017;70(5):620-663.
21.Georgeson S, Linzer M, Griffith JL, et al. Acute cardiac ischemia in patients with syncope: importance of the initial electrocardiogram. *J Gen Intern Med*. 1992;7(4):379-86.
22.Runser LA, Gauer RL, Houser A. Syncope: Evaluation and Differential Diagnosis. *Am Fam Physician*. 2017;95(5):303-312.
23.Zhang Q, Zhu L, Wang C, et al. Value of history taking in children and adolescents with cardiac syncope. *Cardiol Young*. 2013;23(1):54-60.
24.Ghani AR, Ullah W, Abdullah HMA, et al. The role of echocardiography in diagnostic evaluation of patients with syncope-a retrospective analysis. *Am J Cardiovasc Dis*. 2019;9(5):78-83.
25.Madeira CL, Craig MJ, Donohoe A, et al. Things We Do For No Reason: Echocardiogram in Unselected Patients with Syncope. *J Hosp Med.* 2017;12(12):984-988.
26.Satish M, Walters RW, Alla VM. Trends in use of echocardiography in hospitalized patients with syncope. *Echocardiography*. 2019;36(1):7-14.
27.Giada F, Bartoletti A. Value of ambulatory electrocardiographic monitoring in syncope. *Cardiol Clin.* 2015;33(3):361-6.
28.Hadjikoutis S, O'Callaghan P, Smith PE. The investigation of syncope. *Seizure*. 2004;13(8):537-48.
29.Sarasin FP, Carballo D, Slama S, et al. Usefulness of 24-h Holter monitoring in patients with unexplained syncope and a high likelihood of arrhythmias. *Int J Cardiol*. 2005;101(2):203-7.
30.Krahn AD, Klein GJ, Yee R, et al. Cost implications of testing strategy in patients with syncope: randomized assessment of syncope trial. *J Am Coll Cardiol*. 2003;42(3):495-501.
31.Benditt DG, Ferguson DW, Grubb BP, et al. Tilt table testing for assessing syncope. American College of Cardiology. *J Am Coll Cardiol*. 1996;28(1):263-75.
32.Kohno R, Adkisson WO, Benditt DG. Tilt table testing for syncope and collapse. *Herzschrittmacherther Elektrophysiol*. 2018;29(2):187-192.
33.Barón-Esquivias G, Martín AJD, Del Castillo ÁM, et al. Head-up tilt test diagnostic yield in syncope diagnosis. *J Electrocardiol.* 2020;63:46-50.
34.Day SC, Cook EF, Funkenstein H, et al. Evaluation and outcome of emergency room patients with transient loss of consciousness. *Am J Med*. 1982;73(1):15-23.
35.Davis TL, Freemon FR. Electroencephalography should not be routine in the evaluation of syncope in adults. *Arch Intern Med.* 1990;150(10):2027-9.
36.İdil H, Kılıc TY. Diagnostic yield of neuroimaging in syncope patients without high-risk symptoms indicating neurological syncope. *Am J Emerg Med.* 2019;37(2):228-230.
37.Dantas FG, Cavalcanti AP, Rodrigues Maciel BD, et al. The role of EEG in patients with syncope. *J Clin Neurophysiol*. 2012;29(1):55-7.