Research Article

Evaluation of Diagnostic Workup in Patients of Syncope

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Abstract

Objective: *Evaluation of patients following a syncopal episode is challenging because there is a wide spectrum of possible cardiac and non-cardiac etiologies. Patients with syncope are usually evaluated based on multiple algorithms, yet most of these tests fail to have a favorable cost-benefit ratio. The objective of the present study is to evaluate the yield of various tests in patients with syncope.*

Methods: *A total of 255 patients aged 18 years and above admitted with a history of syncope from Mar 2015 to Mar 2016 were enrolled in a retrospective, non-randomized, observational study. Data were collected from hospital records, discharge summary, patient's old documents, and if needed on follow up by taking the history, physical examination, and obtaining results of various tests. At the end of the study, data were analyzed and the yield of the various diagnostic test was evaluated.*

Results: *Major finding of this study was the relatively low diagnostic yield of neurological tests and the high number of unexplained cases. Cardiac testing also had low yields overall. Conversely, postural BP recordings, tilt testing, and carotid sinus massage had very high yield but the fact remained that these tests were performed infrequently. Advanced second or third-degree AV block and sick sinus syndrome were the most frequently reported etiologies***.**

Conclusion: *Overall diagnostic yield of various tests was relatively low. A cost-effective approach to syncope requires a thorough history, physical examination, and prioritizing higher yield tests while avoiding low yield tests.*

1.Introduction

Syncope is an important clinical problem as it markedly reduces the quality of life, results in traumatic injury and a few cases can be the only warning sign before sudden cardiac death. **(**1-3**)** Patients with syncope account for 1% of hospital admissions and 3% of emergency department visits. The prevalence of the first episode of syncope in young adults is particularly high between the ages of 10 and 20 years. **(**4**)** and an additional peak occurs at approximately 60 and 80 years of age. **(**4,5**)**.

Evaluation of patients following a syncopal episode is challenging because there is a wide spectrum of possible etiologies, ranging from benign to life-threatening conditions. **(**6**)** Despite thorough evaluation the etiology of syncope frequently remains undetermined. **(**7,8**)** Studies **(**9-13**)** have attempted to reduce unnecessary testing by the use of algorithms to improve syncope evaluation methods. The algorithms increased the percentage of patients in whom an etiology was identified but did not decrease the use of low-yield testing or reduce the cost associated with diagnostic testing.

The few studies **(**14,15**)** examining the utility of individual tests found that cardiac enzymes test, electroencephalography (EEG) **(**16**)**, head computed tomographic (CT) scan **(**17**)** and carotid ultrasonography (US)**(**18**)** seldom identified the etiology. The contribution of magnetic resonance

imaging (MRI), echocardiogram, telemetry, and other tests remains unknown, as does the cost of tests relative to their effect on diagnosis or management. It is unclear whether the yield and cost-effectiveness of evaluation can be improved by identifying patients in whom test results are likely to affect diagnosis or management.

2.Methods

2.1 Study Population

255 consecutive patients aged 18 years or more who were admitted with syncope to the Max Super specialty hospital from march 2015 to march 2016 were enrolled in the study with prior informed consent. Patients less than 18 years of age, those presenting with near syncope, patients with head trauma before the onset of syncope, and patients not consenting were excluded from the study.

2.2 Study Protocol

A retrospective, non-randomized, observational study was conducted and the protocol was approved by the institutional scientific and ethical committee. Data was collected by taking the history, physical examination, and obtaining results of various tests. Hospital records, discharge summary, and patient's old documents were also evaluated to collect data. At the end of the study, data were analyzed and the yield of the various diagnostic test was evaluated.

2.3 Definition Of Terminologies

Syncope is a sudden and transient loss of consciousness (LOC) due to loss of postural tone leading to transient global cerebral hypoperfusion. It is characterized by rapid onset, short duration, and spontaneous recovery. **(**19**)** Abnormal cardiac enzyme results were defined as any troponin I level greater than 0.04 ng/mL (the hospital's reference value).

Postural hypotension was defined as a drop in systolic BP of at least 20 mm Hg, or a drop in diastolic BP of at least 10 mm Hg within 3 minutes of changing from a lying position to a standing position. A test was considered *abnormal* if any abnormality, no matter how minor, not seen on prior testing as written in the test reports (for example, mild mitral valve regurgitation on echocardiogram and mild slowing on EEG). If no mention was made of prior testing, the result was assumed to be new. A test result was considered to have *affected diagnosis* if it was noted in

any test reports, progress notes, or discharge summaries that the test has contributed to, confirmed or established any diagnosis. This definition included all diagnoses, including those not related to syncope. We also recorded whether a test result has *identified the etiology* of the syncopal episode.

2.4 Diagnostic criteria with initial evaluation were as follows:19

Vasovagal syncope (VVS) was diagnosed if syncope was precipitated by emotional distress or orthostatic stress and is associated with a typical prodrome. *Situational syncope* was diagnosed if syncope occurred during or immediately after specific triggers. *Orthostatic syncope* was diagnosed when it occurred after standing up and there is documentation of OH. *Arrhythmia-related syncope* was diagnosed by ECG in the presence of the following: Persistent sinus bradycardia <40 bpm in the wake or repetitive sinoatrial block or sinus pauses ≥ 3s, Mobitz II second or third-degree AV block, Alternating left and right BBB, VT or rapid paroxysmal SVT, Non-sustained episodes of polymorphic VT and long or short QT interval, Pacemaker or ICD malfunction with cardiac pauses. *Cardiac ischemia-related syncope* was diagnosed when syncope presented with ECG evidence of acute ischemia with or without myocardial infarction. *Cardiovascular syncope* was diagnosed when syncope presented in patients with prolapsing atrial myxoma, severe aortic stenosis, pulmonary hypertension, pulmonary embolism, or acute aortic dissection.

2.5 Static Analysis

Statistical analysis was in terms of descriptive statistics whereby the percentage positivity of various tests in syncope patients was reported. Significance levels ($p<0.05$) were used when appropriate. We also found out the 95% confidence interval for each one of these percentages.

3.Results

The characteristics of the patients are presented in **Table 1**. The mean age was 68.3 years; 74% were male. A history of hypertension was present in 55%, coronary artery disease in 27%, diabetes in 30%, and atrial fibrillation in 7%. 8% of the patients suffered serious injuries including head injury.

Table 1. Baseline Characteristics

Characteristics	**Total (%)**
Number of patients	255(100)
Male	189(74)
Age years (average)	68.3
Previous h/o syncope	45(18)
Serious injuries	20(8%)
Comorbidities	
Ischemic heart disease	68 (27)
Previous myocardial infarction	10 (3.9)
Systemic hypertension	140 (55)
Previous or current atrial fibrillation	18 (7)
Previous stroke	25 (10)
Valvular heart disease	06 (2)
Diabetes	**76 (30)**
Previous PCI or CABG	35 (14)
Cardiac pacemaker or ICD	9 (3.5)
Pharmacotherapy	
Beta blockers	95 (37)
ACEi/ARB	113 (44)
Alpha blockers	19 (7)
Digoxin	09 (3)
Nitrates	80(31.3)
Calcium channel blockers	103 (40.3)
Diuretics	46 (18)
Class Ic/III Antiarrhythmic drugs	16 (6)

The frequencies of tests obtained, abnormal findings, and yields are shown in **Table 2**. The most commonly used test was Electrocardiogram (100%), Echocardiogram (88%), Coronary angiography (49%), Holter monitoring (43%), and Cardiac enzymes (41%).

Table 2. Diagnostic tests obtained in evaluation of syncopal episodes in older patients (n = 255)

Tests	Obtained	Abnormal Findings n (%)	Affected diagnosis/ Management n (%)	Helped determine etiology. n(%)
Postural BP recording	15(6)	05(33)	00	05(33)
Electrocardiogram	255(100)	209 (82)	131 (51)	55 (22)
Cardiac enzymes	104(41)	25 (24)	21 (20)	04 (4)
Echocardiogram	225(88)	92 (41)	62 (27)	18 (8)
Tilt test	13(5)	5 (38)	00	5 (38)
Coronary angiography	126(49)	88 (70)	37 (29)	8 (6)
Holter	109(43)	67 (61)	20 (18)	47 (43)
Carotid Doppler	18(7)	12 (66.6)	02 (11)	00
Stress test	23(9)	07 (30)	01 (4.3)	06 (26)
EP Study	45(18)	32 (71)	03 (6.6)	30 (67)
Carotid sinus massage	07(2.7)	04 (57)	00	04 (57)
CT Head	25(9.8)	04 (16)	02 (08)	00
MRI Head	46(18)	18 (39)	08 (17)	00
EEG	23(9)	04 (17.4)	01 (4.3)	00

ECG was abnormal in 82% of patients. As shown in **Table 2a** the most common abnormalities on the ECG were RBBB (17%) and Complete heart block (13%). LBBB was present in 10% of cases. Other common abnormalities were ST-T changes (10%) and bifascicular block (8.2%). Isolated first degree and second-degree heart blocks were present in 4.3% and 5% cases respectively. In 51% of patient, ECG revealed significant abnormalities which affected the further management. ECG helped in determining the etiology of syncope in 22% of patients.

225 patients underwent echocardiography and of these 41% of patients showed abnormal findings. The most common abnormalities on echo were regional wall motion abnormality (43%) and global hypokinesia (30%). In 8% of patients, echocardiography helped in identifying the etiology of syncope.

Table 2a. ECG findings in patients with syncope, (n=255)

ECG findings	No of patients (%)
1st degree HB	11 (4.3)
RBBB	16 (6.2)
RBBB + 1st degree HB	11 (4.3)
RBBB + LAHB	08 (3)
RBBB + LPHB	02 (0.7)
RBBB + 1st degree HB + LAHB	07 (2.7)
LAHB	03 (1)
LBBB	21 (8.2)
LBBB + 1st degree HB	05 (2)
2nd degree HB	13 (5)
CHB	31 (12)
IVCD	03 (1)
Pathologic Q waves	19 (7.4)
ST-T changes	26 (10)
S. Bradycardia	15 (5.8)
S. Tachycardia	05 (2)
Ventricular Tachycardia	02 (0.7)
Atrial Fibrillation	05 (2)
Sinus pauses	04 (1.5)
QT prolongation	03 (1)
Others	22 (8.6)
Normal	46 (18)

Out of 126 coronary angiographies (CAG), 70% revealed abnormal findings. The most common abnormalities were noncritical coronary artery disease (31%) and single-vessel disease (20%) as shown in **Table 2b**. Only in 29% of cases, CAGs showed significant findings and thereby affected the final management or clinical decision making. CAG helped in identifying the etiology of syncope in 6% of cases. These cases included patients with acute coronary syndrome and those with an abnormal stress test. Only 24% of patients had abnormal values for cardiac enzymes, defined as an elevation in troponin I level.

Table 2b. CAG findings in patients with syncope, (n=126)

CAG findings, n=126	**No of patients (%)**
Non obstructive CAD	39(31)
Single vessel disease	25(20)
Double vessel disease	09(07)
Triple vessel disease (including P/CABG patients)	15(12)
Normal	38(30)

Of note, Holter monitoring and EP study showed abnormal findings in 61% and 71% respectively and had a high diagnostic yield for etiology of syncope (43% and 67% respectively). As shown in **Table 4** overall most common findings on holter were sick sinus syndrome (25%), S. Bradycardia (8%), paroxysmal AF (7%), and second/third-degree AV block (7%). Holter monitoring was normal or revealed no new abnormality in 38% cases. 26% of patients who underwent Holter monitoring, had normal baseline ECG. Sick sinus syndrome (21%) was the most common abnormality among these patients. Importantly 3.5% of patients with normal baseline ECG showed significant ventricular arrhythmias (NSVT/VT) on holter monitoring. However, holter was normal or revealed no new abnormality in 57% of patients with normal baseline ECG. The most common finding on the EP study was AV nodal disease (51%). Postural BP recording (6%), Tilt test (5%), and carotid sinus massage (2.7%) were performed very infrequently. However, they were abnormal in the majority of patients and had high diagnostic yield (33%, 38% & 57% respectively) as far as the etiology of syncope is concerned.

CT Brain, MRI Brain & EEG were obtained frequently but very few of them helped in diagnosis or management and did not help in determining the etiology of syncope. Carotid ultrasound was abnormal in 66% of patients, however, only 11% were significant enough to affect the management. The tests with the lowest likelihood of determining etiology were cardiac enzymes, CAG, Carotid Doppler & echocardiogram.

Table 2c. Holter findings in patient with syncope (n=109)

Holter findings	With normal baseline ECG (n=28)	With abnormal baseline ECG (n=81)	Total (n=109)
Significant Ventricular arrhythmias(NSVT/VT)	01(3.5)	03(3.7)	04(3.6)
Paroxysmal AF	01(3.5)	07(8.6)	08(7)
Sick sinus syndrome	06(21.4)	19(23.4)	25(23)
Advanced second- or third-degree AV block	01(3.5)	07(8.6)	08(7)
VPCs	00	07(8.6)	07(6)
Atrial tachycardia	00	01(1.2)	01(0.9)
S. Bradycardia	01(3.5)	07(8.6)	08(7)
S. Tachycardia	02(7.1)	04(5)	06(5.5)
Normal/No new abnormality	16(57)	26(32)	42(38.5)

Table 3. Number of Tests Performed in the 143 (56%) Patients Where the Etiological Diagnosis was Made During Admission

Tests	Obtained	Abnormal Findings n (%)	Helped determine etiology, n (%)
Postural BP recording	15(10.4)	05(33)	05(33)
Electrocardiogram	143(100)	119(84)	55(39)
Cardiac enzymes	53(37.5)	18(34)	04(7.5)
Echocardiogram	125(87.4)	51(40)	18(14.4)
Tilt test	06(4.1)	05(83)	05(83)
Coronary angiography	80(56)	54(67.5)	08(10)
Holter	57(40)	49(86)	47(82)
Carotid Doppler	09(6.2)	05(55.5)	00

Stress test	12(8.3)	06(50)	06(50)
EP Study	36(25)	31(86)	30(83)
Carotid sinus massage	06(4.1)	04(66.6)	04(66.6)
CT Head	14(9.7)	03(21)	00
MRI Head	15(10.4)	06(40)	00
EEG	11(7.6)	04(36)	00

Table 3 shows the diagnostic yield of various tests in 143 patients in whom the etiology of syncope was determined. Holter monitoring, EP study & tilt testing had the highest diagnostic yield. (82%, 83% & 83% respectively.) Carotid sinus massage & baseline ECG identified etiology in 66% & 39% patients respectively.

Table 4. Etiology of Syncope (n=255)

Etiology	Number (%), n=255	Age < 65 yrs, n=104	Age ≥ 65 yrs, n=151	p value
Neurocardiogenic syncope	06(2.3)	04(4)	02(1.3)	0.229
Orthostatic hypotension	05(2)	01(0.9)	04(2.6)	0.651
Cardiac				
Significant Ventricular arrhythmias(NSVT/VT)	08(3.1)	04(3.8)	04(2.6)	0.719
supraventricular arrhythmias	04(01.5)	01(0.9)	03(2)	0.647
Sick sinus syndrome	29(11.3)	10(9.6)	19(12.5)	0.549
Advanced second- or third-degree AV block	68(27)	27(26)	41(27)	0.833
Structural cardiac disease	04(1.5)	02(1.9)	02(1.3)	1.00
Coronary artery disease	08(3.1)	05(5)	03(2)	0.277
Pulmonary embolism	04(1.5)	04(3.8)	00	0.027
Mixed	07(3)	02(1.9)	05(3.3)	0.704
Undiagnosed	112(44)	44(42)	68(45)	0.667

As shown in **Table 4**, advanced second & third-degree AV Block (27%) and sick sinus syndrome(11%) were the most common etiology of syncope. Approximately 3% of patients had more than one etiology and in 3% of cases, significant ventricular arrhythmias (NSVT/VT) were responsible for syncope. An excess of 112 (44%) patients remained undiagnosed. Coronary artery disease (5%) and Neurocardiogenic syncope (4%) were more common in the younger age group (age < 65 yrs) whereas sick sinus syndrome was more common in the older age group(age > 65 yrs), however the difference was not statistically significant. Pulmonary embolism was significantly more common in the younger age group(p-value-0.027).

Table 5. Etiology of Syncope in patient with normal ECG on presentation (n=46)

Etiology	Number (%)
Neurocardiogenic syncope	03(6.5)
Orthostatic hypotension	00
Cardiac	
Significant Ventricular arrhythmias(NSVT/VT)	02(4.3)
supraventricular arrhythmias	00
Sick sinus syndrome	05(11)
Advanced second- or third-degree AV block	02(4.3)
Structural cardiac disease	00
Coronary artery disease	01(2.1)
Pulmonary embolism	00
Mixed	02(4.3)
Undiagnosed	31(67.4)

Baseline ECG was normal in 46(18%) patients. In these patients, sick sinus syndrome (11%) was the most common etiology as shown in **Table 5**. However, an excess of 67% of patients with normal baseline ECG remained undiagnosed. Neurocardiogenic syncope (6.5%) was relatively more common in these patients.

Table 6. Correlation between EP study and baseline ECG (n=45)

Findings on EP study(n=45)	Total no n, (%)	**Baseline ECG findings. n (%)**				
		Normal (n=09)	**First degree HB (n=02)**	**Bundle branch block (n=20)**	**Pathologic Q waves (n=02)**	**Other (n=12)**
AV nodal disease SA nodal disease	23(51) 01(2.2)	02(22.2) 01(11.1)	02(100) -	14(70) -	- -	05(41.6) -
AV + SA nodal disease	02(4.4)	-	-	02(10)	-	-
VT	02(4.4)	01(11.1)	-	-	01(50)	-
Accessory pathway	03(6.6)	01(11.1)	-	-	-	02(16.6)
Ectopic AT	01(2.2)	-	-	-	-	01(8.3)
Dual AV nodal physiology	01(2.2)	-	-	01(05)	-	-
Normal	12(27)	04(44.4)	-	03(15)	01(50)	04(33.3)

As shown in **Table 6**, a total of 20 patients had bundle branch block in baseline ECG and of these 14(70%) patients demonstrated AV nodal disease on EP study. Approximately 22% of patients with normal baseline ECG showed AV nodal disease. However, the EP study was normal in 44% of patients with normal baseline ECG. Two patients showed ventricular tachycardia on EP study, one had normal baseline ECG and the other had pathological Q waves.

4.Discussion

The major findings of this study were the relatively low diagnostic yield of neurological tests and the high number of unexplained cases. Only in the few cases, the neurological tests were helpful and they did not help in the etiological diagnosis of syncope. Cardiac testing also had low yields overall. Conversely, postural BP recordings, tilt testing, and carotid sinus massage had very high yield but were performed in only 6%, 5%, and 2.7% of admissions respectively. A study done by Prakash et al **(**20**)** found that tilt testing is very helpful in the evaluation of patients with syncope. The results of our study are consistent with this.

Overall reflex (neurocardiogenic) syncope is the most common etiology however, in our study advanced second or third-degree AV block and sick sinus syndrome were the most frequently reported etiologies. This may be due to the inclusion of only in-patients (hospitalized) in the study. The lack of an etiology in almost half of the patients despite extensive testing was also similar to prior reports of older adults. **(**6,21-23**)** EEG, head CT or MRI scans, carotid ultrasound, and cardiac enzymes tests were found to be least useful. Many of our findings are consistent with prior studies. Grossman et al1 **(**4**)** and Link et al1 **(**5**)** found that serial cardiac enzymes tests had little impact on diagnosis in syncope. Head CT scans, carotid US, and EEG are all known to rarely identify lesions contributing to syncope. **(**16-18**)** Our findings confirm these earlier reports that neurological imaging is not warranted in the evaluation of syncope unless a neurological disease or event is suspected.

The high yield of postural BP recordings in our study supports guideline recommendations that the initial evaluation of syncope should entail medical history, physical examination, electrocardiogram, and postural BP measurements. **(**23-26**)** The evaluation of syncope entails identifying the presence of underlying diseases in addition to determining the etiology of the syncopal episode. Therefore, we complemented existing research by determining the effect the tests had on establishing any diagnosis or on any management decision.

In our study, the holter monitoring, EP study, and tilt table test proved useful in the workup. Short-term holter monitoring appears to establish a diagnosis in only less than 4 percent of patients with syncope, **(**27,28**)** however in our study the diagnostic yield of holter monitoring was much higher (43%) possibly related to the overall advanced age and selection of a sicker group of patients. Common etiologies identified by holter monitoring were advanced second or third-degree AV block and sick sinus syndrome, however, holter was normal or detected no new abnormality in 38% of patients. These findings are comparable to the study done by Sarkar et al. **(**29**)** Our study also showed that patients with bundle branch block are at higher risk of developing high degree AV block as demonstrated in the EP study. This finding is consistent with previous reports.30 Patients with prior ischemic heart disease are at high risk of developing ventricular arrhythmias and EP study is recommended in these patients. **(**19**)** Our study is consistent with these recommendations by demonstrating the induction of VT in 50% of patients with pathologic Q wave on baseline ECG. Many patients with normal baseline ECGs were subsequently found to have serious AV conduction disturbances and significant ventricular arrhythmias (NSVT/VT) on holter monitoring and EP study, highlighting the importance of these tests in patients with normal baseline ECG. Furthermore, we found no obvious age-dependent

variation, but we found an increasing prevalence of orthostatic and cardiac syncope in the elderly and more reflex syncope in the young.

One goal of the evaluation of syncope is to detect conditions, particularly life-threatening ones such as arrhythmias, which may be present in patients with syncope. Because patients who experience a syncopal episode often have serious injuries, such as a hip fracture, and head injury during the episode, **(**31**)** another goal is to identify non–life-threatening, but treatable etiologies, such as postural hypotension. Our study suggests that inexpensive postural BP testing is greatly underutilized, resulting in many missed opportunities to institute effective treatment strategies such as medication reduction.

5.Limitations of Study

First**,** we report the experience of a single hospital.

Second**,** we could not account for factors that might have influenced the attending physician in ordering certain tests for establishing the etiology of syncope.

Third**,** all clinical decisions may not have been documented in the medical record. For example, we likely underestimated the contribution of negative results to diagnosis or management.

Finally**,** a majority of syncope cases are treated in outpatient and general practice. Therefore, data from those individuals who do not seek medical attention or who are only seen in the outpatient clinic are not captured. For syncope, this results in a slight bias to more severe cases of syncope because patients with milder/less severe symptoms may not seek medical attention.

6.Conclusion

The overall diagnostic yield of various tests was relatively low. Neurological tests e.g. MRI/CT head, EEG, and Carotid doppler were not helpful. The contribution of cardiac enzymes, CAG, and stress testing in the diagnosis and management was relatively low, although CAG was performed more frequently than required. Postural BP recordings, tilt testing and carotid sinus massage had very high yield but were performed infrequently. The baseline ECG was very much helpful as advanced second or third-degree AV block and sick sinus syndrome were the most frequently reported etiologies. Holter monitoring and EP study proved very useful in the workup especially in patients showing intraventricular conduction disturbances, bundle branch blocks, and prolonged PR intervals as they were subsequently found to have significant AV conduction disturbances and ventricular arrhythmias (NSVT/VT) on these studies.

In summary, the baseline clinical tests like Postural BP recordings, HUTT, and Carotid sinus massage had a high yield of positivity but were underutilized in comparison with the costlier and invasive tests like CAG, CT/MRI, Carotid ultrasound which was over-utilized with less yield. A robust algorithm wherein the test with a high yield of positivity and are cost-effective need to be designed for the evaluation of syncope.

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Conflicts of Interest

There are no conflicts of interest.

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