Original Articles

Admission for Syncope: Evaluation, Cost and Prognosis According to Etiology

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Abstract

Background: Syncope is a common clinical problem that often remains undiagnosed despite extensive and expensive diagnostic evaluation.

Objectives: To assess the diagnostic evaluation, costs and prognosis of patients hospitalized for syncope in a tertiary referral center according to discharge diagnosis.

Methods: We retrospectively reviewed the medical records of patients with a diagnosis of syncope discharged from a tertiary referral center in 1999. In addition, mortality data were obtained retrospectively a year after discharge for each patient.

Results: The study group comprised 376 patients. Discharge etiologies were as follows: vasovagal 26.6%, cardiac 17.3%, neurological 4.3%, metabolic 0.5%, unexplained 47.3%, and other 4%. A total of 345 patients were admitted to the internal medicine department, 28 to the intensive cardiac care unit, and 3 to the neurology department. Cardiac and neurological tests were performed more often than other tests, with a higher yield in patients with cardiac and neurological etiologies respectively. The mean evaluation cost was 11,210 ± 8133 NIS, and was higher in the ICCU than in internal medicine wards (19,210 ± 11,855 vs. 10,443 ± 7314 NIS, respectively; P = 0.0015). Mean in-hospital stay was 4.9 ± 4.2 days, which was longer in the ICCU than in medicine wards (7.2 ± 5.6 vs. 4.6 ± 3.5 days, respectively; P = 0.024). Short-term mortality rates (30 days after discharge) and long-term mortality rates (1 year after discharge) were 1.9% and 8.8% respectively, and differed according to discharge etiology. LTM rates were significantly higher in patients discharged with cardiac, neurological and unknown etiologies (not for vasovagal), compared with the general population of Israel (1 year mortality rate for the age-adjusted [65 years] general population = 2.2%). The LTM rate was higher in patients discharged with a cardiac etiology than in those with a non-cardiac etiology (15.4% vs. 7.4%, P = 0.04). Higher short and long-term mortality rates were associated with higher evaluation costs.

Conclusions: Hospitalization in a tertiary referral center for syncope is associated with increased mortality for most etiologies (except vasovagal), cardiac more than non-cardiac. Despite high costs of inpatient evaluation, associated with more diagnostic tests, longer in-hospital stay and higher mortality rates, nearly half of the patients were discharged undiagnosed. Outpatient evaluation should be considered when medically possible.

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Syncope, defined as a sudden and brief loss of consciousness associated with the inability to maintain postural tone, followed by spontaneous recovery [1-6], is a common clinical problem accounting for up to 3% of emergency department visits and 6% of all hospital admissions [2]. Syncope is caused by a broad diversity of etiologies [1,3,7] and hence is encountered by physicians from various fields of medicine. The most common identified cause of syncope is vasovagal [1,3,7] (also termed neurocardiogenic). Other common etiologies are cardiac (e.g., ischemia and arrhythmias), neurological (stroke, transient ischemic attack), and metabolic (medication or toxin-induced syncope and hypoglycemia). Less common causes are psychiatric illnesses [1] (mainly hysteria and conversion disorder) and visceral reflexes; deglutition [5], cough [6] (relatively rare causes), and micturition (a common cause). However, despite intensive investigation in inpatient series, 40–55% of patients remain undiagnosed [4,7,8]. The pathophysiology of all forms of syncope consists of a sudden decrease or brief cessation of cerebral blood flow [1]. While many clinical algorithms for the evaluation of syncope have been published, none has been widely implemented [2,9,10]. A serious problem in the evaluation of syncope is the absence of a gold standard against which to validate the sensitivity of test results [1,2]. Consequently, when clinical evaluation and non-invasive testing are not helpful, a broad array of investigations is conducted, which may be: unpleasant, potentially dangerous and expensive. Most of the health care costs associated with syncope are due to recurrent hospitalizations and investigation [2,11,12]. Reduced survival was reported among patients with syncope of all causes except those with syncope that was vasovagal, orthostatic and medication-induced [3]. We conducted a study to evaluate the

NIS = New Israeli Shekels
ICCU = Intensive Cardiac Care Unit
LTM = long-term mortality

inpatient diagnostic evaluation, the costs and the prognosis of patients admitted to a tertiary referral center with syncope, according to the discharge etiology.

Patients and Methods

In this observational retrospective cohort study we reviewed the medical records of all patients admitted via the emergency department of the Soroka University Medical Center between 1 January and 31 December 1999, to one of three ward types: Internal Medicine (six wards overall), Neurology (one ward) and the Intensive Cardiac Care Unit (one ward), and discharged with a diagnosis of syncope according to the hospital ATD (Admission, Transfer and Discharge) information system. Soroka is the only tertiary referral center (1000 beds) serving the whole metropolitan area of Beer Sheva (over 500,000 residents). Patients were excluded from the study if they had not lost consciousness during the event (pre-syncope), were experiencing a typical recurrence of a known seizure disorder, had a malignant arrhythmia (e.g., ventricular tachycardia/fibrillation) documented during the episode, or were admitted to a ward not included in the study. In addition, patients were excluded if data were insufficient. Except for these exclusion criteria, all medical findings and diagnoses as obtained from the medical files were accepted without additional adjudication.

The following data were obtained and analyzed from patient files and medical hospital records: medical history, physical examination, and diagnostic evaluation tests that were classified into three categories as follows:

- cardiac tests: 12-lead electrocardiography, Holter monitoring, exercise test, coronary angiography, electrophysiology studies, radionuclide stress scan, transthoracic echocardiography and tilt-table test
- neurological tests: electroencephalography, cranial computed tomography scan and carotid Doppler
- other tests: chest X-ray and blood pressure Holter.

The rate of abnormal findings was obtained and analyzed for some of the tests mentioned (an abnormal finding is one that can theoretically explain the syncope, for example infarct on cranial CT was considered abnormal while general atrophy was not). Post-discharge mortality data were collected retrospectively from the hospital's mortality database, updated on a weekly basis by the Ministry of the Interior. These data include out-of-hospital mortalities for a period of one year for each patient and are classified as: short-term mortality – i.e., within 30 days after discharge, and long-term mortality – within one year post-discharge. Evaluation costs were calculated based on the prices obtained from the Ministry of Health basket of services data on 1 April 2002, and presented as the sum of the cost of all evaluation tests and hospitalization itself (= average price of a hospitalization day x number of days). It is important to emphasize that these costs include theoretical estimations (e.g., work force revenues, support services, equipment wear-out) and do not necessarily equal true costs; however, this is an acceptable and comparable estimation of health services costs in our country.

Reports of syncope were classified into six categories according to cause: cardiac (ischemia, arrhythmias, conduction abnormalities, pacemaker dysfunction and organic heart diseases), neurological (stroke, transient ischemic attack, intracranial bleeding and space-occupying lesions), vasovagal (including orthostasis), metabolic (medication or toxin-induced syncope and hypoglycemia), other (all identified causes that could not be classified under the above categories, e.g., psychiatric etiologies), and unknown.

Statistical analysis

All statistical analyses were performed with SAS software for windows (version 6). Numerical data were compared by Student's t-test, chi-square, or Fisher exact tests. Continuous variables are presented as mean with standard deviation unless otherwise indicated. Mortality rates were compared to those of the age-adjusted general population in Israel for the years 1996–1999, as obtained from the Central Bureau of Statistics website [13]. All tests of hypotheses were considered significant when two-sided probability values were $P < 0.05$.

Results

Altogether, 519 patients were discharged from the Soroka University Medical Center in 1999 with a diagnosis of syncope. We excluded 143 patients (27.6%) for the following reasons: 116 (81%) had no loss of consciousness (pre-syncope), 8 (6%) had typical recurrence of a known seizure disorder, 4 (3%) were admitted to a ward type not included in the study, 2 (1.5%) had insufficient data, 2 (1.5%) were not admitted in the year 1999, and 11 (8%) whose files were not found. Accordingly, 376 patients qualified for the study. Table 1 presents their characteristics and admitting wards.

Discharge etiologies were vasovagal in 100 patients (26.6%),

Table 1. Patient characteristics and admitting wards

Mean age	62.8 ± 18.7
Gender	
Males	212 (56.4)
Females	164 (43.6)
Risk factors	
Diabetes mellitus	79 (21)
Hypertension	162 (43.1)
Dyslipidemia	194 (51.6)
Smoking	93 (24.7)
Heart disease	
Ischemic heart disease	144 (38.3)
History of myocardial infarction	52 (13.8)
Valvular heart disease	8 (2.1)
Implanted pacemaker	9 (2.3)
First syncope episode	279 (74.2)
Admitting wards	
Internal Medicine	345 (92)
Intensive cardiac care unit (ICCU)	28 (7)
Neurology	3 (1)

Values are No. (%), except for age

Table 2. Diagnostic tests and abnormal findings according to discharge diagnosis

Tests/abnormal findings*	Unknown N (%)	Metabolic N (%)	Neurologic N (%)	Vasovagal N (%)	Cardiac N (%)	P
Cardiac tests						
ECG	178 (100)	2 (100)	16 (100)	100 (100)	65 (100)	NS
Holter monitoring	135 (75)	2 (100)	8 (50)	56 (56)	36 (55.3)	< 0.001
Abnormal findings		0 (0)	1 (12.5)	2 (3.6)	12 (33.3)	< 0.05
Exercise test	17 (9.5)	0 (0)	0 (0)	7 (7)	14 (21.5)	0.053
Abnormal findings		0 (0)	0 (0)	2 (28.6)	6 (42.9)	NS
Coronary angiography	9 (5)	0 (0)	0 (0)	4 (4)	16 (24.6)	< 0.001
Abnormal findings		0 (0)	0 (0)	1 (25)	15 (93.7)	0.008
EPS	2 (1.1)	0 (0)	0 (0)	0 (0)	3 (4.6)	NS
Abnormal findings		0 (0)	0 (0)	0 (0)	2 (66.7)	NS
Tilt-table test	7 (3.9)	0 (0)	0 (0)	9 (9)	0 (0)	NS
Radionuclide stress scan	2 (1.1)	0 (0)	0 (0)	6 (6)	7 (10.7)	NS
TTE	90 (50.5)	1 (50)	5 (31.2)	38 (38)	47 (72.3)	< 0.001
Abnormal findings		1 (100)	1 (20)	17 (44.7)	18 (38.3)	NS
Neurological tests						
EEG	53 (29.7)	0 (0)	7 (43.7)	12 (12)	0 (0)	< 0.001
Abnormal findings		0 (0)	5 (71.4)	0 (0)	0 (0)	0.018
Cranial CT	64 (35.9)	1 (50)	15 (93.7)	20 (20)	16 (24.6)	< 0.001
Abnormal findings		0 (0)	9 (60)	1 (5)	1 (6.25)	< 0.001
Carotid Doppler	64 (35.9)	2 (100)	6 (37.5)	23 (23)	18 (27.6)	NS
Other tests						
Chest X-ray	143 (80.3)	1 (50)	13 (81.2)	81 (81)	52 (80)	NS
Blood pressure Holter	1 (0.27)	0 (0)	0 (0)	1 (1)	0 (0)	NS

* Percentages presented for abnormal tests are out of the total number of same test, for the mentioned etiology.

TTE = transthoracic echocardiography, EPS = electrophysiological studies,
EEG = electroenchephalography

Table 3. Short and long-term mortality rates according to discharge etiology

Discharge etiology (N)	STM N (%)*	LTM N (%)*
Cardiac (65)	3 (4.6)	10 (15.4)
Neurological (16)	0 (0)	2 (12.5)
Vasovagal** (117)	1 (0.85)	3 (2.5)
Unknown (178)	3 (1.7)	18 (10.1)
Total (376)	7 (1.9)	33 (8.8)

* Percents presented are out of total number of patients discharged with the mentioned etiology
**Including "Metabolic" and "Other" categories.

discharged with cardiac etiology than in those with non-cardiac etiology (15.4% vs. 7.4%, P = 0.04).

The mean evaluation cost was 11,210 ± 8133 NIS (range 1767–57,202), and the mean hospitalization cost accounted for 7245 ± 6134 NIS of that sum. The cost was significantly higher in the ICCU than in internal medicine wards (19,210 ± 11,855 vs. 10443 ± 7314 NIS, respectively, P = 0.0015). Mean in-hospital stay was 4.9 ± 4.2 days (1–37) and was significantly longer in the ICCU than in internal medicine wards (7.2 ± 5.6 vs. 4.6 ± 3.5 days, respectively, P = 0.024). The neurology ward was excluded from the previous two analyses due to its small number of hospitalized patients. Evaluation costs were higher for the deceased patients compared with the survivors, both 30 days and 1 year post-discharge [Figure 1]. No statistically significant difference was found in the cost of evaluation between patients deceased within 30 days and those deceased within 1 year. In-hospital stay was longer in deceased patients compared with the survivors, both 30 days and
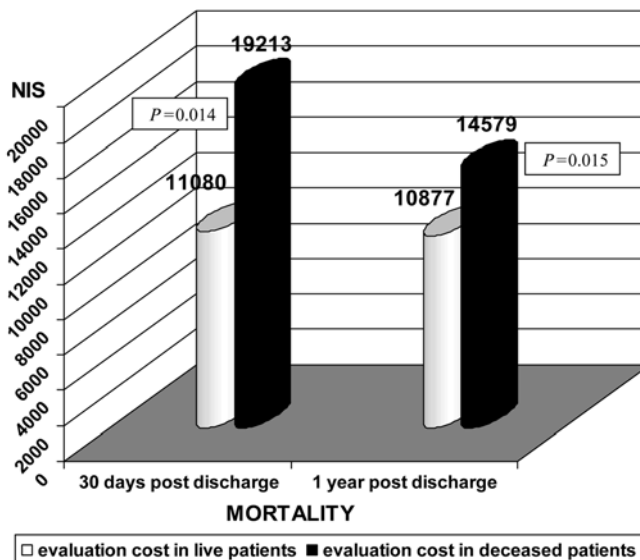
cardiac in 65 (17.3%), neurological in 16 (4.3%), metabolic in 2 (0.5%), unexplained in 178 (47.3%), and other in 15 (4%). The latter category was excluded from all analyses.

A mean of 4 (range 2–8) types of diagnostic tests were performed, although every patient underwent an ECG. The diagnostic tests, the frequency of their use and the rate of some of the abnormal diagnostic tests were compared according to discharge etiology [Table 2]. Unknown etiology was excluded from the analysis of the abnormal diagnostic tests. As presented in Table 2, cardiac tests were performed more frequently and with higher yield in patients discharged with a cardiac etiology. Similarly, neurological tests were conducted more often with higher yield in patients discharged with neurological etiology. No statistically significant difference was found in the frequency of use of tests defined as "other" tests, according to the discharge etiology. Abnormal rates of these tests were not analyzed.

Short-term and long-term mortality rates (within 30 days and 1 year since discharge respectively) were 1.9% and 8.8%, and differed according to discharge etiology [Table 3]. LTM rates were significantly higher for all discharge etiologies presented in Table 3 (except vasovagal), compared with the general population in Israel (1 year mortality rate for the age adjusted [65 years] general population = 2.2%) [13]. The LTM rate was higher in patients

Figure 1. Diagnostic cost (in New Israeli Shekels, NIS) according to outcome

1 year post-discharge (11.4 vs. 4.8, *P* < 0.001 and 7.9 vs. 3.5, *P* = 0.01, respectively). No statistically significant difference was found in the in-hospital stay length between patients who died within 30 days and those who died within 1 year after discharge.

Discussion

The distribution of causes of syncope in our study is consistent with previous reports in inpatient series [4,7,8]. However it differs from the distribution reported by Soteriades et al. [3] in a population-based sample as follows: vasovagal + orthostatic etiology (30.6% vs. 26.6% respectively), cardiac etiology (17.6 vs. 9.5% respectively), and unknown (47.3 vs. 36.6% respectively). We believe this can be explained by the assumption that patients with worse etiologies (cardiac) have a higher chance of being admitted than those with more benign causes (vasovagal + orthostatic). Moreover, although consistent with previous reports in inpatient series (40–55%) [4,7,8], the higher rate of undiagnosed patients would probably have been similar to the lower rates reported by Soteriades and colleagues [3] had these patients undergone further post-discharge outpatient evaluation as reported by Getchell et al. [7]. Among patients with identified cause, the largest group consisted of syncope of vasovagal etiology.

The relatively specific and sensitive use of cardiac tests in patients discharged with cardiac etiology, and neurological tests in patients discharged with neurological etiology, suggests that both neurological and cardiac testing were probably guided by initial findings of history and physical examination, making the evaluation more prudent and efficient (saving both time and money) at least for patients discharged with an identified diagnosis. In a study of 1516 hospitalized patients Getchell and co-workers [7] compared the performance rate of investigational tests between cardiovascular, non-cardiovascular and unexplained syncope. The tests differing according to etiology are very similar to our results, but most tests were used less frequently for most etiologies compared with our study, which may be partially attributed to the fact that not all patients in their study cohort were admitted to tertiary referral centers where sophisticated tests are usually more widely used. Nevertheless, it seems that lower yield, expensive tests like cranial CT, carotid Doppler and electroencephalogram were overused in our study, thus increasing costs substantially. In patients without focal neurological findings or a history consistent with seizures, these tests should be of limited use [4,14,15]. However, in concordance with other previous reports [9,16,17], high yield tests like the tilt-table test and electrophysiology studies were underused, both in our study and in that of Getchell et al. [7], which can partially explain the high rate of undiagnosed cases. These tests when used in properly selected groups made it possible to diagnose up to 90% of cases [18-20]. This shows that the investigation was partially based on the availability of diagnostic tests and obsolete instead of new guidelines and algorithms.

Syncope was found to be associated with worse short and long-term survival prognosis (all etiologies, except vasovagal), cardiac etiology more substantially than non-cardiac. Since we did not perform co-morbidity adjustment, these findings could potentially be confounded by an underlying illness. Nevertheless, they are consistent with the findings of Soteriades and co-authors [3] and Kapoor [21], who reported higher mortality in patients with syncope of all etiologies except vasovagal, orthostatic and medication-induced, and higher mortality in patients with cardiac causes than non-cardiac etiologies.

We found high costs for syncope evaluation in all ward types. In agreement with previous reports [12,22], in-hospital stay and care accounted for a major part of these costs. Mean evaluation cost was found to be significantly higher in the ICCU than in the internal medicine wards, which can be attributed to the additional cost of the significantly longer in-hospital stay in the ICCU.

High evaluation cost was found to be associated with a worse prognosis (higher short and long-term mortality rates). However, this was not adjusted to age and co-morbidity of the patients, and can partially be explained by the longer in-hospital stay associated with worse prognosis, probably due to a worse underlying clinical status requiring a longer and more intensive evaluation. Evaluation costs and length of in-hospital stay were similar in patients who died within 30 days compared to those who died within one year.

Limitations

Our study involves inpatients in a tertiary referral center and does not include ambulatory patients. Obviously, many individuals will suffer syncope and never see a physician (about 50%) [1], while others will see a physician and not be admitted. Therefore, the applications of this study are limited to inpatients in similar centers.

Statistical analyses were hard to perform on some of the evaluation tests especially the non-standard ones (e.g., electrophysiological tests) due to their low frequency in our study, which may account for some of the not statistically significant results. We believe that further study with larger sample size is warranted.

Another important limitation of this study is that we retrospectively reviewed and relied on the treating physicians' findings and diagnoses (after excluding patients according to exclusion criteria) that may be biased or incorrect in some cases. We chose not to create new homogenous criteria as did Pires et al. [9], because we felt that overruling and "second guessing" the treating physician might introduce more inaccuracies.

Although this study involved patients hospitalized throughout 1999, and new syncope guidelines from the European Society of Cardiology were published in 2001 [23] and updated in 2004 [24], and from the American Heart Association and American College of Cardiology Foundation in 2006 [25], these guidelines are based largely on data published in the last decades of the previous century and were already available when this study was conducted. Moreover, we believe that these new guidelines are still not being implemented and followed properly by physicians. In addition, the costs of the evaluation tests in this study have not changed much in the last decade. In view of the above, the results and conclusions of this study are as relevant today, if not

more so, than they were in 1999, when the guidelines had not yet been established.

Summary

In this study we found that despite high costs of inpatient evaluation, associated with more diagnostic tests, longer in-hospital stay and higher mortality rates, nearly half the patients were discharged without an identified cause. Because the cost of the hospitalization itself comprises the major part of the total cost, we recommend considering outpatient evaluation when hospitalization criteria are not met [1]. A multidisciplinary syncope clinic might improve the evaluation efficacy and reduce its cost. For inpatients, a prudent and efficient evaluation based on new guidelines and algorithms [23-25] should be applied to minimize inpatient stay, inconvenience and costs. Additional study comparing the prognosis, evaluation and costs in hospitalized patients versus outpatients with syncope is warranted.

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> *Foreign aid might be defined as a transfer of money from poor people in rich countries to rich people in poor countries*
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> Douglas Casey, American free market economist, best-selling financial author, and international investor and entrepreneur