The value of multidisciplinary team in syncope clinic for the effective diagnosis of complex syncope

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Abstract

Background: Syncope is a perplexing challenge that often receives thorough evaluation, yet the diagnosis remains unclear. Usually, the emergency department is the first point at which patients present with syncope. However, diverse medical factors, including low diagnostic rates and inconsistent management by doctors, add to healthcare costs and delay diagnosis for syncope patients.

Methods: Patients who had been to the emergency department at least once but were not given a clear diagnosis of syncope were recruited into our study at the time they visited syncope clinic staffed by a multidisciplinary team. Complete medical histories and clinical examinations were conducted by both experienced cardiologists and neurologists. If patients were not given a conclusive diagnosis at the syncope clinic on the basis of outpatient examinations, they were admitted for further evaluation.

Results: A total of 209 consecutive patients claiming “syncope” visited the syncope clinic, yet only 167 patients were formally diagnosed with syncope. For these 167 patients, the mean age was 55.93 ± 17.40 years old, and 41.3% were male. The proportions of cardiac syncope, reflex syncope, orthostatic hypotension (OH), and syncope of uncertain etiology were 19.8%, 64.1%, 7.8%, and 8.4%, respectively. The diagnostic rate was 91.6%, and the hospitalization rate was 23.4%. Patients with reflex syncope and OH were younger than patients with cardiac syncope. Cardiac syncope tends to occur more frequently in males, while reflex syncope is more likely in females.

Conclusions: The cooperation of professional cardiologists and neurologists will play an important role in improving diagnostic rates, lowering admission rates, and reducing medical costs.

KEYWORDS
diagnosis, multidisciplinary team, syncope, syncope clinic

1 | INTRODUCTION

Syncope is defined as a transient loss of consciousness (TLOC) due to cerebral hypoperfusion and characterized by rapid onset, short duration, and spontaneous complete recovery.1 It is experienced by almost half of the population during a lifetime and accounts for significant morbidity.2 The incidence of a first report of syncope was 6.2 per 1,000 person-years,3,4 which accounts for approximately 3% of emergency department (ED) visits and 6% of hospital admissions.5 Diagnosis of syncope is always challenging because most patients are asymptomatic upon arrival at the hospital, and the causes of syncope are diverse, ranging from relatively benign conditions to potentially life-threatening diseases. Usually, patients will visit an emergency room in response to their first blackout. However, the rate of etiological diagnosis is low, and rates of admission for syncope are high in EDs, leading to increased hospital expenses (i.e., total annual costs related to syncope are estimated at 2.4 billion dollars in the United States).5 In addition, the risk of life-threatening events associated with syncope is extremely low, and most episodes of syncope are transient, benign, and self-limited.6,7 Due to the lack of education about syncope for patients
in the ED, most patients will visit the ED every time syncope occurs, and these frequent visits inevitably give rise to anxiety.

To reduce excessive hospital procedures, improve diagnostic efficiency for syncope or uncertain etiology, decrease hospital admission rates, and provide unified management for syncope patients, we formed a designated multidisciplinary team for syncope evaluation in syncope clinic consisting of experienced cardiologists and neurologists. Here, we describe the experience of providing syncope services in the context of a multidisciplinary team in syncope clinic from January 18, 2017 to February 7, 2018 in Shanghai Sixth People's Hospital, specifically focused on the etiology of complex syncope.

2 | METHODS

From January 18, 2017 to February 7, 2018, 209 patients who had already gone to the ED at least once but had not received a clear diagnosis visited syncope clinic in Shanghai Sixth People's Hospital. At the time of arrival at the syncope clinic, complete medical histories were obtained, and clinical examinations were conducted on all patients by both a cardiologist and neurologist. Since all patients had been to the ED before, most of them would receive a primary diagnosis after evaluation in the syncope clinic in accordance with the guideline of 2017 ACC/AHA/HRS. Often, key tests had already been performed in the ED, such as blood tests, electrocardiogram (ECG), cardiac ultrasounds, 24-hour electrocardiographic monitoring, cranial computed tomography (CT), and cranial magnetic resonance imaging (MRI). Those patients who did not receive a stated diagnosis and those with established diagnoses but in need of treatment because of high risk were referred to the hospital for an inpatient evaluation. Patients with syncope were classified by diagnosis, including cardiac syncope, reflex syncope, orthostatic hypotension (OH), and syncope of uncertain etiology. The diagnostic standards of syncope are shown below.

Reflex syncope:

Reflex syncope is highly probable if the patient’s history of syncope fits the criteria below:

1. Long history of recurrent syncope, in particular that occurring before the age of 40.
2. Occurring after unpleasant pain, fear, sight, sound, taste, and/or smell.
3. Occurring while in a crowded and/or hot place.
4. Autonomic activation before syncope: pallor, sweating, faint, and/or nausea/vomiting.
5. Occurring in association with prolonged standing.
6. Occurring during or immediately after eating, micturition, gastrointestinal stimulation (swallow, defecation), cough, sneeze, exercise, laughing, and/or brass instrument playing.
7. Occurring with head rotation or pressure on carotid sinus (as in tumors, shaving, tight collars).
8. Carotid sinus massage is positive or head-up tilt testing is positive if the patient is without prodromes and/or without apparent triggers and/or shows atypical presentation.

Syncope due to OH:

Syncope due to OH is highly probable if the patient’s history of syncope fits the criteria below:

1. Occurring during exercise, after meals, and/or prolonged bed rest.
2. Occurring in association with overdose of vasodilators, diuretics, phenothiazine, and/or antidepressants.
3. Occurring in association with volume depletion (hemorrhage, diarrhea, vomiting, etc.).
4. Occurring in association with primary autonomic failure (pure autonomic failure, multiple system atrophy, Parkinson’s disease, dementia with Lewy bodies).
5. Occurring in association with secondary autonomic failure (diabetes, amyloidosis, spinal cord injuries, autoimmune autonomic neuropathy, paraneoplastic autonomic neuropathy, kidney failure).
6. Orthostatic challenge is positive.

Cardiac syncope:

Cardiac syncope is highly probable if the patient’s history of syncope fits the criteria below:

1. Occurring during exertion or when supine.
2. Sudden onset palpitation immediately followed by syncope.
3. Family history of unexplained sudden death at young age.
4. Presence of structural heart disease, coronary artery disease, prolapsing atrial myxoma, left atrial ball thrombus, severe aortic stenosis, pulmonary embolus, or acute aortic dissection.
5. ECG or electrocardiographic monitoring findings suggests arrhythmia syncope (bifascicular block, other intraventricular conduction abnormalities, Mobitz I second-degree atrioventricular [AV] block, and 1 degree AV block with markedly prolonged PR interval, asymptomatic mild inappropriate sinus bradycardia, or slow atrial fibrillation in the absence of negatively chronotropic medications, nonsustained ventricular tachycardia [VT], preexcited QRS complexes, long or short QT intervals, early repolarization, ST-segment elevation with type 1 morphology in leads V1–V3, negative T waves in right precordial leads, epsilon waves suggestive of arrhythmogenic right ventricular cardiomyopathy [ARVC], left ventricular hypertrophy suggesting hypertrophic cardiomyopathy).
6. Positive electrophysiological study.

3 | STATISTICS

Using IBM Statistical Product and Service Solutions 20.0 (IBM SPSS 20.0, IBM Corp., Armonk, NY, USA) for the primary analysis, we calculated the mean, standard deviation, and 95% confidence intervals of patient age. Analysis of variance was used to compare continuous variables (age of patients in different groups), while two-tailed Pearson’s χ² tests, two-tailed continuity correction tests, and Fisher’s exact tests were used to compare categorical variables (recurrence rate, gender of patients in different groups). A P-value of less than 0.05 was considered statistically significant.
FIGURE 1  Flow of the observational study

4 | RESULTS

For all people claiming “syncope” (209 persons) who visited syncope clinic, 189 patients experienced TLOC, including 167 syncopal patients who received a formal diagnosis of syncope after evaluation. The remaining 22 patients were nonsyncopal, including 11 epileptic patients and 11 vertebrobasilar transient ischemic attack (TIA) patients (Figure 1).

For the 167 patients in the study, the mean age was 55.93 ± 17.40 years old; 69 (41.3%) were male. Thirty-nine patients (23.4%) were admitted to the hospital. Of all the patients reporting syncope, 114 (68.3%) had recurrent episodes, and 46 (27.5%) had syncopal symptoms more than three times. However, there were no significant differences among all groups in terms of recurrence rate (P = 0.122). When classified according to the criteria recommended above, the number of patients diagnosed with cardiac syncope, reflex syncope, OH, and syncope of uncertain etiology were 33 (19.8%), 107 (64.1%), 13 (7.8%), and 14 (8.4%), respectively (Table 1). Final diagnoses were carefully collected and are shown in Table 2. The total diagnostic rate was 91.6%, with a 72.5% rate of established diagnosis after initial evaluation at syncope clinic. The number of admitted patients diagnosed with cardiac syncope, reflex syncope, OH, and unexplained reasons were 12 (7.2%), 22 (13.2%), two (1.2%), and three (1.8%), respectively. There were 11 patients without a clear diagnosis who refused hospitalization (Table 1). Of all 39 patients hospitalized, 35 patients were admitted for diagnosis, while the other four patients were admitted for treatment. Out of 33 patients diagnosed as cardiac syncope, eight patients were admitted for diagnosis, four patients were hospitalized for treatment, two patients were advised to have outpatient drug therapy, and the rest 11 patients refused hospitalization.

The mean age of patients in the different classification categories was 65.70 ± 12.70 years old (cardiac syncope), 64.43 ± 21.48 years old (uncertain etiology), 52.45 ± 16.60 years old (reflex syncope), and 47.77 ± 15.50 years old (OH). There were significant differences among all groups (F = 8.771, P < 0.001). Patients with reflex syncope and with OH were younger than patients with cardiac syncope (P < 0.001/P = 0.001) and patients with syncope of uncertain etiology (P = 0.011/P = 0.009) (Table 3).

Across diagnostic categories, the ratio of men and women was significantly different ($\chi^2 = 13.038, P = 0.004$). Men are more likely to present with cardiac syncope (66.7%), while women are more likely to present with reflex syncope (67.3%) (P = 0.001) (Table 4).

5 | DISCUSSION

This study was carried out by a multidisciplinary team in the syncope clinic, who collected data on the diagnostic yield, specific diagnosis of TLOC, proportion of syncope type, hospitalization rate, recurrence rate of syncope, and age and gender distribution across diagnostic categories of syncope. The diagnostic rate was 91.6%, with an admission rate of 23.4%. Reflex syncope was shown to be the most common
form of syncope in patients visiting syncope clinic (64.1%), followed by cardiac syncope (19.8%). A total of 68.3% of syncope patients had recurrent episodes; nevertheless, there were no significant differences among groups in recurrence rate. With respect to demographic characteristics, patients with reflex syncope and OH were younger than patients with cardiac syncope. Moreover, cardiac syncope tended to occur in males, while reflex syncope was likely to occur in females.

### 5.1 Syncope clinic and diagnosis

Despite the development of several clinical guidelines, current strategies for the diagnosis of syncope vary widely among physicians and among hospitals. Evaluation and treatment of syncope are often hap-

| Diagnostic category | Mean age | F/P | Reflex syncope (P-value) | OH (P-value) | Uncertain etiology (P-value) |
|---------------------|----------|-----|--------------------------|--------------|-----------------------------|
| Cardiac syncope     | 65.70 ± 12.70 | 8.771/ < 0.001 | <0.001 | 0.001 | 0.663 |
| Reflex syncope      | 52.45 ± 16.60 | ___ | ___ | 0.329 | 0.011 |
| OH                  | 47.77 ± 15.50 | ___ | ___ | 0.009 |
| Uncertain etiology  | 64.43 ± 21.48 | ___ | ___ | ___ |

Note: ANOVA = analysis of variance; OH = orthostatic hypotension.

The comprehensive, professional nature of syncope clinic consisting of cardiologists and neurologists with the implementation of guideline of 2017 ACC/AHA/HRS clearly pays dividends in terms of the number of positive diagnoses made in our patients, with a 91.6% established diagnostic rate. Conventional services reported positive diagnostic rates ranging from 57.9% to 87%, which were lower than that in our study. Moreover, the syncope clinic is only open once a week, and the patients enrolled in our study were those who lacked clear diagnoses after having visited the ED. Thus, the diagnostic rate would be even higher if our study sample included patients whose clinical test results were positive enough to make a definite diagnosis upon arrival at the ED.
After initial evaluation in the syncope clinic, 72.5% patients got definitive diagnosis. This is because of the high proportion of reflex syncope patients, which account for 64.1% of syncope patients. Most of reflex syncope can be diagnosed just based on the appropriate and detailed clinical history of syncope patients. In this study, 85 of 107 reflex syncope patients were diagnosed in the syncope clinic and need no further investigations. Another reason is that when patients came to the syncope clinic, they already took a series of medical investigations at the ED. That explains why so many cardiac syncope patients got stated diagnosis in syncope clinic without inpatient evaluation.

Fedorowski et al revealed that there was overlap among vasovagal syncope, situational syncope, and carotid sinus syndrome, and head-up tilt test and carotid sinus massage were helpful to distinguish them. However, it is not recommended to take further investigations if diagnosis is nearly certain or highly likely based on medical history of patients after initial evaluation. Since not every reflex syncope patient had head-up tilt test or carotid sinus massage, it is inevitable that there may be some misdiagnosis of reflex patients.

### 5.2 Syncope clinic and admission rate

Syncope represents a common and challenging symptom complex for practicing physicians, and it can be debilitating and associated with high healthcare costs. Sun and Emond reported that in the United States, the total annual costs for syncope-related admissions were about $2.4 billion, with a mean cost of $5,400 per hospitalization. In a study consisting of 116 patients without intervention taken in South Korea, the admission rate was 21.5%, and the cost for syncope evaluation was 542,000 Korean won per patient (approximately 1,000 won = 1 United States dollar). However, for the other 128 patients enrolled in the intervention group, their admission rate decreased by 8.3%, resulting in a cost reduction of about 30% during the intervention period. Similar conclusions can be found in many researches. Therefore, it is obvious that decreasing syncope-related admissions can result in substantial costs saving. But it is unreasonable to reduce admission rates by risking patients’ safety. The Syncope Evaluation in the Emergency Department Study (SEEDS) indicated that a dedicated syncope unit could decrease admitted patients safely. They randomized intermediate-risk patients to an ED-based explicit syncope protocol versus routine inpatient admission. At the end, hospital admissions were reduced by 56% without affecting recurrent syncope and all-cause mortality among intermediate-risk patients. Many researches also showed similar results that comparing to conventional management, the utilization of a standardized approach could increase the number of low-risk patients (reflex syncope) and decrease the amount of high-risk patients (cardiac syncope). In our study, 107 of 167 syncope patients were diagnosed as reflex syncope, which is the most common form. Up to 85 reflex syncope got established diagnosis after initial evaluation in the syncope clinic and were discharged without hospitalization. The high diagnosis rate and the high proportion of reflex syncope explain the low admission rate.

Probst et al conducted an analysis of the ED portion of the National Hospital Ambulatory Medical Care Survey ED database from 2001 through 2010, they found the admission rates for syncope patients ranged from 27% to 35%. Other investigations showed that the hospitalization rates of syncopal patients ranged from 46.5% to 51.4%, if the patients did not receive specific medical care from syncope unit or some other similar departments. In our study, the admission rate was 23.4%, which was lower than many prior studies.

#### 5.3 The value of syncope clinic

As the guideline of 2018 ESC recommend, patients presenting with probable TLOC will be categorized into no TLOC, syncope, and TLOC-nonsyncopal groups according to their rough medical history. Thereafter, syncope patients will go through initial syncope evaluation including detailed history and physical examination, ECG, and supine and standing blood pressure. Then some patients can get certain or highly likely diagnosis, and treatment can be started. The other patients with uncertain diagnosis will be grouped based on risk stratification. Those in the high-risk group are advised for early inpatient evaluation and treatment, while those in the low-risk group need no further evaluation. The syncope clinic in our study is a little different from the guideline of 2018 ESC.

First, in our study, all patients have been to the ED before due to urgent loss of consciousness and have underwent a series of investigations but could not get stated diagnosis from the ED. That means a high proportion of these patients would get definite diagnosis after initial evaluation in the syncope clinic because of the sufficient medical information and they were not advised to be admitted if they were diagnosed as reflex syncope or OH, thus reducing admission rate. McCarthy et al reviewed 18,898 patients who presented to the ED of a Dublin teaching hospital from November 10, 2005 to April 13, 2006. In that research, up to 78.5% patients with syncope did not require admission, which concluded that hospitals should develop outpatient
We believe that the syncope clinic composed of cardiologists and neurologists is an effective form to manage syncope patients. Second, the syncope clinic consisted of both cardiologists and neurologists. Blanc et al conducted a research to evaluate the impact of an educational process on the use of unnecessary neurological investigations and found out that education of physicians in charge of patients with syncope is inadequate to improve the cost effectiveness of the management of these patients. Maybe this is because implementing published syncope management guidelines is difficult for physicians working in the ED. The multidisciplinary collaboration of both cardiologists and neurologists, who are experts in syncope complex, can benefit syncope patients compared to similar services provided by single-organ specialists, such as only cardiologists, neurologists, or physicians in the ED. Syncope patients who visit the ED always present with loss of consciousness. However, it is hard for ED physicians to differentiate syncope from neurological conditions, and an abundant of healthcare cost was used on neurologic investigations ineffectively. In our syncope clinic, with the help of neurologists, 11 patients were diagnosed as TIA and 11 patients were diagnosed as epilepsy based on their medical history and past investigation reports, reducing unnecessary neurological investigations in return.

There is no doubt that a standardized syncope management can on the one hand improve the quality of life of syncope patients and, on the other hand, incur lower health and social care costs, unnecessary hospitalizations, diagnostic procedures, and higher diagnostic rates. Our results also provide evidence for the importance of standardized outpatient evaluation and care for syncope. Besides, the resources available in our syncope clinic are likely suitable for large referral centers equipped with experienced cardiologists and neurologists. With head-up tilt testing and electrophysiological assays commonplace worldwide, these resources could conceivably be available in most hospitals.

6 | LIMITATIONS

There are potential limitations to our findings. First, selection bias exists in the research. Patients who presented at the syncope clinic had already been to the ED, so the patients recruited into our study were those who had received unclear diagnoses from ED. These patients do not represent all those with syncope. Many patients with OH were easily diagnosed in the ED due to evident symptoms; thus, only patients with obscure presentations were included in our study. Second, as the idea of syncope clinic is novel to the public, our specific clinic was not widely known to patients with syncope during the period of our research, thereby limiting the sample size. We expect future research to employ larger samples. Third, the absence of a follow-up visit is a major limitation. Relevant clinical outcomes, such as mortality, major adverse events, and recurrence of syncope after treatment, were not included. The present study did not have sufficient power to assess these events due to the low event rates; larger sample size will be needed to evaluate these outcomes in the future.

7 | CONCLUSION

Syncope clinic is a multidisciplinary unit with efficient and effective procedures that can elevate diagnostic rates, lower admission rates, reduce medical costs, and therefore reduce waste of medical resources. Although diagnostic rates improved in the syncope clinic, some cases remain undiagnosed. Specific efforts should be made to further decrease the number of patients discharged without an established diagnosis. Additionally, careful monitoring is warranted to maintain standards of care that have been thus far achieved.

CONFLICTS OF INTEREST

The authors have no conflicts of interest. All authors have read and approved the final version of this manuscript.

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