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Syncope Protocols and Units Improve Diagnosis and Risk Stratification and Reduce Costs

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Causes of transient loss of consciousness include trauma, syncope, seizures, intoxications, and metabolic disturbances. False transient loss of consciousness can occur due to psychogenic causes, pseudosyncope or pseudoseizure, "drop attacks," or cataplexy. True syncope can be due to neurally mediated reflex, orthostatic hypotension, cardiac arrhythmia, structural cardiopulmonary conditions, or unexplained causes.

The Signature Group developed an algorithm for rapid prediction of syncope onset by analyzing heart rate and blood pressure in 1155 patients with previous syncope [Virag N et al. *Heart Rhythm*. 2007]. In this study, electroencephalogram video studies showed that heart rate parameters changed in different ways during episodes of syncope, epilepsy, and psychogenic pseudosyncope. The objective of the study was to find a quicker, less expensive way to diagnose syncope. To accomplish this, the researchers recorded electrocardiograms (ECGs) of patients during electroencephalogram video monitoring with the hypothesis that if the type of syncope could be identified using ambulatory ECG, the same principles could be applied to medium-term external or long-term implantable loop recorders (ILRs). Dr Richard Sutton, DSc, MBBS, Imperial College, London, United Kingdom, presented results. Among 45 patients, syncope was diagnosed as epilepsy (n = 17), psychogenic pseudosyncope (n = 8), or vasovagal syncope (n = 20) on the basis of a measure called marginality, a new approach to imaging in syncope diagnosis methods. The study results are summarized in Table 1, showing that marginality was low (< 4%) for tachycardia and reflex syncope but higher (> 10%) for focal epilepsy and nonepileptic attack disorder.

David G. Benditt, MD, University of Minnesota, Minneapolis, Minnesota, USA, discussed assessing risk in patients presenting with syncope, and he indicated that patients with syncope may be at increased risk of mortality, including sudden cardiac death. Other risks include serious injury and loss of independence in elderly patients. There is no universal consensus on how to assess risk, but several studies are ongoing. Studies of major syncope risk stratification systems are summarized in Table 2.

The EGSYS study had the most robust data and employed a point score that is useful in the clinic, according to Dr Benditt. The EGSYS 2 follow-up data demonstrated an approximately 20% syncope recurrence rate at 2 years, regardless of the underlying cause [Ungar A et al. *Eur Heart J*. 2010]. Predictors of mortality included age ($P < .0001$), trauma ($P = .018$), heart disease or abnormal ECG ($P < .0001$), male sex ($P = .030$), and hypertension ($P = .002$). An international meta-analysis including 43 315 patients from 11 studies identified high-risk markers of adverse

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Table 1. Details of Syncope Diagnoses Made by Electrocardiogram Marginality

Type of Syncope	Presence of Tachycardia	Marginality, %	Heart Rate Variability	LF/HF Ratio
Tachycardia	Yes	< 4	Moderate changes (mostly sympathetic)	No changes
Reflex syncope	Some before faint	< 4	Reduced sympathetic before faint	Reduced before faint
Focal epilepsy	No	10-35	Increased sympathetic activity	Increased (10)
NEAD	Yes, irregular	≤50	High sympathetic and parasympathetic activity	Increased (10-40)

LF/HF, low frequency/high frequency; NEAD, nonepileptic attack disorder.

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Table 2. Major Syncope Risk Stratification Systems

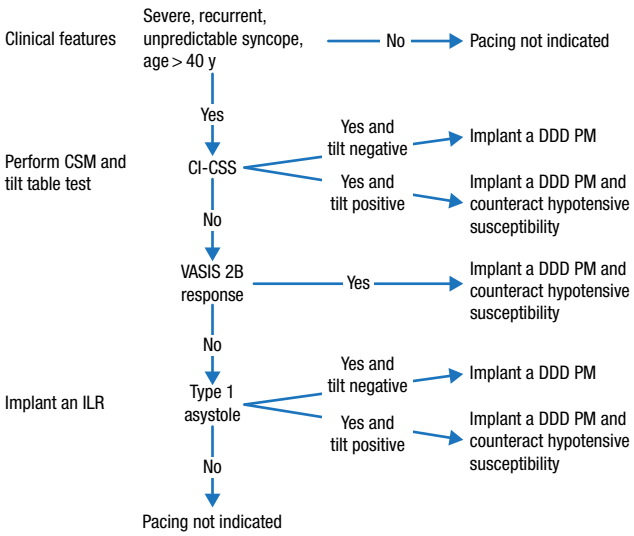
Study	
Design/Patients	**Results/Limitations**
Boston [Grossman SA et al. *J Emerg Med*. 2007]	
201 patients with syncope followed 30 d Clinical decision rule applied to identify risk Primary end point: critical intervention or adverse event	69% had ≥1 risk factor and were admitted 66 of 68 patients met primary outcome Sensitivity, 97%; specificity, 62% Small study, short follow-up, utility limited by complexity No external validation
OESIL [Colivicchi F et al. *Eur Heart J*. 2003]	
270 consecutive patients with syncope 328 patient validation cohort Application of point score to determine risk, based on age > 65 y, history of cardiovascular disease, syncope without prodromes, abnormal ECG Primary end point: death from any cause within 12 mo	Mortality increased as score increased in original and validation cohorts No external validation
EGSYS [Del Rosso A et al. *Heart*. 2008]	
260 consecutive patients with syncope evaluated Point score developed and validated in 256 patients Predictors of cardiac syncope identified by univariate and multivariate analysis and a score from +4 to −1 assigned to magnitude of regression coefficient Primary end point: cardiac syncope, mortality	Predictors of cardiac syncope: abnormal ECG or cardiopathy, palpitations before syncope, syncope during effort or while supine, absence of neurovegetative signs during recovery, absence of precipitating or predisposing factors Score ≥3, original/validation cohort: sensitivity, 95%/92%; specificity, 61%/60% Score ≥3 vs < 3: higher mortality (original cohort, 17% vs 3%, $P < .001$; validation cohort, 21% vs 2%, $P < .001$) External validation
San Francisco [Quinn JV et al. *Ann Emerg Med*. 2004]	
684 consecutive patients with syncope 50 predictor variables for serious outcomes evaluated	26 variables associated with serious outcome on univariate analysis San Francisco rule developed based on presence of abnormal ECG, shortness of breath, congestive heart failure, hematocrit < 30%, blood pressure < 90 mm Hg Sensitivity, 96%; specificity, 62% External study but results not reproduced [Sun BC et al. *Ann Emerg Med*. 2007]
ROSE [Reed MJ et al. *J Am Coll Cardiol*. 2010]	
550-patient derivation cohort; 550-patient validation cohort Development of clinical decision rule to predict serious outcomes and death in patients presenting with syncope	Independent predictors of serious outcome or death: elevated brain natriuretic peptide, chest pain, abnormal ECG, fecal occult blood, hemoglobin ≤90, oxygen saturation ≤94 Sensitivity, 87.2%; specificity, 65.5%; negative predictive value, 98.5% No external validation

ECG, electrocardiogram.

outcomes, including palpitations preceding syncope, heart disease, and syncope during effort [D'Ascenzo F et al. *Int J Cardiol*. 2013].

The risks associated with syncope might be reduced with cardiac pacing in appropriate cases. Michele Brignole, MD, Ospedali del Tigullio, Lavagna, Italy, studied the benefits of cardiac pacing for patients with reflex syncope. The SUP2 study [Brignole M et al. *Eur Heart J*. 2015] evaluated 253 patients with severe unpredictable recurrent reflex syncope with carotid sinus massage (CSM), tilt testing (TT) if CSM was negative, and ILR if TT was negative. Patients with an asystolic response to 1 of the tests received a dual-chamber pacemaker (n = 120). The recurrence rate among these patients was 9% at 1 year and 15% at 2 years, compared with 22% at 1 year and 37% at 2 years among patients with an ILR and no pacemaker ($P = .004$).

Figure 1. Decision Tree: Pacing for Neurally Mediated Syncope



CI-CSS, cardioinhibitory carotid sinus syndrome; CSM, carotid sinus massage; DDD PM, dual-chamber pacemaker; ILR, implantable loop recorder; VASIS 2B, Vasovagal Syncope International Study 2B.

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The prevalence of carotid sinus syndrome was 2 to 5 times higher than in the general syncope population. Syncope was more likely to recur in patients with mixed forms of carotid sinus syndrome or positive mixed or vasodepressor TT. A positive TT might indicate hypotensive susceptibility, which can cause syncope recurrence regardless of the etiology and mechanism of syncope [Solari D et al. *Europace*. 2014; Sutton R, Brignole M. *Eur Heart J*. 2014].

The algorithm used to identify patients for pacemaker implantation in the SUP2 study was revised on the basis of evidence from this and other studies (Figure 1).

Standardization of syncope management through the introduction of syncope protocols such as this decision tree can help reduce the number of admissions, tests performed, and rate of unexplained syncope. Mohamed H. Hamdan, MD, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, USA, discussed how syncope protocols and clinics can improve the cost-effectiveness of syncope management.

The cost of syncope management is determined by hospital admissions, test utilization, and the rates of unexplained syncope and misdiagnosis. According to the European Society of Cardiology guidelines, high-risk criteria requiring prompt hospitalization or intensive evaluation are as follows: severe structural heart disease, clinical or ECG features suggesting arrhythmic syncope, and important comorbidities [Moya A et al. *Eur Heart J*. 2009]. A comparison of standardized admission criteria (Faint-Algorithm) with clinical practice found that in a single center, 58% of admissions and 6% of discharges were inappropriate [Daccarett M et al. *Europace*. 2011]. Other data demonstrated high rates of inappropriate testing among patients presenting with syncope [Edvardsson N et al. *Europace*. 2011; Mendu ML et al. *Arch Intern Med*. 2009; Pires LA et al. *Arch Intern Med*. 2001]. Studies have demonstrated rates of unexplained syncope of 52% [Brignole M et al. *Pacing Clin Electrophysiol*. 2011] and misdiagnoses of 12.9% [Josephson CB et al. *Can J Neurol Sci*. 2007] and 39% [MacCormick JM et al. *Ann Emerg Med*. 2009].

Several studies have shown that establishing syncope protocols and units can improve diagnosis, reduce hospitalizations, and lower costs (Table 3).

The evidence shows that differential diagnosis between epilepsy and syncope may be difficult, especially in retrospect. Cardiovascular evaluation including CSM, TT, and ILR may identify an alternative diagnosis in many patients with apparent epilepsy.

Appropriate use of syncope protocols and syncope units can increase the rate of appropriate diagnoses and decrease admission rates, hospital stays, and unnecessary testing. The University of Wisconsin established a Faint and Fall Clinic that provides better care while being profitable. Despite the decrease in admissions and tests per diagnosis, hospitals could have increased margins due to improved quality of care and associated increase in market share.

Table 3. Studies Comparing Syncope Protocols and Unit Care vs Conventional Diagnosis and Care

Study	
Design/Patients	**Results**
Shen WK et al. *Circulation*. 2004	
103 intermediate-risk syncope patients randomized to evaluation in the Syncope Unit (6-h ECG monitoring, echocardiography, TT) vs standard care	Admission rate lower in Syncope Unit vs standard care (43% vs 98%; $P < .001$) Diagnosis rate higher in Syncope Unit vs standard care (67% vs 10%; $P < .001$)
Sun BC et al. *Ann Emerg Med*. 2014	
124 patients randomized to emergency department observation syncope protocol vs routine inpatient admission Primary end points: admission rate and LOS	Admission rate lower with syncope protocol (15% vs 92%; 95% CI, −88% to −66%) LOS lower with syncope protocol (29 vs 47 h; 95% CI, −28 to −8) Similar serious outcome rates after discharge Facility costs $629 less per index visit in syncope protocol group
Brignole M et al. *Europace*. 2006	
Standardized pathway (European Society of Cardiology Guidelines; n = 745) vs usual management (n = 929)	Standardized pathway had lower hospitalization rate (39% vs 47%; $P = .001$), shorter LOS (7.2 ± 5.7 vs 8.1 ± 5.9 d; $P = .04$) vs usual care Mean cost per patient and per diagnosis 19% and 29% lower with standardized pathway ($P = .001$)
Krahn AD et al. *Circulation*. 2001	
60 patients randomized to 1-y ILR monitoring vs conventional testing Crossover to alternate group offered if remained undiagnosed	Diagnosis rate higher with ILR vs conventional (52% vs 20%; $P = .012$) Prolonged monitoring (including crossover data) resulted in diagnosis in 55% vs 19% ($P = .0014$)
Krahn AD et al. *J Am Coll Cardiol*. 2003	
60 patients randomized to 1-y ILR monitoring vs conventional testing Crossover to alternate group offered if remained undiagnosed Cost analysis performed	Cost per patient: ILR followed by conventional testing vs conventional followed by ILR ($2937 ± 579 vs $3683 ± 1490; $P = .013$) Cost per diagnosis: ILR followed by conventional testing vs conventional followed by ILR ($5875 ± 1159 vs $7891 ± 3193; $P = .002$)
Rockx MA et al. *Am Heart J*. 2005	
Patients with community-acquired syncope Cost-effectiveness of 1-mo ILR (n = 49) vs 48-h Holter monitor with crossover if failed activation or no symptoms	Symptom recurrence and successful activation with ILR vs Holter (63% vs 24%; $P < .0001$)
Zaidi A et al. *J Am Coll Cardiol*. 2000	
Value of cardiovascular testing in 74 patients with apparent treatment-resistant epilepsy TT and carotid sinus massage during continuous ECG, electroencephalogram, and blood pressure monitoring 10 patients received ILR	Alternative diagnosis found in 41.9% of patients, including 36 patients taking antiseizure medications
Farwell DJ, Sulke AN. *Heart*. 2004	
Prospective analysis of syncope protocol (n = 421) vs retrospective analysis (n = 660) in consecutive patients with syncope	Rate of diagnosis increased in syncope protocol group, but nondiagnostic tests still commonly used Cost of testing and hospital stay increased with syncope protocol

ECG, electrocardiogram; ILR, insertable loop recorder; LOS, length of stay; TT, tilt test.