Prognosis of patients with syncope seen in the emergency room department: an evaluation of four different risk scores recommended by the European Society of Cardiology guidelines

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\textbf{Aim} To apply, analyze, and evaluate the four syncope risk scores recommended by the 2009 European guidelines and the different parameters that they use to predict death, syncope recurrence, and hospital readmission in the population seen in the emergency room department (ERD) for syncope.

\textbf{Methods and results} A total of 323 patients aged older than 14 years [mean age 59 (32–75) years] and seen in ERD for syncope over a 2-month period were included in the study; 50.7\% were women. Patients were evaluated using the four risk scores and were followed up for at least 2 years. In all, 275 patients (85.2\%) were discharged directly from ERD after evaluation. During 28 ± 5 months of follow-up, 8\% died, 18.3\% presented a further syncopal episode, and 18.6\% were readmitted to hospital. Only two of the four risk scores were useful in risk discrimination, but no statistically significant differences were detected between predicted risk and observed risk. Multivariate analysis indicated relationships between age and death, a history of cardiovascular disease and syncope recurrence, and between presyncopal palpitations and hospital readmission.

\textbf{Conclusion} Although a large number of events occur after syncope, the risk scores recommended by guidelines overestimate risk, but there were no statistically significant differences between observed and predicted risk. European Journal of Emergency Medicine 00:000–000 Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.

Keywords: accident and emergency department, risk, syncope

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different parameters they use to predict death, hospital readmission and syncope recurrence in patients treated for syncope in ERD.

Methods
The study was a prospective, single-centre observational study carried out in a tertiary hospital between 1 November and 31 December 2009. We included all patients aged older than 14 years admitted to ERD for a syncopal event (defined as a sudden and transient loss of consciousness with complete recovery) occurring during the 24 h before their admission. Patient screening criteria were similar to those described in previous studies [1]. In accordance with our observational study design, no restrictions were placed on the responsible physicians in terms of diagnostic tests or management decisions.

Data collection
Each day, four of the authors of this article reviewed all patients seen in ERD with a diagnosis of syncope or collapse. A specifically designed data collection form (Supplementary Appendix, Supplemental digital content 1, http://links.lww.com/EJEM/A120) was filled in for each patient who fulfilled the enrollment criteria. This form covered all the items included in the four risk scores evaluated including, in particular, age, family and personal medical history, detail of the syncopal event, clinical examination, and ECG interpretation on arrival at ERD. The criteria used to define each item were identical to those specified by the authors of each score in their respective publications [2,8,10,11]. In addition, the investigators reviewed the patient destination to determine the results of the diagnostic test results, management and, when provided, the clinical course during the hospital stay. Etiology of the syncope was classified according to the ESCGS criteria as reflex syncope (RS), orthostatic syncope (OS), cardiac syncope, or syncope of unknown etiology [9].

Follow-up
After discharge from ERD or hospital, patients were followed up every 6 months as outpatients or by telephone contact if they could not attend in person. All patients were followed up for at least 2 years to enable an adequate analysis of the results.

Risk evaluation
The four different scores predict different events and use different follow-up periods: the SFSR score predicts serious events within 7 days of hospital discharge; MK predicts severe arrhythmias or arrhythmic death over the following year; OESIL predicts 1-year total mortality; and EGSYS predicts 2-year total mortality. We calculated the four different scores and compared them with the number of events that we detected during follow-up. Our work is not comparing the fourth scores among them. As ESCGS recommend, we analyze separately all those serious events that the four scores predict, but also we looked into those clinical events that could worsen the quality of life of our patients such as syncopeal recurrence and hospital readmission. We are using them to evaluate their utility and efficacy in events prognosis in real clinical practice. We also carried out univariate and multivariate analyses of the different items and events to estimate risk.

Statistical analysis
Qualitative variables are presented as absolute or relative frequencies and quantitative variables as mean ± SD or as the median with the interquartile range depending on the distribution of the variable evaluated using the Kolmogorov–Smirnov test. The $\chi^2$-test or Fisher’s exact test was used to compare qualitative variables and Student’s $t$-test or the Mann–Whitney $U$-test was used to compare quantitative variables, as appropriate. We evaluated the differences between the observed and the predicted risk by four scores using the Hosmer–Lemeshow test. Risk assessment during follow-up was performed using the value of each of the four scores in each patient and a stepwise logistic regression model was constructed with the four risk scores and with the 18 parameters in an independent model. In this model, the dependent variables were the relationship with death, syncope recurrence, and hospital readmission and the independent variables were the 18 criteria and the values for each risk score. The statistical power was determined after categorization of the population into low-risk and high-risk groups. For event prediction in the MK score, patients were grouped according to their scores: 1–2 points or 3–4 points. For mortality prediction in the OESIL score, patients were divided into groups with 1–2 points and ≥3 points. For the EGYS score, we grouped patients according to their scores (<3 or ≥3 points). To calculate the sensitivity and specificity of the scores, we used the criteria applied in the source studies. A $P$-value less than 0.05 was considered significant. The statistical analysis was carried out using the SPSS, version 18.0 software (SPSS Inc., Chicago, Illinois, USA).

Results
Clinical characteristics
Between 1 November and 31 December 2009, 20 592 patients were seen in the ERD of our hospital; 323 (1.5%) of these patients had syncope and were included in the study. The mean age of these patients was 59 (32–75) years and 164 (50.7%) were women. There were no differences in age between men and women: 59 (30–74.25) years in men versus 60 (34–77) years in women ($P=0.594$).

Forty-eight (14.8%) patients were admitted, 26 (8%) to hospital wards and 22 (6.8%) to the ERD observation ward, with subsequent discharge after 7 ± 5 h. The other 275 patients (85.2%) were discharged from ERD after
evaluation. Forty-three of the 275 patients discharged were referred to cardiology outpatient offices for follow-up, one to neurology outpatients, and the rest were sent to their general practitioner (Table 1).

The final diagnosis in ERD was RS in 211 patients (64%), OS in 29 (9%), cardiac syncope in 30 (9%), and syncope of unknown etiology in 59 (18%). One female patient was initially diagnosed with syncope in ERD, but follow-up showed that she had epilepsy, and thus had experienced a transient loss of consciousness, but not a syncopal episode (0.3%).

**Follow-up**

Follow-up was possible for 309 patients (95.7%). After a mean follow-up of 28 ± 5 months, 26 patients (8%) died, 59 (18.3%) presented an additional syncopal event, and 60 (18.6%) required a further hospital admission. Five of the 26 patients died of the following cardiovascular conditions: severe aortic stenosis with a low ejection fraction \((n = 1)\), acute myocardial infarction \((n = 3)\), and heart failure \((n = 1)\). The cause of death in the remaining 21 patients was stroke \((n = 1)\), Alzheimer’s disease \((n = 2)\), cancer \((n = 7)\), infectious diseases \((n = 4)\), and mesenteric ischemia \((n = 1)\); the cause was unknown in six cases. When we analyzed the evolution in those 26 patients who were admitted to the hospital ward, three of them (11.3%) died, two (7.7%) had an additional syncopal event, and six (23.1%) required a further hospital admission. There were no differences in the follow-up with the other patients who were not admitted to the hospital ward.

**Risk evaluation**

The frequency of the syncope characteristics in the 323 patients is shown in Table 2. The most common characteristic was an autonomic prodrome (67.4% of patients) and the least common characteristic was hematocrit below 30%.

**Risk prediction on the basis of four scores**

After calculation of the frequencies, we developed a risk prediction with three of the risk scores (MK, OESIL, and EGSYS); the SFSR score was not included as none of the 323 patients had a serious event within 7 days of hospital discharge. The risk estimations are shown in Fig. 1.

MK predicts severe arrhythmias or arrhythmic death over the following year; as there were neither severe arrhythmias nor arrhythmic deaths during the follow-up period of our study, we used the overall number of deaths. There was no significant difference between the survival curve of the 1–2 point group [mean survival: 11.95 ± 0.39 months; 95% confidence interval (CI), 11.87–12.03] and the survival curve of the 3–4 point group [mean survival: 11.7 ± 0.106 months; 95% CI, 11.5–11.91] \((P = 0.156)\).

OESIL predicts the 1-year total mortality. A significant difference was detected between the survival curve of the 1–2 points group [mean survival: 29.90 ± 0.28 months; 95% CI, 29.13–30.24] and the survival curve of the ≥3 points group (mean survival: 27.859 ± 0.631 months; 95% CI, 26.62–29.09) \((P = 0.004)\).

EGSYS predicts 2-year total mortality. The difference between the survival curve for the group with less than 3 points (mean survival: 29.44 ± 0.303 months; 95% CI, 28.85–30.03) and the survival curve for the group with at least 3 points (28.028 ± 0.676 months; 95% CI, 26.7–29.35) was not significant \((P = 0.055)\).

We also calculated the sensitivity and specificity of the scores using the criteria applied in the source studies. The area under the curve \((C\text{ statistic})\) was low for all scores and thus did not show an adequate discriminatory capacity (a standard value of 0.7 was considered adequate discrimination). The sensitivity and specificity were determined in accordance with the cut-off scores chosen for the high-risk and low-risk groups (Table 2).

Three of the four risk scores classify the population into different risk groups. We compared the results of the risk prediction on the basis of the baseline data with the true risk figures obtained on follow-up. This was not performed with the SFSR scale because there were no serious events within 7 days of hospital discharge, nor with the MK scale because there were no severe arrhythmias or arrhythmic deaths during the follow-up period, and there were no significant differences between the risk curves. When comparing the observed OESIL risk with the predicted risk score, we found a linear increase in risk in both cases, but the true risk score derived from the follow-up data was lower than the predicted risk. Using the EGSYS score, we also observed a linear increase in risk, but this was higher than predicted in the low-risk population and lower than predicted in the high-risk population. When we compared the observed and the predicted risk using the actual data of our population in the two scores (OESIL and EGSYS) with the risk described by the authors of those scores, we found a real lowest risk in our population (Fig. 2).

We evaluated the differences between the observed and the predicted risk using the Hosmer–Lemeshow test. None of these differences reached statistical significance.
Table 2  Univariate analysis between risk characteristics and evolution

<table>
<thead>
<tr>
<th>Prevalence (%)</th>
<th>Death [P-value&lt;br&gt;RR (95% CI)]</th>
<th>Syncope [P-value&lt;br&gt;RR (95% CI)]</th>
<th>Hospital admission [P-value&lt;br&gt;RR (95% CI)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sudden death familiar history</td>
<td>0.4</td>
<td>NP</td>
<td>NP</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>15.8</td>
<td>0.005</td>
<td>2.501 (1.373–4.556)</td>
</tr>
<tr>
<td>Ventricular arrhythmia history</td>
<td>0.7</td>
<td>0.158**</td>
<td>NP</td>
</tr>
<tr>
<td>Heart failure history</td>
<td>3</td>
<td>0.029**</td>
<td>1.000**</td>
</tr>
<tr>
<td>Syncope during effort</td>
<td>5.1</td>
<td>1.000**</td>
<td>0.477**</td>
</tr>
<tr>
<td>Syncope while supine</td>
<td>2.6</td>
<td>0.400**</td>
<td>0.617**</td>
</tr>
<tr>
<td>Predisposing factors?</td>
<td>39.7</td>
<td>0.927</td>
<td>0.050</td>
</tr>
<tr>
<td>Precipitating factors?</td>
<td>39.9</td>
<td>0.867</td>
<td>0.827</td>
</tr>
<tr>
<td>Palpitations before syncope</td>
<td>5.1</td>
<td>1.000**</td>
<td>0.473</td>
</tr>
<tr>
<td>Autonomic prodome?</td>
<td>67.4</td>
<td>0.979</td>
<td>0.431</td>
</tr>
<tr>
<td>Lack of prodrome</td>
<td>16.3</td>
<td>0.752</td>
<td>0.799</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>2.4</td>
<td>NP</td>
<td>0.318**</td>
</tr>
<tr>
<td>Systolic blood pressure (&lt; 90 mmHg)</td>
<td>11</td>
<td>0.853</td>
<td>0.379**</td>
</tr>
<tr>
<td>Abnormal ECG</td>
<td>26.1</td>
<td>0.985</td>
<td>0.431</td>
</tr>
<tr>
<td>Hematocrit &lt; 30%</td>
<td>0</td>
<td>NP</td>
<td>NP</td>
</tr>
<tr>
<td>Age</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0.433</td>
</tr>
</tbody>
</table>

Age: we have used different ages for each calculation of score value. Bold values denote P < 0.05. CI, confidential interval; NP, not performed because some values = 0. **Fisher’s exact test.

Risk prediction on the basis of risk items

Univariate and multivariate analyses were carried out with the inclusion of the items evaluated in all patients to predict death, syncope recurrence, and hospital readmission (Tables 2 and 4). For the prediction of death, the univariate analysis showed a significant correlation with a history of cardiovascular disease, congestive cardiac failure, and age; however, the multivariate analysis only showed an independent correlation with age. Syncope recurrence was associated with a history of cardiovascular disease and the presence of predisposing factors in the univariate analysis, but the multivariate analysis only showed a relationship with cardiovascular disease. Finally, hospital readmission was associated with six different items in the univariate analysis, but only presyncopeal palpitations were confirmed in the multivariate analysis, with an odds ratio of 15.123 (P < 0.004) (Table 4).

Discussion

Clinical characteristics of syncope

The prevalence of syncope in our study (1.5%) was similar to figures reported previously for Spain and in the ESCGS, which describes a stable frequency of syncope in community-based ERDs in Europe, with an incidence of around 1% of all patients seen (range, 0.9–1.7%) [1,9]. Final diagnoses were also similar to those reported previously, with three of every four patients being diagnosed with RS or OS. Interestingly, only 14.8% of patients were admitted to hospital, 26 (8%) of them to a hospital ward and 22 (6.8%) to the ERD observation room for 7 ± 5 h before being discharged. The other 85.2% of patients were discharged directly. Our admission rate was much lower than the figures reported previously for Spain (25%) and considerably lower than the 43 to 98% reported by other authors [1–8]. For example, of 94168 patients evaluated for syncope in emergency departments in the USA, only 2.3% of patients were discharged immediately and 21.9% remained in ERD for a day. The remaining 75.8% of patients were admitted to hospital for 2 days (23.2%), 3 days (16.8%), 4 to 6 days (23.4%), or more than 7 days (12.4%) [12]. We agree with Brignole and Hamdan [13], who reported that only a small minority of patients with syncope referred to ERD were likely to benefit from urgent assessment, and even fewer required hospitalization. It is unlikely that there is a relation between the low admission rate (14.8%) with the readmission rate (18.6%); our readmission rate is exactly the same after 12.5 ± 2.5 months of follow-up in a Canadian study in which 100% of patients were admitted in the hospital ward for syncope [14]. It is possible that our population could be at a lower risk as fewer patients had no prodromal symptoms, but these characteristics have only been used in one study [2]. There were also fewer patients with an abnormal ECG or with a history of coronary artery disease compared with other prospective...
studies involving patients in ERD, although some other studies have reported a similar prevalence of heart disease [15]. These differences could have influenced the results, although we did not modify or select our population – we included 323 consecutive patients seen in ERD for syncope.

Follow-up
During 28±5 months of follow-up, 59 patients (18.3%) presented a further episode of syncope; this figure is lower than that reported in certain population studies, in which approximately a third of patients have a recurrence of syncope during the first 3 years of follow-up [9]. Our data show an 8% mortality, which was much higher than the 1.4% annual overall mortality reported by a recent Danish national register with a mean follow-up of 4.5 years [16], but it was lower than the mortality reported in many recent studies in ERDs, with mean annual mortalities of 10% [17–19]. We cannot explain these differences on the basis of our results, but the evaluation performed in ERD and in hospitalized patients, the treatment provided to patients, and the low admission
rate are likely to be determining factors in the actual clinical course of this population. Our data thus also suggest the idea that this could be a low-risk population.

Risk evaluation

Three of the four scores were found to be useful in distinguishing between low-risk and high-risk populations. However, in our study, only OESIL and EGSYS could predict the actual clinical course when comparing predicted and observed risk in our population between low-risk and high-risk patients, but none of these differences reached statistical significance. One of the reasons for the failure of the MK and SFSR scores was probably related to the overall number of patients. In fact, if our study had more patients, it would probably have greater statistical power; on comparison of predicted data with observed data, we found that these scores were useful for the prediction of risk in our setting, but that the number of events was lower than originally estimated. In our study, patients with syncope thus had a lower risk than initially estimated. However, use of a high-quality statistical tool (the Hosmer-Lemeshow test) to analyze the difference between the observed risk and the risk predicted with each of the four scores showed that this difference did not reach statistical significance in any case. Other authors who have compared these scores have concluded that the methodological quality and prognostic accuracy of current clinical decision guidelines for syncope are limited [20].

Univariate analysis of the items in the scores and the probability of death, recurrent syncope, or hospital readmission indicated relationships between a number of items and each event; however, multivariate analysis showed that just one of each item was related to each event. Age was associated with mortality, the presence of cardiovascular disease was associated with syncope recurrence, and presyncopal palpitations were associated with hospital readmission. The relationship between age and mortality was also found in a younger population (median age, 47 years) in a Danish survey [16], although mortality in that study was 8.2% at 4.5 years compared with 8% at 28 months in our study.

Many authors draw attention to the fact that the presence of structural heart disease and a family history of sudden unexplained death are associated with a poorer prognosis and warrant more comprehensive cardiac investigations [21]. This was not the result in our series. There is evidence that symptoms associated with syncope in patients with genetic arrhythmias may help establish their prognosis and the overall mortality during follow-up, but the low cardiovascular mortality in our series (only five of 323 patients) is probably one of the reasons for the low predictability of this serious event in our study [22]. In contrast to previous reports by other authors and by our group, syncope recurrence in the present study was related to a history of cardiovascular disease; previous reports have related this event to age and the number of

| Table 3 | Statistical prediction capability of the four different risk scores |
| --- | --- | --- | --- | --- | --- |
| Endpoint | Statistic C | Cut-off point | Sensitivity (%) | Specificity (%) |
| Martin | Severe arrhythmias (1 year) | 0.622 | 1 | 84.60 | 32.00 |
| OESIL | Mortality (1 year) | 0.683 | 1 | 100.00 | 2.70 |
| EGSYS | Mortality (2 years) | 0.586 | 1 | 88.50 | 24.00 |
| EGSYS | Syncopal recurrence (2 years) | 0.51 | 1 | 78.00 | 23.80 |

| Table 4 | Multivariate analysis between risk characteristics and death, syncope recurrence, and hospital readmission |
| --- | --- | --- | --- | --- | --- |
| Effect | P-value | OR | 95% CI |
| Death | History of cardiovascular disease | 0.989 | 1.007 | 0.351–2.886 |
| History of congestive heart failure | 0.298 | 2.285 | 0.488–10.557 |
| Age | 0.0001 | 0.932 | 0.898–0.968 |
| Syncopal recurrence | History of cardiovascular disease | 0.002 | 0.270 | 0.118–0.618 |
| Predisposing factors? | 0.182 | 0.615 | 0.302–1.205 |
| Hospital readmission | History of cardiovascular disease | 0.143 | 2.074 | 0.762–5.503 |
| Palpitations before syncope | 0.004 | 15.123 | 2.433–93.999 |
| Autonomic prodrone | 0.144 | 0.567 | 0.265–1.213 |
| Shortness of breath | 0.054 | 11.879 | 0.958–147.253 |
| History of congestive heart failure | 0.789 | 0.774 | 0.118–5.073 |
| Age | 0.063 | 0.991 | 0.952–1.000 |

Bold values denote P < 0.05. CI, confidence interval; OR, odds ratio.
previous episodes of syncope, particularly in the population with RS [3,23,24]. The association between presyncopal palpitations and hospital readmission has not been described by other authors, but a recent meta-analysis in patients presenting with syncope in ERD found this item to be the most powerful predictor of an adverse outcome [25].

An interesting finding was that an abnormal ECG (observed in 26.1% of our patients) was not related to death, syncope recurrence, or hospital readmission, although we have not studied individual ECG findings. This contrasts with reports by other authors and with data from a previous study by our group. Data from the GESINUR study found that an abnormal ECG was common in patients with syncope, but only a wide QRS complex, ventricular pacing, and an elevated heart rate worsen the prognosis [26].

Conclusions

In our hospital, 85.2% of patients with syncope seen in ERD are discharged directly from ERD after evaluation. During 28±5 months of follow-up, only five of 323 patients died because of a cardiovascular event and this would explain why only two of the four risk scores were useful in risk discrimination. The true risk observed during follow-up was lower than the predicted risks, but the analysis showed no statistically significant differences between observed risk and predicted risk. Only age was associated with death, a history of cardiovascular disease with syncope recurrence, and presyncopal palpitations with hospital readmission. Our data therefore show that there are a large number of events after syncope and that some risk scores are useful, but probably overestimate the true risk in patients with syncope.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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