Europace (2008) **10**, 471–476
doi:10.1093/europace/eun061

Management of syncope: clinical and economic impact of a Syncope Unit

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Received 12 September 2007; accepted after revision 13 February 2008

KEYWORDS
Syncope Unit;
Guidelines;
Loss of consciousness;
OESIL risk score;
Pacemaker

Aims Aim of this observational study is to evaluate the clinical performance of a Syncope Unit, in order to assess whether the implemented organization really improves syncope management.
Methods and results The study enrolled patients with unexplained syncope who were consecutively referred to our Syncope Unit, either as outpatients or during hospitalization, in a 2-month period. The design of this observational study consists in three phases: a retrospective analysis of their clinical management in the 9 months prior to the first attendance at the Syncope Unit (phase one), their subsequent clinical management in the Syncope Unit (phase two) and a 9-month follow-up (phase three). The retrospective analysis of phase one showed that 25% of patients had already been hospitalized without diagnosis. After Syncope Unit evaluation, diagnosis was obtained in 82% of patients, with 15% of patients indicated to pacing. In the follow-up, 23% of patients experienced a syncopal recurrence. Our analysis indicated an 85% reduction of hospital costs in the follow-up period.
Conclusion The clinical and economic analysis of the three phases of our study demonstrates that a Syncope Unit allows an improved management of patients with syncope.

Introduction

Syncope is a relatively common problem, affecting over one million people in the US each year, with an annual incidence greater than 500 000 patients.[1] Similarly, in Europe syncope is recognized as one of the most common reasons for hospital admissions (1–6% of the total) and for emergency room (ER) visits (3–5% of the total).[2–5] No difference in the 15-year probability of survival has been observed between patients with vasovagal (VV) syncope and those without syncope. The risk of death for any cause is doubled in subjects with cardiac syncope as compared with those without syncope, with a 15-year mortality higher than 80%.[6] Therefore, identifying the cause of syncope assumes an important prognostic significance.

Currently, the main problems in syncope management are the lack of a 'Gold Standard' clinical test, the lack of a standard clinical 'pathway', and a poor adherence to guidelines.[7,8] The ISSUE[9–11] and ISSUE 2[12,13] studies indicate the implantable loop recorder (ILR) as a possible tool for the diagnosis of syncope due to rhythm disorders. The inappropriate use of diagnostic tests and a high rate of misdiagnosed and unexplained syncope cause over-utilization of medical resources and increase costs.[4,14] A standardized strategy based on the application of current guidelines and the use of dedicated facilities yield better results and reduce the consumption of healthcare resources.[3,15–17] In this context, it appears necessary to set up a Syncope Unit, in which a methodological approach, aimed at a structured and cost-effective clinical management of syncope, can be implemented in order to reduce the number of unexplained syncope and to identify those at 'high risk' of mortality. A correct diagnosis and therapy should imply a reduction of syncopal recurrences; at the moment, it is still debated whether a Syncope Unit may allow an adjunctive benefit in reducing syncopal recurrences: only little data on a selected intermediate-risk population are available and do not support this hypothesis.[18]

The aim of this observational study is to evaluate the clinical performance of a Syncope Unit, in order to assess whether the implemented organization really improves syncope management.

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Methods

Clinical pathway applied in our Syncope Unit

Our Syncope Unit consists of a dedicated team of a physician and two nurses who operate in two dedicated rooms physically located in the Cardiology Department. Physicians operating at the ER have been trained to follow some limited guidelines on syncope.

Patients presenting with transient loss of consciousness (TLOC) at the ER are evaluated based on current European Society of Cardiology (ESC) guidelines. Additionally, in order to obtain a prognostic stratification of the potential risk of mortality at 1 year,[19] the ER physician calculates the OESIL risk score (ORS), which is based on four parameters: age more than 65 years, altered ECG, syncope without prodromes, and history of previous cardiovascular disease (including hypertension). A score of 1 is attributed to each of these parameters: a total score ≥ 2 indicates an increased risk, the risk being greater as the score increases.[19] If the ORS is 2 or more, the patient is potentially at high risk, and therefore hospitalized for further investigations. During a stay of 24–48 h in the Department of Emergency Medicine, the patient is referred to the Syncope Unit. If these investigations suggest a structural cardiac or neurological disease, the patient is transferred to the relevant departments for second-level diagnostic tests and/or specific therapy. Patients with a risk score <2 are considered to be at low risk; they are discharged from the ER and referred to the ambulatory of the Syncope Unit, where they are reassessed within 24–48 h in accordance with the ESC guidelines.[7,8] Outpatients referred to the Syncope Unit are managed in accordance with the ESC guidelines (*Figure 1*).

Study design

The study enrolled patients with TLOC who were consecutively referred to our Syncope Unit, either as outpatients or during hospitalization, in a 2-month period (October–December 2005). This observational study complies with the Declaration of Helsinki, and its design consists of three phases which have been compared: the 9 months prior to the first attendance at the Syncope Unit (phase one), the subsequent clinical management in the Syncope Unit (phase two) and a 9-month follow-up (phase three). All patients signed an informed consent approved by the local Ethics Committee.

At the first visit in Syncope Unit, the following information was recorded:

- clinical characteristics of syncope, clinical history and ORS score;
- with regard to the preceding 9 months, the number of visits to the general practitioner and/or specialist, admissions to ER and/or hospitalizations, instrumental and diagnostic laboratory examinations performed, and any therapy undertaken;
- outcome of clinical evaluation, ECG, carotid sinus massage in supine and upright positions, tilt test and, when indicated, of pharmacological tests (atropine, flecainide, and adenosine), other instrumental and clinical tests (invasive and non-invasive);
- department of hospitalization, if applicable;
- any therapies undertaken.

At the 9-month follow-up examination, the following data were recorded:

- recurrences of syncope;
- further visits to the general practitioner and/or specialist, ER admissions and/or hospitalizations and therapies undertaken.

Economic analysis

The economic impact of the Syncope Unit was assessed by calculating the healthcare costs during the three phases of the study.[20] The analysis was conducted retrospectively and did not consider indirect costs (loss of earnings by the patient or family members, etc.) or

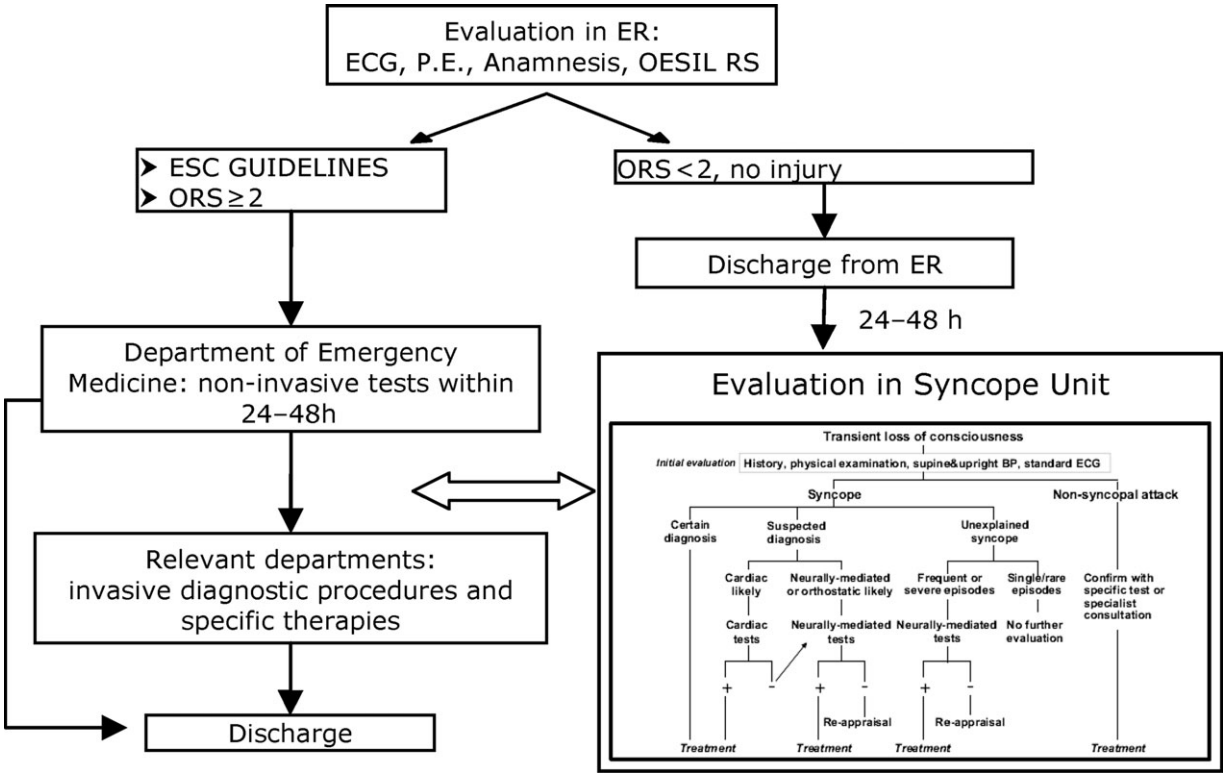

Figure 1 Management of syncope applied in our organization.

costs sustained by the patients outside the National Healthcare Assistance. Costs were calculated on the basis of reimbursement tariffs for ambulatory activity and hospitalizations (DRG).[21–23]

In the three periods considered, the cost items were classified as 'Costs for diagnosis' (refers to the diagnostic examinations performed) and 'Costs for therapy' (refers to the hospitalization costs for bypass surgery and pacemaker implantation). Comparisons were made only in terms of overall costs; indeed, as the statistical distribution of the data was non-normal—the costs being mainly concentrated above the 75th percentile—neither the mean nor the median cost would have been representative.

Statistical analysis

Continuous data are reported as mean ± standard deviation, and categorical data as percentages. Comparisons between costs before and after management in the Syncope Unit were carried out by means of non-parametric tests (Wilcoxon test); the same tests were utilized to compare costs during follow-up between patients with certain and those with unexplained syncope.

Results

Study population

We enrolled 102 consecutive patients referred to the Syncope Unit in a 2-month period (October–December 2005). As 6 patients were lost to follow-up, data from the remaining 96 patients were analysed: in *Table 1* demographics and clinical characteristics are reported. The majority of patients were female; the mean age was 50 ± 21 years, and 26% were aged over 65 years.

Clinical results

Analysis of phase one: the 9 months prior to the Syncope Unit

Syncope was recurrent in 71 patients (74%); only one syncopal episode occurred in the remaining 25. The ORS was ≥2 in 14 patients with recurrent syncope and in 10 patients with a single syncopal episode.

Almost a quarter of the patients (26%) had undergone a mean of 1.1 ± 0.4 hospital admissions for syncope and a mean of 3.6 ± 2.5 examinations. In the same period, 5 patients (5%) had been admitted to the Day-Hospital for syncope and had undergone a mean of 3.2 ± 1.9 examinations.

None of these patients had a conclusive diagnosis.

Analysis of phase two: management in the Syncope Unit

Of the 96 patients, 63 were outpatients, while the remaining 33 underwent evaluation at the Syncope Unit during hospitalization.

Twenty-one per cent of the patients had been referred to the Syncope Unit by other hospitals, 37% by other departments of the same hospital (either during hospitalization or as outpatients following discharge), and 5% directly by the ER; the remaining 37% presented on their own initiative.

Admission to the Syncope Unit allowed a conclusive diagnosis in 82% of cases: in *Table 2* is reported the distribution of patients according to the conclusive diagnosis formulated by the Syncope Unit. Fifty-eight patients (60%) were affected by VV syncope, while the second cause of syncope was cardiac (6%). In 17 patients (18%) the origin of syncope remained unexplained: according to the ORS, 5 had to be considered at high risk, i.e. with indication for hospitalization for further diagnostic investigation and therapy.

Syncope management during hospitalization

Thirty-three patients were evaluated by the Syncope Unit during hospitalization: 14 of them were hospitalized in the Cardiology department, 4 in Internal Medicine, 4 in the ER department, 2 in Neurology, 1 in the Surgery department. Eight patients have been evaluated in Day-Hospital.

A conclusive diagnosis was obtained in 27/33 patients (82%). In only one case the diagnosis of Syncope Unit was tentative and not confirmed by further tests that followed: then, on-discharge diagnosis was different from that initially provided by the Syncope Unit.

In 21% of the patients, hospitalization could be considered inappropriate according to the indications provided by the ESC guidelines[7,8] and the ORS.[19] On the contrary, 15 (62%) of the 24 (out of 96) patients with ORS ≥2 underwent ambulatory evaluation without hospitalization.

Table 1 Demographic and clinical characteristics ($N = 96$)

Age	
<45 years	36 (38%)
46–64 years	35 (36%)
>65 years	25 (26%)
Mean ± SD	50 ± 21
Sex	
Male	30 (31%)
Female	66 (69%)
No. of syncopes prior to enrolment	
$N \geq 2$	71 (74%)
$N = 1$	25 (26%)
OESIL risk score	
ORS = 0	35 (36%)
ORS = 1	37 (38%)
ORS = 2	19 (20%)
ORS = 3	5 (4%)
ORS = 4	0 (0%)

Table 2 Distribution of patients according to the conclusive diagnosis ($N = 96$)

Diagnosis	Number
Vasovagal	58 (60%)
Cardiac	6 (6%)
Situational	3 (3%)
Carotid sinus syndrome	2 (2%)
Orthostatic hypotension	1 (1%)
Not syncopal TLOC	1 (1%)
Psychiatric	1 (1%)
Vasovagal + cardiac	3 (3%)
Carotid sinus syndrome + cardiac + vasovagal	2 (2%)
Carotid sinus syndrome + epilepsy	1 (1%)
Vasovagal + carotid sinus syndrome	1 (1%)
Unexplained	17 (18%)
Total	96 (100%)

Table 3 Patients with recurrent transient loss of consciousness ($N = 96$)

Diagnosis	No. of patients without recurrence	No. of patients with recurrence	Total
Vasovagal	45 (78%)	13 (22%)	58
Cardiac	5 (83%)	1 (17%)	6
Situational	3 (100%)	0 (0%)	3
Carotid sinus syndrome	1 (50%)	1 (50%)	2
Orthostatic hypotension	1 (100%)	0 (0%)	1
Not syncopal TLOC	1 (100%)	0 (0%)	1
Psychiatric	1 (50%)	1 (50%)	1
Vasovagal + cardiac	2 (67%)	1 (33%)	3
Carotid sinus syndrome + cardiac + vasovagal	1 (50%)	1 (50%)	2
Carotid sinus syndrome + epilepsy	0 (0%)	1 (100%)	1
Vasovagal + carotid sinus syndrome	1 (100%)	0 (0%)	1
Unexplained	14 (82%)	3 (18%)	17
Total	74 (76%)	22 (24%)	96

Invasive diagnostic and therapeutic procedures

In 5 patients, evaluation was completed by an electrophysiological study. One patient underwent coronary-aortic bypass and 14 patients (15%) underwent pacemaker implantation. Neuromediated syncope was the major indication for pacing (13 out of 14). Eight of them suffered from cardio-inhibitory VV syndrome, 1 from carotid sinus syndrome (CSS), 1 from CSS and epilepsy, and one from VV syncope associated to CSS. In 3 patients, pacemaker implantation was undertaken for arrhythmic causes (sick sinus syndrome associated to a bifascicular block), 2 of whom were also affected by neuromediated syncope. Due to the typical end-of-year depletion of financial resources no ILR were purchased and consequently not implanted.

Analysis of phase three: the follow-up

The diagnoses initially made by the Syncope Unit were confirmed in 95 of the 96 patients interviewed. In 1 patient with an initial diagnosis of 'unexplained syncope', the tests prescribed by the Syncope Unit and carried out during follow-up led to a diagnosis of 'cardiac syncope'; the patient was thus submitted to coronary-aortic bypass.

During follow-up, 22 patients (24%) suffered syncopal recurrences, as reported in *Table 3*; of these patients, 2 were hospitalized for further tests during follow-up. Following pacemaker implantation, 2 out of 14 patients suffered a total of 3 syncopal recurrences; in this subgroup of patients, the number of episodes experienced in the 9 months before enrolment was 80 (*Figure 2*).

Statistical analysis did not reveal any factors predictive of syncopal recurrence during follow-up, when comparing the two groups of patients – with and without syncopal recurrences.

Five patients with unexplained syncope at high-risk did not suffer any syncopal recurrence during follow-up. On the contrary, in the remaining 12 patients with unexplained syncope at low-risk, recurrences were recorded in 2 patients with previous recurrent syncope, and in 1 patient with a single syncopal spell.

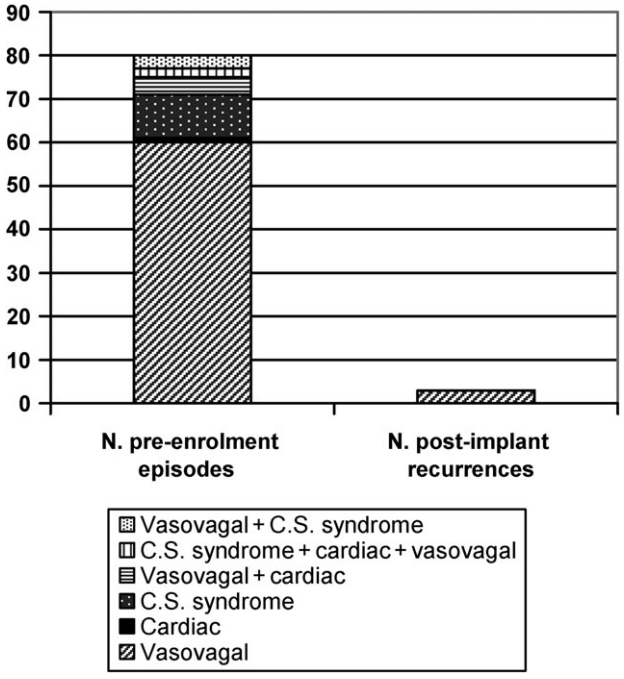

Figure 2 Number of syncopal recurrences before and after pacemaker implant ($N = 14$).

Results of economic analysis

The consumption of resources in the periods before and after admission to the Syncope Unit has been compared. During the latter period, a significant reduction in both the number of accesses to the general practitioner (overall number: 7 vs. 57) and to the hospital for diagnostic purposes (overall number: 2 vs. 25) has been observed, while there are no significant differences considering the number of ambulatory diagnostic tests (overall number: 104 vs. 63) or visits of a specialist (overall number: 5 vs. 65). This latter finding may be linked, on the one hand, to the lower number of hospitalizations and, on the other hand, to therapy-related visits, such as pacemaker follow-up visits.

On the basis of resource consumption, the healthcare costs were calculated as described above; these are reported in *Figure 3*. The total costs for diagnosis (examinations, tests, hospitalizations) fell from €63 938 in the 9 months prior to enrolment to €57 236 during attendance at the S.U. (Syncope Unit) and to €9 711 in the subsequent 9-month follow-up period. Hospitalizations costs accounted

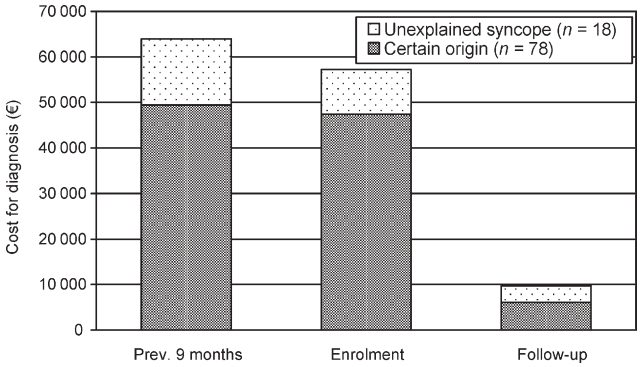

Figure 3 Total costs for diagnosis in the 9 months before enrolment, at enrolment and in the 9-months follow-up period ($N = 96$).

for 82, 93, and 46% of the total of these costs in the three periods, respectively.

The cost for diagnosis during S.U. attendance can be attributed to the large number of hospitalized patients. This cost could be considerably reduced: indeed, as mentioned above, 21% of these hospitalizations were seen to be inappropriate on the basis of the ESC guidelines.

Comparison between the pre- and post-enrolment periods showed a statistically significant 85% reduction in the costs for diagnosis ($P < 0.001$). The same comparison carried out in patients with syncope of certain origin showed an even greater reduction of 88% ($P < 0.001$). Moreover, it is interesting that, even in patients with syncope of unexplained origin, a significant 75% cost reduction was observed ($P < 0.03$).

The comparison of total costs for diagnosis during follow-up between patients with syncope of certain and unexplained origin shows a trend of higher costs in the latter group. However, the small size of the sample did not allow statistical significance to be reached.

Costs for therapy amounted to €119 112 and were accounted for by the hospitalizations required for the implantation of 14 pacemakers and for 1 coronary-artery bypass surgery. It should be pointed out, however, that these costs were occurred during the first 3 months after enrolment and that this value is not constant in the long term.

Discussion

The results of this study show that the utilization of the guidelines improves the diagnostic yield. Our study confirms that the leading cause of syncope is neuromediated, while the second is cardiac. The Syncope Unit displayed a high diagnostic performance, providing a diagnosis in 82% of overall population. This result is similar to those obtained in the OESIL 2 and EGSYS studies (unexplained syncope: 19.5 and 18%, respectively); moreover, it was obtained during routine clinical management and not during a controlled clinical study.

In 15% of patients, the Syncope Unit recommended pacemaker implantation: in these patients, the total number of episodes fell from 80 in the 9 months before enrolment to 3 in the follow-up. However, without a control group, this result does not allow to confirm the efficacy of pacemaker in reflex syncope, considering that pacemaker may have a potential placebo effect and that VV episodes can be clustered and not occurring in the follow-up period.

The retrospective analysis of the 9 months before the enrolment indicates that, in spite of numerous investigations, a conclusive diagnosis was not obtained. About one quarter of patients had been hospitalized for syncope, accounting for the 82% of total costs. The remaining 18% of costs should be considered underestimated: they were based on the patient's recollection and did not include expenses sustained by the patients themselves, such as private visits to specialists, and indirect costs, such as loss of earnings on the part of the patient and/or family members. During the follow-up, the number of hospitalizations and visits to the general practitioner were significantly fewer, while the number of diagnostic tests and visits of specialist remained almost unchanged; probably, this latter finding should be correlated to the number of mandatory examinations (e.g. pacemaker follow-up visits) or of examinations scheduled during hospitalization and performed after discharge. The reduced number of hospitalizations that we observed determined a reduction in the costs of diagnosis: however, the absence of a control group, followed by doctors who are not expert in syncope, does not allow demonstrating that the Syncope Unit effectively reduces hospitalizations and then costs.

Greater attention should be paid to risk stratification, in order to improve the appropriateness of the diagnostic-therapeutic pathway. On the basis of the hospitalization criteria indicated by the ESC guidelines and of the ORS, 21% of hospitalized patients could have been managed in a more efficient and less costly manner as outpatients. In contrast, 24% of the patients referred to the Syncope Unit as outpatients should have been regarded as being at high risk, and therefore evaluated during hospitalization.

Finally, almost 60% of the patients were referred to the Syncope Unit by other hospitals or outpatient clinics for clinical evaluation; this demonstrates the scarce availability of an organized model for the management of syncope.

Limitations of the study

The design of the study was partly prospective and partly retrospective: this type of design may have influenced the results. Our data seem to indicate a reduction in costs and hospitalizations after evaluation in the Syncope Unit, with respect to the previous 9 months in which the same patients have not been managed by experts in syncope. The lack of a control group, followed by doctors who are not experts in syncope, could be considered the main limitation of our study: in spite of encouraging data, we are not able to demonstrate that the observed reduction can be effectively attributed to the activity of the Syncope Unit. Moreover, the absence of a control group does not allow confirming the efficacy of pacemaker therapy in reflex syncope.

The costs incurred prior to admission to the Syncope Unit may have been underestimated; indeed, the retrospective analysis was based on the recollection of the patient, and, moreover, did not consider direct costs sustained by the patient, or the indirect costs resulting from the impact on his working activity.

During the study, no ILR were implanted for administrative reasons. However, in the population observed during the 2-month study, 6 out of a total of 96 patients would

conventionally have been candidates to ILR (syncope of unexplained origin even after the usual diagnostic procedures, recurrent or severe syncope, age $>$ 40 years): probably, the ILR could have allowed a reduction of unexplained syncopes. According to the indications given by the ISSUE 2 study (age $>$ 30, three or more episodes of suspected neuromediated syncope with a severe clinical presentation in the prior 2 years and requiring treatment initiation. Patients with induced carotid sinus syncope were excluded from this study),[12,13] published during the follow-up phase, 18 patients would have been candidates for ILR implantation.

Finally, in order to ensure a constant and rigorous application of the guidelines, no shared tools such as flowcharts or dedicated decision-making software were used.

Conclusions

The analysis of the clinical and economic results of the three phases of our study demonstrates that a Syncope Unit allows an improved management of patients with syncope. In particular, clinical results show a good diagnostic-therapeutic performance and a consistent reduction of syncopal recurrences. The economic results seem to indicate a possible reduction of costs in the follow-up. Finally, the analysis indicates that further improvement in the management of patients with syncope could be achieved, through a corrective intervention based on an appropriate clinical pathway.

Acknowledgements

We wish to thank Sara Napoleone, Anna Sassi, Maria Grazia Romano, and Paola Di Stefano for their support in the collection and processing of data.

Conflict of interest: A.D.S., I.C., T.D.S., and E.T. are employees of Medtronic. R.R. is currently conducting research sponsored by Medtronic and is a member of the speakers' bureau for Medtronic. M.S. is conducting research sponsored by Medtronic.

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