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Posted Date: 3 March 2026

doi: 10.20944/preprints202603.0146.v1

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 doi:10.20944/preprints202603.0146.v1

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Cardiac Syncope: An Underestimated Cause of Unexplained Syncope in the Elderly. Data from a Single High-Volume Syncope Unit

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Abstract

Background/Objectives*:** Syncope remains a common problem in the elderly, adversely affecting quality of life, morbidity and mortality. Diagnosis is challenging due to the atypical presentation, multifactorial aetiology, overlap with non-syncoptic falls and increased prevalence of cardiac disease. This study aims to investigate the impact of cardiac syncope in this high-risk population. ***Methods: A retrospective single-center observational cohort study, including 171 patients ≥ 65 years-old with syncope of unknown origin or other falls. Different diagnostic tests and strategies were utilised during the investigational process investigation, based on clinical judgement and the latest guidelines. Patients were classified either in the 'high risk' ('cardiac') or 'low-risk' ('autonomic') pathway. ***Results:*** Mean age was 76.4±6.6 years (range: 65-92 years-old) and the mean follow-up period was 40.5 months. Our study population was characterised by a high incidence of comorbidities and underlying heart disease, and polypharmacy. One third of the patients did not report prodromals, 81.9% had no recognizable trigger and 43.3% had various 12-lead ECG abnormalities. Overall, 67.8% of the patients were stratified in the 'cardiac pathway'. Eventually, a final diagnosis was established in 126 patients (73.7%). The cause was cardiac syncope in 56.4%, reflex syncope in 26.2%, orthostatic hypotension in 7.9% and non-syncopal falls in 9.5%. An ILR was implanted in 90.1% with a diagnostic yield of 43%. ECG-based diagnosis occurred in 53.2% whereas time to diagnosis was 4.8±3.3 months. ***Conclusions***: Cardiac disease, mostly arrythmias, represent a common and possibly underestimated cause of unexplained syncope in the elderly. A structured approach including a targeted use of ILRs improves investigational process.

Keywords: syncope unit; implantable loop recorder; unexplained syncope; cardiogeriatric assessment; elderly patients

Introduction

According to recent estimates, the population of elderly people (usually defined as those over 65 years old) in Europe is expected to increase significantly, rising from 90.5 million in 2019 (20.3% of the population) to 129.8 million (nearly 30% of the population) by 2050 while, those aged 75-84 years are expected to expand by 56.1 %.[1] Syncope, on the other hand, defined as a self-limited transient loss of consciousness and postural tone due to rapid onset global cerebral hypoperfusion with a short duration and complete recovery, has a higher incidence in the elderly than in any other age group. [2,3] The incidence of syncope is significantly increasing from 5.7 episodes/1000 individuals per year

 doi:10.20944/preprints202603.0146.v1

between 60 and 69 years-old to 11.1 episodes/1000 individuals per year between 70 and 79 years, showing a further increase to 19.5 episodes per 1000 individuals in the age-group over 80 years-old.[3,4] Importantly, in adults over 65, syncope is associated with increased mortality, irrespectively of the cause. [5] In addition, syncope is a major cause of morbidity. Hospitalizations occur relatively more often in older patients, with 58% of sufferers over 80 years being admitted to hospital, and are associated with increased health economic costs.[6,7] Moreover, syncope and the subsequent fear of falling has a particularly adverse impact on the quality of life (QoL) of older adults. [8] Finally, injurious events such as fractures and head injuries, are also more common in this patient group.[9]

In contrast to younger patients, syncope in the elderly is often characterised by atypical presentation. Patients often do not report prodromes and may have amnesia for the events. History is often unreliable and frequently unwitnessed and therefore there might be an overlap with drops. Moreover, syncoptic episodes in this patient group are usually multifactorial and may be associated with many predisposing factors. Polypharmacy and presence of co-morbidities is also frequent.[7–9]

Diagnosis and treatment of syncope in older patients is challenging, due to the atypical presentations, the wide range of differential diagnosis, polypharmacy, the increased incidence of comorbidities, as well as the physiological changes associated with ageing. Advanced clinical skills and expertise are required to reduce hospital admissions and improve quality of life in this increasingly complex population.

We have observed that cardiac causes and syncope attributed to more than one possible cause are common in the clinical practice in older subjects with unexplained syncope assessed in our Syncope Unit, which is based in the Cardiology Clinic of a tertiary hospital. Therefore, we speculate that cardiac arrhythmias are an underdiagnosed cause of syncope of unknown origin. The objective of this study is to determine the incidence of cardiac syncope, particularly due to arrhythmias, in the elderly population in the era of modern algorithms for diagnostic investigation and an extended albeit targeted, use of implantable cardiac loop recorders (ILRs).

Methods

Study design and patient population

A single-centre, retrospective, observational cohort study undertaken in a tertiary Syncope Unit. Individuals ≥ 65 years-old with Syncope of unknown origin or other possible Falls admitted in our clinic from March 2019 until December 2024 were recruited in the study.

The Syncope Unit is located at the Cardiology Department of Hippokration Hospital, Athens, Greece, operating mainly as an Outpatient clinic in line with the European Society of Cardiology (ESC) guidelines.[2,10] In addition, patients admitted in the hospital may also be reviewed if requested by the treating physicians. Outpatient referrals for further assessment and consulting, originate either from the various outpatient departments of our hospital or other hospitals, or from the emergency department, however, the possibility of self-referral is also offered.

In addition to age ≥ 65 years-old, the study inclusion criteria were: (a) individuals with pre-syncope or syncope episodes [2] assessed in our clinic, (b) individuals with episodes of TLOC[2] assessed in our clinic, (c) individuals referred from other facilities for episodes of 'unexplained syncope' (US) or unexplained 'falls', (d) absence of severe co-morbidities or systematic diseases limiting prognosis to less than 1 year.

All patients presented in our facility were investigated according to the current European Society of Cardiology (ESC) guidelines.[2] Firstly, individuals were assessed according to the 'initial evaluation' scheme, including an extensive history of both the conditions of occurrence of the syncoptic episode, any additional health problems and the patient's medication list. Initial evaluation also included a detailed clinical examination, performing active standing test and carotid sinus massage when clinically relevant, and a 12-lead electrocardiogram (ECG). Patient data were stored in both electronic and paper forms.

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Assessment scheme was subsequently individualised based on clinical judgement and subjects were recruited either in the 'cardiac' ('high-risk') or 'autonomic' ('low-risk') pathways. Stratification process followed the ESC guidelines.[2] The presence of a high probability for arrhythmia as the underlying mechanism in combination with the presence of ECG abnormalities guided our decision for selecting the most adequate test for further investigating syncope. Novel algorithms based on up-to-date research were followed for patients categorized in the 'cardiac' and 'autonomic' pathways.[11,12] 24-hour ECG ambulatory monitoring and blood tests including full blood count, kidney function tests and electrolytes and hepatic function tests as well as a transthoracic echocardiogram were performed in all cases. Despite its emerging significance, 24-hour ambulatory blood pressure monitoring (24hABPM) was underutilised in our practice.

Further assessment was performed according to clinical judgment and included Tilt Table Test (TTT), Electrophysiological Study (EPS), and/or long-term ECG recording with an ILR. For TTT, either the standard 20 minutes Italian Protocol or the new 'fast' Italian protocol was selected, including provocation by means of nitrogen triglyceride sublingual spray. A functional ischaemia test (e.g. Treadmill Test, Stress echocardiography or Scintigraphy) in order to investigate the presence of myocardial ischemia and to assess possible exercise or post-exercise syncope was considered after case-by-case assessment. A coronary angiogram was programmed in the case of an increased possibility of ischaemia. Depending on the patient history, referrals to internal medicine or neurology clinics were possible.

In those patients in whom a Loop Recorder was favoured, implantation of a Reveal LINK™ or a LINK II ™ Insertable Cardiac Monitoring System (Medtronic Inc., Minneapolis, MN, USA) occurred. Remote Monitoring (CARELINK™ NETWORK, Medtronic Inc., Minneapolis, MN, USA) was utilised for remote day-by-day assessment. Arrhythmias recorded by the device were classified according to the ISSUE study criteria.[13] Patient triggered events, marked as 'symptoms', were recorded and after contacting the patient, the nature of the symptom was assessed. Patients were also advised to contact the center in the presence of unexplained symptoms. ECG-diagnosis occurred in the case that an arrhythmia was recorded in combination with clinically relevant symptoms or when serious arrhythmias occurred. Arrhythmias not considered relevant to the investigation of syncope were also recorded.

Follow-up visits in our facility were programmed depending on the clinical condition of the patient. During follow-up assessment, history was obtained and clinical examination was performed, and the investigation scheme was revised. Unscheduled visits could also occur accordingly. On the other hand, urgent, or elective inhospital admissions occurred according to the clinical findings. Follow-up was performed for at least 12 months after initial assessment in all subjects.

The primary endpoint of the study was the definite diagnosis of syncope. Secondary endpoints were (a) ECG-based diagnosis, (b) the initial presentation to final diagnosis time, (c) incidence of syncope relapse.

Ethical considerations

This study was conducted in compliance with the Declaration of Helsinki and the ethical guidelines for research involving human subjects. The study design was reviewed and approved by the Institutional Review Board (IRB)/Ethics Committee of our hospital. Ethical approval was not considered necessary since the study included only anonymized data from patient medical records managed according to our standard practice without any intervention. Personal data were stored in electronic and paper forms and were psedonymised.

Statistical analysis

Data are presented as absolute numbers and percentages if categorical and as mean ± standard deviation if continuous. All variables were tested for normality of distribution with p=p plots and Kolmogorov-Smirnov test. For categorical variables differences between different studied groups were tested with chi square test or fisher exact test as appropriate and for continuous variables with

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analysis of Variance (ANOVA). Statistical calculations were performed in SPSS software (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism (version 8, GraphPad, Boston, MA, USA).

Results

During a 70-month period, from March 1st, 2019, until December 31st, 2024, a total of 171 patients over 65 years-old were referred to our Syncope Unit. The mean age of this population was 76.4 ± 6.6 years (ranging 65-92 years-old) and 81 individuals (47.4%) were female. Sixty-two patients were older than 80 years (36.3%). Subjects were referred from the emergency department in 20 cases (11.7%), from our outpatient clinic in 48 cases (28.1%), from other hospitals and primary care structures in 92 cases (53.8%) whereas self-referrals occurred in 11 cases (6.4%). Mean follow-up period was 40.5 months (ranging from 12 to 70 months) (**Table 1**). Patient demographic data, clinical characteristics and investigational strategies are presented in **Table 1 and 2**.

Table 1. Patient demographics and clinical characteristics.

Characteristics	Population (n=171)
Female, n (%)	81 (47.4%)
Age, years	76.4 ± 6.6
Characteristics of syncope/presyncope	
Syncope ± presyncope	158 (92.4%)
Presyncope only	13 (7.6%)
Traumatic syncope, n (%)	127 (74.3%)
Number of episodes	6.2 ± 3.8
Prodromes[1], n (%)	114 (66.7%)
Predisposing factors[2]	31 (18.1%)
Position, n (%)	
• Supine	17 (9.9%)
• Sitting	91 (53.2%)
• Standing	122 (71.3%)
• changing	15 (8.8%)
Exertion status, n (%)	
• Rest	117 (68.4%)
• Mild	90 (52.6%)
• Intense	9 (5.3%)
• Post exertion	1 (0.6%)
Presyncope, n (%)	109 (63.7%)
Palpitations, n (%)	25 (14.6%)
Post syncope symptoms, n (%)	141 (82.5%)
Mean recovery time (min)	5.6 ± 4.1
Clinical Characteristics	
Arterial Hypertension, n (%)	106 (62%)

 doi:10.20944/preprints202603.0146.v1

Dyslipidaemia, n (%)	95 (55.6%)
Diabetes Mellitus, n (%)	26 (15.2%)
Smoking, n (%)	37 (21.6%)
Coronary Heart Disease, n (%)	30 (17.5%)
Non-Ischaemic Dilated Cardiomyopathy, n (%)	1 (0.6%)
Hypertrophic Cardiomyopathy, n (%)	2 (1.2%)
Atrial Fibrillation[4], n (%)	28 (16.4%)
Pacemaker, n (%)	3 (1.8%)
Valvular Heart Disease[3], n (%)	11 (6.4%)
Mitral Valve Prolapse, n (%)	3 (1.8%)
AVNRT, n (%)	1 (0.6%)
Previous Stroke, n (%)	6 (3.5%)
Carotid stenosis not requiring operation, n (%)	11 (6.4%)
History of cancer, n (%)	9 (5.3%)
History of thyroid disease, n (%)	33 (19.3%)
History of Parkinson disease on medication, n (%)	6 (3.5%)
History of prostate hyperplasia on medication, n (%)	12 (7.1%)
Receiving medication for dementia, n (%)	14 (8.2%)
Receiving antiepileptic therapy, n (%)	4 (2.3%)
Receiving any chronic medication, n (%)	164 (96%)
Receiving antiplatelet or anticoagulant medication, n (%)	67 (39.2%)
12-lead ECG abnormalities on presentation, n (%) (Sinus Bradycardia, 1st degree AV block, Bifascicular block, Atrial Fibrillation, Left Anterior Fascicular Block ,Right Bundle Branch Block, Left Bundle Branch Block, n Incomplete Right Bundle Branch Block, Left Ventricular Hypertrophy, Ischaemic Changes, T-wave inversion, Prolonged QT, Early Repolarization, remature Atrial Contractions, Premature Ventricular Contractions, Paced)	74 (43.3%)

[1]Prodromes included symptoms such as dizziness, nausea, sweeting, abdominal pain, shortness of breath, palpitations, difficulty in maintaining body stature, tinnitus etc or a combination of the above symptoms.[2]Predisposing factors included situations such as psychological stress, acute pain, long-standing, post-prandial period, post urination/defecation period, standing, hot or crowded environment.[3]Valvular heart disease included 5 patients with moderate aortic or mitral regurgitation, 2 patients with bioprosthetic aortic valve, 3 patients with mechanic aortic valve and 1 patient with mechanic mitral valve.[4]Atrial Fibrillation was permanent in 22 cases and paroxysmal in 6 cases. One patient underwent ablation 8 years prior presentation.

Table 2. Additional Tests performed after initial evaluation with History, Clinical examination and ECG.

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Test performed	Population (n=171)
Carotid Massage, n (%)	58 (33.9%)
Active Standing, n (%)	171 (100%)
Haematology/ Biochemistry, n (%)	171 (100%)
Echocardiogram, n (%)	171 (100%)
Left Ventricular Ejection Fraction	54 ± 10 %
ECG Monitoring, n (%)	24 (14%)
24-hour ambulatory ECG recording, n (%)	171 (100%)
Treadmill ECG stress test, SPECT or stress echo test, n (%)	42 (24.6%%)
Coronary Catheterization, n (%)	12 (7.2%)
Tilt Table Test, n (%)	26 (15.2%)
Electrophysiological Study, n (%)	13 (7.6%)
Implantable Loop Recorder insertion, n (%)	154 (90.1%)
Central Nervous System Computerised Tomography and/or Magnetic Resonance Imaging performed for syncope investigation, n (%)	4 (2.3%)
24-hour Ambulatory Blood Pressure Monitoring (24hABPM), n (%)	6 (3.5%)

Our study population was characterised by a high incidence of comorbidities such as arterial hypertension (62%), diabetes mellitus (15.2%), dementia (8.2%), history of cancer (5.3%), history of thyroid disease (19.3%), prior stroke (3.5%), moderate carotid disease (6.4%), Parkinson disease (3.5%) and prostate hyperplasia on medication (7.1%). In addition, presence of preexisting heart disease, mostly ischaemic heart disease (17.5%), atrial fibrillation (16.4%) and significant valvular heart disease (6.4%) was not uncommon. Polypharmacy was present, as only 7 of the 171 patients did not receive any medication at all. Interestingly, the incidence of patients receiving medication affecting coagulation (i.e. either antiplatelets or anticoagulants) was 39.2%.

Presentation without prodromes was not rare, as prodromes were recorded in 114 patients whereas 1/3 of the patients (n=57) did not report prodromals. On the other hand, most of the patients (81.9%) experienced syncope without reporting a recognizable triggering factor. Moreover, syncope at supine or sitting position was common (9.9% and 53.2% respectively). Furthermore, presence of palpitations was not uncommon (14.6%). Importantly, elderly patients reported a high incidence of injury in our study of 74.3%, including head injury and limb fractures. Finally, patients were commonly presenting with electrocardiographic abnormalities (43.3%). During the initial assessment, all patients (100%) underwent an active standing test, revealing orthostatic hypotension in 21 subjects (12.3%), however this drop of arterial pressure was not accompanied by symptoms in any of the subjects, and history of syncope during rising from supine to standing position was not present. Moreover, Carotid Sinus Massage (CSM) was performed in 58 subjects (33.9%), where it was considered clinically relevant. In 12 subjects the diagnosis of carotid sinus hypersensitivity was established, albeit without reproduction of symptoms in any case. CSM was insignificant in the other 46 cases.

Furthermore, ambulatory 24-hour ECG monitoring was performed in all (100%) cases, being insignificant in 68 individuals (39.8%) and had minor, albeit not pathognomonic, findings in the rest of 103 patients. Common findings were the presence of atrial or ventricular extrasystoles and runs of supraventricular or non-sustained ventricular tachycardia as well as a low mean heart rate. Admission in the hospital wards and continuous monitoring was performed in 24 cases without significant findings. A transthoracic echocardiogram was prescribed in all 171 patients or performed

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in our laboratory, in order to assess the structural condition of the heart. In none of the 171 patients was echocardiography diagnostic for syncope in our cohort, however it did play a pivotal role for selecting the subsequent diagnostic steps.

More than 2/3 of the patients in our study group (n=116, 67.8%) were considered to be 'high-risk' according to the risk stratification process and they were subsequently stratified in the 'cardiac pathway' whereas the remaining 55 were 'low-risk' and were stratified in the 'autonomic pathway'. Tilt Table Test was performed in 26 patients (15.2%), in 10 of which it was considered to be diagnostic, revealing cardioinhibitory reaction in one patient, vasodepresive reaction in 6 subjects and a mixed cadioinhibitory/ vasodepresive reaction in 4 cases. Typical symptoms were reproduced during the test in all 10 cases. Electrophysiological study was performed in 13 patients (7.6%). Abnormalities such as an HV interval >70ms, a prolonged corrected Sinus Node Recovery Time (cSNRT) and an atrioventricular block occurring early during fast atrial pacing were recorded. Programmed ventricular stimulation (PVS) was performed in these patients with a protocol that included an eight-beat drive train at a cycle length of 550ms followed by two and three extrastimuli sequentially. The procedure was repeated using a drive train at a cycle length of 400ms. In 3 individuals with ischaemic heart disease PVS resulted in the induction of ventricular tachycardia. In 2 other subjects with bifascicular block, HV interval was significantly prolonged and an early 2:1 atrioventicular block was induced during pacing. One of these 2 patients had additionally a prolonged cSNRT with secondary pauses recorded post-pacing.

In our study population, most of the participants eventually underwent an ILR implantation (154 of 171 patients, 90.1%). There were no ILR implant-related complications. In 66 cases, an ILR based diagnosis was established, in most of the cases accompanied with re-appearance of symptoms of syncope or pre-syncope. In these 66 cases with an arrhythmic cause, 9 patients were recorded with tachycardia (6 with atrial fibrillation, 1 with supraventricular tachycardia and 2 with ventricular tachycardia) and 57 with bradycardia (32 with conduction disorders and 25 with sinus arrest). In another 42 patients the ILR critically assisted diagnosis: More specifically, in 22 cases, the patients reported reproduction of symptoms and a history compatible with vasovagal syncope, without electrocardiographic abnormalities on ILR recordings, thus suggesting the presence of reflex syncope. In 10 cases, reproduction of symptoms was related to rising from the supine position in patients with significant arterial pressure drop during active standing and no electrocardiographic abnormalities on ILR recordings, suggesting orthostatic hypotension. In 8 cases, one or more fall episodes occurred during upright position or walking without electrocardiographic abnormalities on ILR recordings and no significant arterial pressure reduction during active standing, and thus a drop was suggested. One patient was diagnosed with epilepsy and experienced an episode of loss of consciousness with myoclonus and no electrocardiographic abnormalities on ILR recording during the episode. Finally, one patient with implanted ILR showed electrocardiographic abnormalities on ILR recording during an episode of fall and sustained dizziness, however he was diagnosed with significant hyponatraemia and hypokalaemia.

Primary endpoint: determining the cause of syncope and the diagnostic yield of the investigation strategy

Minimum follow-up time was 12 months, ranging between 12 and 82 months. Mean follow-up time was 40.5 ± 20 months. Investigation resulted in a final diagnosis in 126 of 171 patients (73.7%) whereas in 45 patients a certain diagnosis was not established (**Table 3**, **Figure 1**). In 71 of the 126 patients the diagnosis was cardiac syncope (56.4%), based on the ILR recording (n=66) and the findings from the EPS (n=5). Thirty-three patients were diagnosed with vasovagal reflex syncope (26.2%), based on the history and TTT (n=10) as well as ILR (n=22) findings. In 10 patients, orthostatic hypotension was assumed to be the cause (7.9%) according to the history, findings from the active standing test and exclusion of arrhythmic causes at the ILR recording. In addition, a non-syncopal cause was diagnosed in 12 patients (9.5%). In this subgroup, in 8 patients the fall was attributed to a drop due to the history of falling without total loss of consciousness at standing/walking position, multiple comorbidities and exclusion of arrhythmic causes at the ILR recording, in 2 patients epilepsy

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was diagnosed (in one patient the diagnosis was supported by an implanted ILR), one patient had persistent hyponatraemia and hypokalaemia (the diagnosis was also supported by an implanted ILR) and in one patient pulmonary embolism was eventually diagnosed. In all patients in whom syncope remains unexplained an ILR has been implanted (**Figure 2, Table 3**).

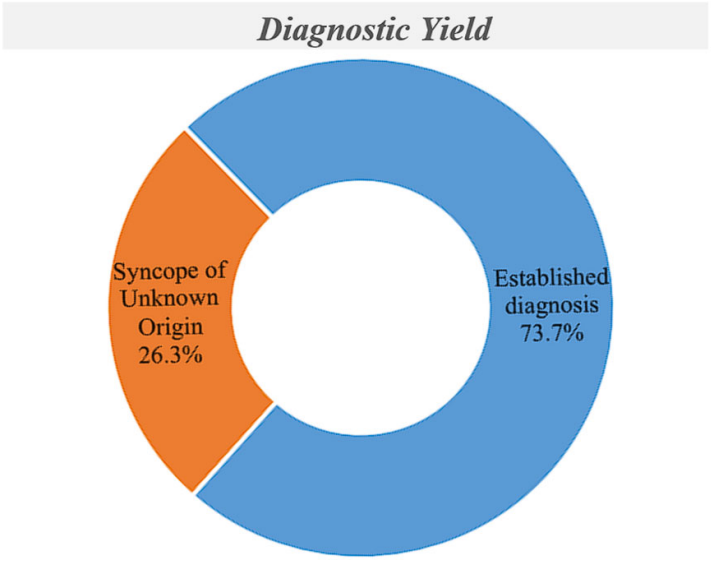

Figure 1. Diagnostic Yield of the investigational process followed in the Syncope Unit in the elderly population, ≥ 65 years-old.

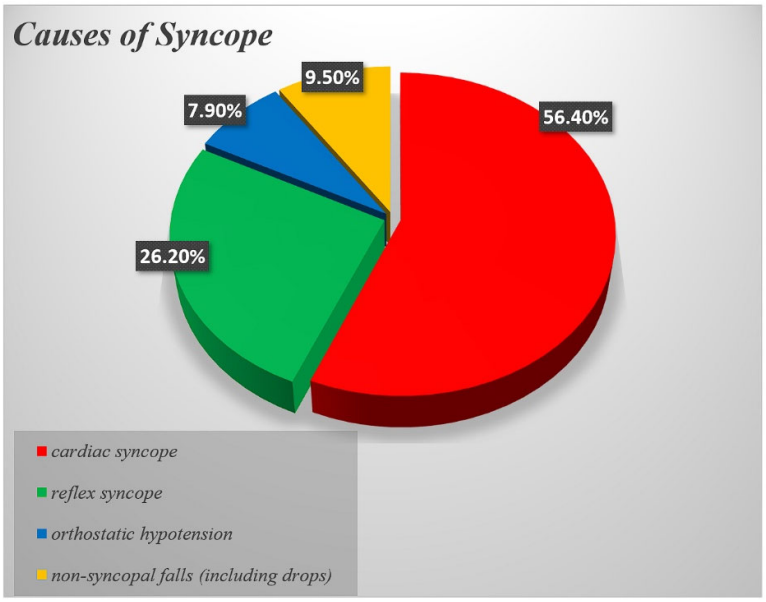

Figure 2. Causes of syncope in the elderly population (i.e. ≥ 65 years-old) of the Syncope Unit.

Table 3. Diagnostic yield and time to diagnosis.

	Population (n=171)
Mean Follow-up time, m	40.5 ± 20
Established final diagnosis, n (%)	126 (73.7%)

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Cause of syncope, n (%)	
• **Reflex**	**33 (26.2%)**
• *cardioinhibitory*	*1 (3%)*[1]
• **Cardiac**	**71 (56.4%)**
• *Bradycardia*	*59 (83.1%)*[2]
• *Tachycardia*	
• *AF*	*6 (8.5%)*[2]
• *SVT*	*1 (1.4%)*[2]
• *VT*	*5 (7.0%)*[2]
• **Orthostatic Hypotension**	**10 (7.9%)**
• **Other (Non-syncoptic)3**	**12 (9.5%)**
Established ECG-based diagnosis, n (%)	67 (53.2%)
Time to final-diagnosis, months	4.8 ± 3.3

AF: Atrial Fibrillation; SVT: Supraventricular Tachycardia VT: Ventricular Tachycardia;[1]Calculated as a proportion of Reflex syncope[2]Calculated as a proportion of Cardiac syncope[3]Other causes included: 8 patients with drops, 2 patients with epilepsy, 1 patient with persistent hyponatraemia and hypokalaemia and 1 patient with pulmonary embolism.

Secondary endpoints

The mechanism of cardiac syncope was most commonly bradycardia; long sinus pauses suggesting sick sinus syndrome or long pauses due to atrio-ventricular block. An ECG-diagnosis, performed by means of a loop recorder, was established in 66 of 71 individuals eventually diagnosed with cardiac syncope. Moreover, a cardioinhibitory event recorded with an ILR, in one of the 33 patients with Reflex syncope confirmed diagnosis. In total, an ECG-based diagnosis occurred in 67 of the 126 individuals (53.2%) (**Table 3**).

Time-to-diagnosis varied significantly; however, final diagnosis was established during a mean 4.8 months after the first visit at our Syncope Unit (**Table 3).**

During a mean follow-up time of 40.5 months a relapse of syncope occurred in 8 of the 71 patients with cardiac syncope (11.6%), 12 of the 33 patients with reflex syncope (36.4%) and in 4 of the 10 patients with orthostatic hypotension (40%).

Finally, in the 154 patients with an ILR inserted, a variety of arrythmias were recorded, that were considered non-relevant to the diagnosis. These arrythmias included, a significant burden of premature ventricular beats of >5%, atrial fibrillation, supraventricular arrythmias, asymptomatic periods of bradycardia <40bpm and single non-conducted P-waves.

Therapy

In the 54 of the 59 patients in whom syncope was attributed to bradycardia a pacemaker was implanted whereas 5 patients declined implantation and are in close follow-up after reviewing of the medical treatment and downgrade of bradycardia-induced medication. Symptomatic atrial fibrillation with rapid ventricular response was recorded in 6 cases and was treated with ablation in 1 case and medically in the remaining 5 cases. Medical treatment was performed with either b-blockers, diltiazem or Ic-antiarrythmics (flecainide or propafenone) or a combination of these drugs. Unfortunately, a relapse occurred in the case of the patient who underwent ablation, that was next treated with pacemaker insertion and atrioventricular junction ablation. In one case a fast supraventricular tachycardia was recorded in the ILR and the patient underwent electrophysiological study and AVNRT ablation. Ventricular tachycardia was recorded in 5 cases, i.e. 3 ischaemic patients

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who underwent EP-studies, 1 ischaemic patient who underwent ILR insertion and 1 patient with Hypertrophic Cardiomyopathy and an ILR. Three patients underwent Implantable Cardioverter Defibrillator (ICD) implantation whereas in two cases a biventricular defibrillator was implanted due to moderate systolic left ventricular dysfunction and co-existing bradycardia/conduction disorders. Of the 33 patients who had reflex syncope, one received a pacemaker, whereas 32 were treated conservatively. Patients with orthostatic hypotension were treated conservatively, without pharmaceutical therapy administration. Moreover, those without true syncopy were treated accordingly. Finally, an additional 4 patients were diagnosed with paroxysmal atrial fibrillation and were initiated on anticoagulation, albeit this arrythmia was considered irrelevant to the cause of syncope.

Discussion

Syncope remains a common problem that has a particularly negative impact on patients' prognosis and quality of life in the elderly. Our data revealed a high incidence of injury of 74.3% in the patients who visited our facility and were over 65-year-old, including head and limb trauma. In addition, syncope represents a challenging clinical entity, due to the wide spectrum of possible causes that could be both benign and potentially life-threatening. The combination of history taking and physical examination, and 12-lead ECG remains the cornerstone for diagnosis.[2] Following initial evaluation, further diagnostic workup of the still unexplained syncoptic episode is based on the classification either to the 'cardiac' or 'autonomic' pathway, utilising a risk stratification algorithm based on clinical judgment. In patients presenting with high-risk features, suggesting cardiac syncope, 'cardiac tests' should be performed as the first step.[11] On the other hand, low-risk patients in whom autonomic, non-cardiac syncope is speculated, should be further investigated in order to identify whether a hypotensive or bradycardic phenotype is responsible for syncope.[11,12] Prolonged ECG monitoring by means of an Implantable Loop Recorder remains the final step of both cardiac and autonomic pathways when the cause of syncope remains unexplained.[11] Furthermore, several studies provide evidence highlighting the importance of dedicated Syncope Units and loop recorders for improving diagnostic yield.[10,14–16]

In our facility, we intend to be as strict as possible in following the above-described strategy, irrespectively of the age of the patient. According to our data, the vast majority (i.e. 116 of 171, 67.8%) of the elderly patients, aged ≥ 65 years, assessed in our Syncope Unit were stratified in the 'cardiac' (high-risk) pathway due to the frequent lack of prodromes or triggers, inadequacy of providing history, amnesia, syncope at supine or sitting position or during exercise, presence of preexisting heart disease, presence of symptoms such as palpitations and presentation with electrocardiographic abnormalities. These patients underwent various tests such as cardiac catheterization (n=12, 7.2%), non-invasive stress tests (n=42, 24.6%) and electrophysiology study (n=13, 7.6%). The remaining 55 patients (32.2%) were stratified in the autonomic pathway, undergoing Tilt Table Test in 26 cases (15.2%), whereas 24-hour blood pressure monitoring was under-utilised (n=6, 3.5%). Irrespectively of the pathway in which the patient was classified, standing test (100% of patients), carotid massage test (33.9% of patients), echocardiogram (100% of patients) and 24-hour ambulatory electrocardiography (100% of patients) were also performed.

An additional finding from our study is the high likeliness of utilizing a loop recorder in this age group. In our study group 154 of the 171 patients (90.1%), eventually, underwent ILR implantation. Similarly to our data, earlier studies had shown that early insertion of an implantable loop recorder is more likely to occur in older subjects and that the ILR, most probably, has a higher diagnostic value in this population.[17,18] In this study the diagnostic yield of the ILR intervention, defined as an ILR-based electrocardiographic diagnosis, was 43% (66 of the overall 154 patients in whom it was implanted). However, importantly, ILR implantation may have an even greater impact and further assist diagnosis by excluding arrythmias in symptomatic patients in whom the ECG is normal during a typical syncoptic event. Of note, in the present study in an additional 42 patients the ILR critically assisted diagnosis by excluding arrhythmic syncope. Overall, in line with other studies [17,19] our

 doi:10.20944/preprints202603.0146.v1

data demonstrate a high diagnostic yield of ILR in elderly patients with unexplained syncope and support assessment with continuous prolonged cardiac monitoring in this population to detect underlying cardiac arrhythmias. Therefore, we may conclude that implantation of an ILR is a safe and effective measure in the investigation of syncope in the elderly population.

Third, an electrophysiological study was performed in 13 elderly patients (7.6%). Despite that several studies have questioned the role of EPS showing a moderate negative predictive value, other authors showed that abnormal ECG findings during non-invasive testing are well correlated with pathognomonic findings in EPS suggesting arrhythmic causes, in patients with undiagnosed syncope.[20,21] Based on our data, we conclude that EPS remains a useful in selected cases, that could potentially assist the investigational process.

Another significant finding from our work is that adoption of a strict algorithmic strategy during investigation in the Syncope Unit, may lead to a high diagnostic yield in this age group. In our study a final diagnosis was achieved in 73.7% of the admitted patients. Moreover, the final diagnosis was cardiac syncope in 56.4% of those patients in whom the investigational process was successful. Therefore, a major finding in this study is that cardiac causes are relatively more common as patients age.

Similarly to other age groups, in the elderly population syncope may be classified as follows [22]:

(a) Reflex syncope, including vasovagal syncope and carotid sinus syndrome. It is considered to be the commonest type of syncope in older adults. In these patients, due to the reduction of the vagal tone, vasodepressor syncope is more common, often occurring without prodromals. In addition, vasovagal syncope may occur under conditions associated with a sudden change of the autonomic tone such as micturition, defecation, exercise, or coughing. Moreover, Carotid Sinus Syndrome is increasingly common at older ages where stiffness of the carotid vasculature is increased due to atherosclerosis and ageing.

(b) Orthostatic hypotension, is also common in the elderly, occurring in up to 30% among patients older than 75 years-old. Underlying autonomic insufficiency, either idiopathic or resulting from comorbid conditions such as diabetes, amyloidosis, or neurological disorders, should be considered in older adults, especially in recurrent syncope. Postprandial syncope (defined as syncope that occurs following a meal) is a common subtype of orthostatic hypotension, attributed to venous pooling in the splanchnic vessels, resulting in reduction of the effective blood volume.

(c) Cardiac syncope, due to arrhythmias or cardiac structural diseases (eg aortic stenosis), is considered to be a less common cause of syncope in older adults compared to reflex syncope; however, it is associated with worse outcomes. The prevalence of bradycardias is increasing with age and may result from medications, sick sinus syndrome, or atrioventricular block, whereas atrial and ventricular tachycardias may also result to syncope through a reduction in stroke volume as a result of incomplete myocardial relaxation and filling.

Previous studies have demonstrated that despite the high incidence of heart disease in the elderly, cardiac syncope does not show increase with age relatively to other causes.[7] In contrast to this perception, in our study, in most of the patients in whom a final diagnosis was achieved, the cause was cardiac syncope (56.4%). Moreover, reflex syncope, orthostatic hypotension and non-syncopal falls (including drops) were the causes in 26.2%, 7.9% and 9.5% of the patients respectively (**Table 3**). Our data suggest that cardiac syncope may be more frequent than previously believed in the elderly population presenting with unexplained syncope. However, we should also appreciate that there is an inhomogeneity in the investigational process of syncope among different health systems. Most of our patients were referred to us at a later stage, having already being investigated in other centers. Therefore, the study population in our facility may not be necessarily a representative sample of the general population although that it is indeed a representative sample of the type of patients referred for further specialised assessment. Our Syncope Unit operates as a tertiary center, and therefore more obvious aetiologies such as carotid sinus syndrome and orthostatic hypotension, may have been identified prior to referral.

 doi:10.20944/preprints202603.0146.v1

An overlap between syncope and drops in older individuals is assumed since amnesia of the event and lack of witnessing the 'fall' event is very common.[19] In the older patients of our study population, mostly in those over 80 years-old, difficulties in obtaining the history of the event were significant. We speculate that a significant subset of the individuals in whom the aetiology remained unidentified probably represent patients with drops and not 'true' syncope. Nevertheless, in line with other investigators [23] we also believe that differential diagnosis among drops and 'true' syncopal causes such as vasovagal syncope, carotid sinus syndrome, orthostatic hypotension and cardiac arrhythmias is challenging if not impossible.

Moreover, we believe that distinguishing between a cardioinhibitory vasovagal reaction and a pause or complete heart block due to sick sinus syndrome or true conduction disorders in the elderly is practically impossible. In most of the cases these findings are characterised as true cardiogenic syncope.

Fifth, our data show that during the mean 40.5 months follow up, the relapse of syncope in those diagnosed with cardiac syncope was dramatically reduced indicating that the initial diagnosis was correct. In those diagnosed with reflex syncope or orthostatic hypotension relapses were also significantly reduced. However, falls did happen in 11.6% of the patients diagnosed with cardiac syncope, a finding that probably indicates the multifactorial mechanism of syncope in elderly patients.

Finally, our data show that, during follow-up by continuous monitoring using ILR, various cardiac arrythmias were detected that were not considered relevant to the cause of the syncoptic episode. However, in some cases the presence of these arrhythmias resulted in treatment interventions, such as in the case of 4 patients diagnosed with paroxysmal atrial fibrillation who received anticoagulation.

The present study has important limitations. First, it is a single-centre retrospective observational cohort study that has recruited a restricted number of participants. Moreover, patients were referred from different facilities (eg primary health-care, cardiology clinics, other medical specialties). Therefore, there was remarkable inhomogeneity regarding the extend of previous investigation with some patients being more extensively investigated than others. Third, the study population may not be representative of the general elderly population, since referrals occurred in already investigated patients. This may have resulted in over-presentation of cardiac syncope cases. The prevalence of cardiac arrhythmia in this cohorts appeared significantly higher, however implication of our findings in other settings, such as in the primary care may not be appropriate. Fourth, despite its emerging significance, 24-hour ambulatory blood pressure monitoring was underutilised in our practice. Furthermore, carotid sinus massage was performed in only 58 subjects (33.9%). Finally, a comprehensive geriatric assessment as well as a cognitive impairment assessment using validated tools such as the mini-mental state examination (MMSE) was not performed.

Conclusions

Syncope remains a common problem with a particularly negative impact on patients' prognosis and quality of life in the older population where, in addition, the cause is often multifactorial. The presence of dedicated Syncope Units as well as the utilisation of modern algorithms has significantly increase diagnostic yield of unexplained syncope. On the other hand, the selective use of ILR represents an effective and safe diagnostic tool that further improves the effectiveness of investigation of a dedicated Syncope Unit, shortening time to final diagnosis and preserving financial resources. According to our data, elderly patients presenting with unexplained syncope are most often classified as high-risk and cardiac syncope may be a more frequent cause than previously believed.

Funding Sources: Hippokration General Hospital is a public hospital receiving financial support from governmental resources. The authors or the Syncope Unit did not receive any additional financial support from any organization and have no financial or non-financial interests to declare.

Conflict of Interest/ Relationship with Industry: The Syncope Unit has received funding from Medtronic, Greece.

 doi:10.20944/preprints202603.0146.v1

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