Review Article

Recurrent transient loss of consciousness in elderly

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To provide physicians with a practical, evidence-based approach to transient loss of consciousness (T-LoC) in the elderly and make a consensus from available research data. Medline, Embase and Cochrane database were searched using terms relevant to T-LoC among the elderly in the community and in institutions. T-LoC is a common and serious health problem with devastating consequences. Several risk factors have been identified in the literature. T-LoC can be prevented through several evidence-based interventions, which can be either single or multicomponent. Proper diagnosis is essential for further management. Physicians should have a rational and evidence-based approach for diagnosis and management of T-LoC patients.

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Key words **: Transient loss of consciousness, elderly, blackout, syncope.**

Blackout is the term commonly used when someone has experienced a sudden loss of consciousness and quickly recovers. Some specialists prefer the technical term transient loss of consciousness (T-LoC). The usual diagnostic dilemma is syncope versus seizure. Since specific therapy depends upon an accurate diagnosis, it is essential for the physician to have a rational approach to the evaluation of this problem. Various guidelines came out in recent years for T-LoC such as National institute Health and Care Excellence (NICE) and Italian Group for the Study of Syncope in the elderly (GIS). Studies suggested that the diagnosis of the underlying cause of T-LoC is often inaccurate, inefficient and delayed. There is huge variation in the management of T-LoC. People experiencing T-LoC may be treated by a range of cliniciansand the lack of a clear pathway may contribute to misdiagnosis and inappropriate treatment. While there was some existing guidance related to T-LoC, for example epilepsy, falls, dual chamber pacemakers and implantable cardioverter defibrillators, guidelines which defined appropriate pathways for the initial assessment, diagnosis and specialist referral were lacking. Such a guideline would help to achieve the correct diagnosis quickly, efficiently and cost effectively, leading to a suitable management plan.

Source of Information :

Medline, Embase and Cochrane database were searched using terms relevant to T-LoC among the elderly in the community and in institutions. Relevant English-language papers published from 1985 to July 2017 were reviewed. Relevant geriatric society guidelines and NICE guidelines were reviewed as well.

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Editorial Comments :

- **In elderly recurrent transient LOC common but may be serious health problem.**
- **Arrythmia, cerebral hypoperfusion, orthostatic hypotension, autonomic failure, metabolic causes have different important etiologies.**
- **Recurrent LOC predict more morbidity and mortality in elderly.**

Epidemiology :

Approximately 3% of urgent visits to the emergency department and 2-6% of hospital admissions are due to syncope or trauma and these patients are aged 65 years or older in 80%.1Incidence of syncope increases exponentially in the elderly and in particular in the 8th and 9th decade of life[2], with an incidence of syncope in an elderly institutionalised population was 6% per year, with a 10-year prevalence of 23% and a recurrence rate of 30%[3]. Hip fractures are one of the most feared consequences of syncope in the elderly, as well as the reduction of functional capacity and hospitalization[4]. Recurrent syncope is associated with fractures and soft-tissue injury in 12% of patients[5]. The mortality for syncope in the elderly, however, ranges between 30% and 50% according to the observation time of follow-up (2-5 years) with a frequency of recurrences in a variable range between 25% and 30%[6]. Unless it is vasovagal, syncope is related to decreased survival[7]. It has been reported that only half of patients over 85 years of age who are hospitalized with syncope surviv e more than 3 years[8].

Etiology and Pathophysiology

Syncope is a T-LoC due to transient global cerebral hypoperfusion characterized by rapid onset, brief duration, and spontaneous complete recovery. Any loss ofconsciousness, even transitory, that does not accurately re?ectthese characteristics, must be considered as "pseudo-syncope" (Table 2). Some pathological conditions, in fact, such as epilepsy, disorders ofmetabolism (hypoxia and hypoglycaemia), and poisoning are characterized by a loss

of consciousness, but in the absence of cerebral hypoperfusion.The differential diagnosis of syncopal T-LoC may be large (Table 1), but bradyarrhythmias, neurocardiogenic syncope, carotid hypersensitivity syndrome, and orthostatic hypotension are the more frequent causes. Primary bradyarrhythmias are mainly due to sinus and atrial node dysfunctions. Sick sinus syndrome is a prototype of such arrhythmias in the older adult and is a main cause for syncope. Neurocardiogenic syncope is due to a sudden sympathetic failure with cardioinhibitory and/or vasodepressor response. It is often preceded by typical "vasovagal symptoms," such as flushing, nausea, and sweating, though older patients frequently do not have such prodromal symptoms. Carotid hypersensitivity is an exaggerated response to carotid sinus stimulation. In one report, almost half of cognitively normal older patients who had experienced non-accidental fall were diagnosed with carotid hypersensitivity[9]. Orthostatic hypotension(OH) is due to a failure of the autonomic nervous system and related cardioregulatory mechanisms. Autonomic failure is mainly due to neurodegenerative disorders, such as multiple system atrophy or Parkinson's disease and diabetes etc. Comorbid conditions such as anemia, any organ failure, and metabolic anomalies can act synergistically to exacerbate syncopal symptoms. Especially important in this respect are the prescription and nonprescription drugs patients take. Through their pharmacological effects and potential for interaction, many drugs may be causally involved in syncope[10]. Severe metabolic disorders can be induced by a number of medications such as steroids, nonsteroidal antiinflammatory drugs, and hypoglycemic agents. Psychoactive agents have been shown to aggravate fall propensity[11].

Diagnostic Pitfalls in T-LoC :

There are certain critical issues that contribute to uncertainty in the diagnostic evaluation such as amnesia for LoCand cognitive impairment makes the acquisition of an accurate history difficult.Gait and balance instability and slow protective reflexes are frequent in older people; in these circumstances moderate haemodynamic changes insufficient to cause syncope may result in falls.It is important, therefore, to make every attempt to obtain a witness account of episodes, although this may not be available in many instances.

In clinical practice, the most common pitfalls in the investigation of syncope are:

- Not spending enough time on the history, including from an eyewitness
- Not clearly differentiating patients with and without structural heart disease
- Doing unnecessary tests (eg, 24-hour Holter monitoring in people with healthy hearts)
- Doing a computed tomography (CT) brain scan, which is not a test for syncope.
- Getting side-tracked by incidental findings, especially in older people.

Table 1 — *Causes of transient loss of consciousness*

Acute illness (causingsyncope)	Syncope attacks	Non-syncopal
• Infection • Acute coronary syndromes • Bleeding • Dissection of the aorta • Pulmonary embolism	•Neurally mediated • Orthostatic • Cardiac arrhythmias • Structural	• Seizure • Hypoglycaemia • Intoxication • Vertebrobasilar migraine or transient ischaemic attack • 'Found lying on floor'

Table 2 — *Causes of Pseudo-syncope : Pseudo-syncope according to the guidelines of the European Society of Cardiology*

With loss of consciousness	Without loss of consciousness
• Epilepsy • Metabolic disorders (hypoxia, hypoglycemia, hypocapnia by hyperventilation) • Poisoning • Vertebrobasilar transient ischemic attack	• Falls • Cataplexy • Drop attacks • Carotid transient ischemic attack

Diagnosis of Syncope in the Elderly :

History-taking in patients with syncope can be difficult, time consuming, and imprecise.12 Some arrhythmias are transient and thus difficult to document. Certain evaluations such as carotid sinus massage and upright blood pressure measurements are frequently not performed and others such as external or internal loop monitoring are not readily available. Consequently, misdiagnosis is frequent and up to 40% of syncopes remain unexplained[8,13,14]. The GIS, by applying the diagnostic algorithm of the European Society of Cardiology (ESC)[1], performed a diagnostic screening in a elderly population[14] (Fig 1). This approach reveals many of those cases considered to be due to unexplained syncope, reducing the prevalence of these to only 10%.

The Diagnostic Algorithm of T-LoC :

First level evaluation

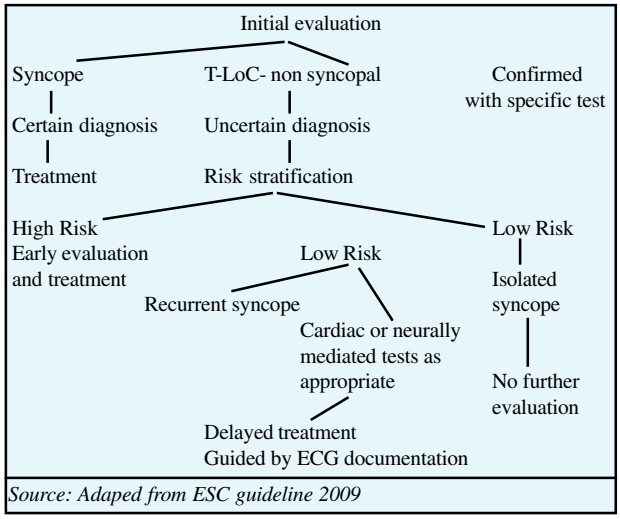
The initial approach to an elderly patient with syncope should take into account three main questions, which should guide the whole diagnostic process:

(1) Has the loss of consciousness a syncopal origin, or is it a syncope-like condition?

(2) Is there heart disease?

(3) How is the history of syncope?

Once detected, the likely origin of syncopal T-LoC is determined through the initial assessment as the key moment in the diagnosis of syncope, especially in elderly. Evaluation of the T-LOC patient starts with a proper history, especially in the older adult. Special attention should be taken to characterize the circumstances and symptoms surrounding the syncope and to get the family's version of the event. A careful and meticulous review of all cardiovascular and neurologic symptoms should be undertaken. All drugs and dosages should be assessed and re-evaluated.The physical examination should be complete



Source: Adaped from ESC guideline 2009

Fig 1 — Algorithm for transient loss of consciousness (T-LoC)-suspected syncope

and thorough. Lying and upright blood pressure and heart rate measurements (at 1, 3, and 5 minutes) will easily detect OH due to dysautonomia. Significant aortic stenosis can almost always be detected with auscultation.Laboratory tests should include basic biochemistry, complete blood count, and electrocardiography. Myocardial ischemia and pulmonary embolus are urgent conditions that should be assessed for with the appropriate testing algorithms. Echocardiography should be ordered when structural cardiac or cardiopulmonary disease is suspected. Carotid sinus massage should be done, provided there are no carotid bruits or known carotid atherosclerotic disease (complication rate <1%)[15]. It should be performed with continuous electrocardiographic recording and, ideally, during tilt table testing with a beat-to-beat pressure monitor. A drop in blood pressure of 50 mmHg or an asystole of 3 seconds or more is diagnostic of carotid hypersensitivity syndrome or, less frequently, sick sinus syndrome. The deep breathing test and a 12-second 40 mmHg Valsalva manoeuvre are bedside procedures that can be performed easily. They may help to identify sinus node incompetence or autonomic failure. The basic purpose of the first level evaluation is to identify patients at risk for cardiogenic syncope, which always has a worse prognosis than the other causes, regardless of age[2,4,6].

Risk stratification in the diagnosis of T-LoC :

A score to predict the risk of cardiac syncope and mortality from the initial assessment was recently validated as derived from the results of the study "Evaluation of Guidelines in SYncope Study 2" (EGSYS 2)[16]. The EGSYS 2 risk score is a method of risk stratification that considers independent clinical predictors of cardiogenic syncope: the abnormal ECG and/or the presence of heart disease, the presence of palpitations prior to syncope, a syncopal episode during exertion or supine, the absence of neuroautonomic prodromes, and the absence of precipitating factors. To each of these variables a score is assigned; a total score of three or more is indicator of cardiogenic syncope. Thus, prodromal symptoms seem to represent a critical point of syncope diagnosis. However, the GIS study has given us important information about the presyncopal prodromal symptoms in the elderly which can predict the type of syncope and address the early diagnosis towards cardiac or non-cardiac etiology. In particular, the presence of nausea, blurred vision, sweating, and premonition of fainting directs the diagnostic suspicion towards a non-cardiac syncope, whereas the presence of dyspnea points towards a cardiac syncope[17].

The Diagnostic Algorithm of T-LOC:

Second level Investigations :

When the initial assessment suggests "pseudo-syncope" diagnostic tests, such as a cranialCT, a Doppler ultrasound of the carotid vessels, or an electroencephalogram (EEG) should be performed. In particular, the CT scan should be performed only in the presence of head injury secondary to the fall, as the EEG, simple or after sleep deprivation, should be reserved only for patients with suspected epileptic nature of loss of consciousness.

Suspected Diagnosis of Cardiac Syncope :

When in the initial assessment there are elements which lead to a syncope of cardiac origin, echocardiography is mandatory and crucial, especially in the presence of aortic stenosis, a dilated or hypertrophic cardiomyopathy, and a pulmonary embolism[18]. In patients with suspected arrhythmic etiology, who have frequent episodes of loss of consciousness or palpitations shortly prior to a syncope episode, only rarely is a dynamic ECG Holter electrocardiogram diagnostic. The ECG Holter, in fact, is diagnostic only in the rare cases in which an event occurs during syncope or presyncope during recording. The presence of a causal association between arrhythmia and symptoms has been demonstrated only rarely; this test may be useful in patients with psychogenic syncope and the demonstration of a normal rhythm during the loss of consciousness can have a good predictive value for excluding a real syncope.1 Electrophysiologic testing may be required to further evaluate life-threatening tachyarrhythmias. Noninvasive loop monitors can be worn for up to 4 weeks and are of relevance for arrhythmias with intersymptom intervals of less than 4 weeks. Invasive loop monitors can be installed for months and have been shown to be the best and most cost-effective diagnostic tool for unexplained syncope. In a recent trial, prolonged (1 year) invasive loop monitoring resulted in a diagnosis rate of 55% compared with 19% for conventional testing[19]. An exercise test is indicated in the case of syncope on exertion, when there is a suspicion of ischemic heart disease. In carefully selected cases in which the suspicion of ischemic syncope is very strong

coronary angiography may be indicated[1].

Suspected Diagnosis of Neurally-mediated Syncope :

When the initial investigation, however, oriented towards a neurally-mediated syncope, as well as when the ?rst-level tests are negative, the diagnostic procedure involves the carotid sinus massage in supine and standing positions, the Tilt Table Test (TTT)[20] and, in selected cases, ambulatory monitoring of blood pressure over 24 hours, which is especially useful in the case of postprandial or night hypotension. The carotid sinus massage is the other instrumental examination of great importance in the diagnosis of neurally-mediated syncope in the elderly; the ESC guidelines propose its performance in examinations of the first level, given the high prevalence of carotid-sinus syndrome as a cause of unexplained syncope and falls in this age group. Carotid sinus massage should be performed only by an experienced physician with electrocardiogram control and after objective and/or sonographic exclusion of carotid atherosclerosis[21]. Contraindications to carotid sinus massage are the presence of carotid bruits, recent myocardial or cerebral ischemia, or previous ventricular tachyarrhythmias. The TTT is the test of greater clinical use for the evaluation of neuromediated reflexes. There are several protocols for the performance of the TTT, but the most popular is enhanced with nitroglycerin, also validated in the elderly by the GIS.22Heart rate reduction with asystole > 3 seconds in TTT is a relative indication to the implantation of a cardiac stimulator[1].

Orthostatic Syncope :

OH is an attributable cause of syncope in up to 30% of older patients. In symptomatic patients, 25% have 'age-associated' or idiopathic OH. OH and related-orthostatic syncope are frequent clinical problems among elderly patients, associated with significant morbidity and mortality[23]. Acute OH is usually secondary to medication, fluid or blood loss, or adrenal insufficiency. By contrast, chronic OH is frequently due to altered blood pressure regulatory mechanisms and autonomic dysfunction. It is very important to exclude diagnoses of neurodegenerative diseases, amyloidosis, diabetes, anaemia, and vitamin deficiency as causes of OH. Elderly patients with symptoms often benefit from a stepped approach with initial non-pharmacological interventions, including avoidance of potentially hypotensive medications and the use of physical counter manoeuvres. Successively, several pharmacotherapeutic agents can be added, including vagolytic substances, such as disopyramide, fludrocortisone, midodrine, and nonsteroidal anti-inflammatory drugs. With a proper evaluation and management, the occurrence of adverse events, including falls, fractures, functional decline, and myocardial ischemia, can be significantly reduced.

Non-Syncopal Causes of T-LoC :

Any loss ofconsciousness, even transitory, that does not accurately reflectcharacteristics of syncope, must be considered as "pseudo-syncope".Some pathological conditions, in fact, such as epilepsy, disorders ofmetabolism, and poisoning are characterized by a loss of consciousness, but in the absence of cerebral hypo perfusion. Differentiation of seizure from syncope is very difficult but thorough history both from the patient and eyewitnesses, prodromal symptoms and relevant investigations can differentiate both the condition.

Paroxysmal Spells and Syncope :

In cases when syncope is still unexplained after testing, psychiatric causes should be sought. Anxiety, panic attacks, depression, and alcohol and drug abuse may explain symptoms in many patients. Paroxysmal spells are non-epileptic, paroxysmal events that may mimic epileptic seizures but are not associated with rhythmic discharges of cortical neurons typical of seizures[24]. They clinically manifest as a T-LoC, often occurring suddenly, with or without a prodrome. Hyperventilation manoeuvres are easy to perform and may be diagnostic. Therapy directed at these causes has been shown to decrease the incidence of syncope.

Treatment of T-LoC in the Elderly :

A proper treatment of T-LoC in the elderly requires an accurate diagnosis. In cardiac syncope, both with organic disease (eg, severe aortic stenosis) and arrhythmias (eg, sinus node disease), the therapeutic indication are unique: valve replacement in the case of aortic stenosis and cardiac stimulator in case of sinus node disease[1]. The treatment of neurally-mediated syncope in elderly patients, however, deserves particular attention. In this regard, it should be stressed that this type of patient presents age-related alterations that make one more vulnerable to this type of syncope and which may significantly influence the effectiveness of therapeutic aids adopted[6,17]. The classic dietary and behavioral approaches indicated in the treatment of neurally mediated syncope (to avoid extreme heat, crowded places and prolonged standing, to increase ?uid intake and salt, to use elastic stockings, to make counter-pressure maneuvers), sometimes overlooked, are to be used early in the elderly[1]. The drug history plays a key role in the management of elderly patients. Sympathomimetic drugs such as midodrine, methylphenidate and etilefrine were completely ineffective in the treatment of vasovagal syncope[25]. Similarly, betablockers are not effective, whereas antidepressants such as paroxetine achieved significant results, even if the data has not been confirmed yet. In some selected cases, the effectiveness of disopyramide, an antiarrhythmic drug with anticholinergic effects, in the prevention of neurally mediated syncope, has been demonstrated. Finally, fludrocortisone, a corticosteroid with marked sodium-retentive activity, has been used successfully in recurrent neurally-mediated syncope. The efficacy of cardiac pacing in preventing syncopal recurrences in patients with neurally-mediated syncope is controversial. In the Third International

Study on Syncope of Uncertain Etiology (ISSUE-3) trial, the 2-year estimated syncope recurrence rate was 57% with pacemaker OFF and 25% with pacemaker ON. The risk of recurrence was reduced by 57%. Thus, dual-chamber permanent pacing is effective in reducing recurrence of syncope in patients 40 years old with severe asystolic neurally-mediated syncope and 57% reduction in syncope recurrence supports this invasive treatment for the relatively benign neurally mediated syncope[26]. Finally, the treatment of syncope in elderly, especially neutrally mediated treatment, is accomplished through a "multiple" approach in order to resolve the various pathogenetic components characteristic of the elderly patient[27].

Conclusions :

Transient loss of consciousness in the elderly is common and is of considerable clinical significance. Since specific therapy depends upon an accurate diagnosis, it is essential for the physician to have a rational approach to the evaluation of this problem. Diagnostic algorithms should be applied with attention, although unknown syncope is still frequent. The therapeutic approach to syncope in the elderly is complicated by the high prevalence of neurally-mediated syncope, in which the therapeutic approach is largley unknown. Unexplained syncope is common but can be decreased by a multidisciplinary approach and the use of various diagnostic procedures. Many therapeutic modalities have been shown to be beneficial. They should be used whenever possible because they can significantly improve symptoms and quality of life, if not survival.

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