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ORIGINAL COMMUNICATION

The prevalence and characteristics of patients with classic locked-in syndrome in Dutch nursing homes

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Abstract To establish the point prevalence and characteristics of patients with locked-in syndrome (LIS), particularly of the classic type, residing in Dutch nursing homes, a cross-sectional survey of Dutch nursing homes was conducted. The classic form of LIS was defined according to the criteria of the American Congress of Rehabilitation Medicine (1995). All Dutch long-term care organisations ($n = 187$) were asked if they had any patients with classic LIS as of December 5, 2011. The treating Elderly Care Physicians were then contacted to provide patient characteristics. Of all organisations, 91.4 % responded, and 11 organisations reported a total of 12 patients. After analysing the questionnaires, it was determined that ten patients had LIS, and two patients were characterised with vegetative state. Only two patients met the criteria for classic LIS, while six patients showed partial LIS. One of these patients was admitted to the nursing home after December 5, 2011, and was therefore, excluded. LIS without accompanying pontine lesion was observed in the remaining two patients. For the first time, the prevalence of classic LIS has been established at 0.7/10,000 somatic nursing home beds in all Dutch long-term care organisations. Possible explanations for this low prevalence could be the Dutch provision of home care or the influence of end-of-life decisions, such as euthanasia and withholding or withdrawing all medical treatment, including artificial nutrition and hydration. These alternate outcomes should be explored in further studies.

Keywords Locked-in Syndrome · Prevalence · Nursing home · Paralysis · Long-term care

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Introduction

Locked-in syndrome (LIS) was first defined in 1966 and is a condition in which patients are awake and conscious but are unable to develop speech or limb or facial movements [1]. According to the criteria of the American Congress of Rehabilitation Medicine (1995), LIS is defined by the presence of sustained eye opening, preserved basic cognitive abilities, aphonia or severe hypophonia, quadriplegia or quadriparesis and a primary mode of communication that uses vertical or lateral eye movements or blinking of the upper eye lids [2].

There are three types of LIS: classic, incomplete and total. Patients with the classic type have quadriplegia and anarthria with preserved consciousness, vertical eye movements and blinking. The incomplete type is the same as the classic type, but with remnants of voluntary movements other than vertical eye movements (such as thumb, finger, neck and head movements). Total LIS is defined by full consciousness and total immobility including all eye movements [3].

In most cases, LIS is caused by a bilateral ventral pontine lesion [1, 4]. A mesencephalic lesion is also possible, but it is rare [3, 5]. Basilar artery occlusion or pontine haemorrhage vascular pathologies are the most common aetiology (86 %) [6]. According to a survey of 44 LIS patients by the Association of Locked-in Syndrome (ALIS)

in France, the most frequent cause of LIS is stroke (86.4 %). Traumatic brain injury is the second-leading cause of LIS (13.6 %), usually resulting in LIS after basilar artery dissection [7, 8]. The syndrome can also be secondary to a subarachnoid haemorrhage, brain stem tumour, central pontine myelinolysis or pontine abscess [9–12]. Transient forms of LIS are very rare and could be the result of a posterior fossa subdural hematoma, a silent aortic dissection or a central pontine and extrapontine myelinolysis [13–15].

Classic LIS is characterised by quadriplegia. Other symptoms include anarthria and bilateral horizontal gaze paresis. Anarthria is caused by facio-glossopharyngo-laryngeal paralysis, which also causes dysphagia and limits the use of facial expression in communication [16, 17]. Sensation is preserved because of spared spinothalamic tracts, which lie dorsal to the pontine lesion [18]. Patients usually retain upper eyelid control and vertical eye movements because the mid-brain tectum is spared, which allows for limited communication [17].

The diagnosis is usually made at approximately the middle of the second month following onset. In 55 % of cases, a family member is the first person to realise that the patient is conscious and can communicate through eye movements [7]. Magnetic resonance imaging (MRI) may show isolated lesions, bilateral infarction, haemorrhage or a tumour of the ventral portion of the pons or midbrain [19]. Electroencephalograms (EEGs) may be normal or abnormal with mostly slowing over the temporal or frontal leads, more diffuse slowing, or cortical resting state rhythms [4, 20, 21]. Positron emission tomography (PET) studies reported preserved metabolic brain levels of LIS patients compared to patients in a vegetative state and to healthy controls. LIS showed dysfunction only in infratentorial regions [22–24].

(Classic) LIS is not a disorder of consciousness, but can be confounded with these disorders if voluntary vertical eye movements are not discovered. This could lead to misdiagnosis if a patient is erroneously considered to have a disorder of consciousness [25]. To establish the prevalence of LIS, it is important to distinguish classic LIS from those disorders of consciousness, particularly coma, unresponsive wakefulness syndrome (the new name for vegetative state) and minimal conscious state. Coma is defined as the absence of consciousness with closed eyes and without reactions [26]. A patient with an unresponsive wakefulness syndrome is awake with open eyes, but is not aware of himself or his surroundings [27]. The minimal conscious state (MCS) is a condition of severely altered consciousness, in which minimal but definite behavioural evidence of self or environmental awareness is demonstrated. Effective communication, however, is not possible [28]. Recently, a subcategorization of MCS patients into "MCS minus" (MCS−) and "MCS plus" (MCS+) has been proposed based on their behaviour. MCS− describes patients with minimal level of behavioural interactions without command following, whereas MCS+ patients show higher-level behavioural responses such as command following [29].

In LIS, recovery of speech and voluntary head and limb movements can be observed. Since its creation in 1997, ALIS registered French LIS patients and according to this database, patients showed moderate to significant recovery of head movement, small degrees of movement in one of the upper limbs and small movements in the lower limbs. There was also recovery of some speech production and vocalisation of unintelligible sounds [6]. In a consecutive sample and follow-up study of 14 LIS patients in whom time from syndrome onset ranged from 5 months to 6 years, significant motor recovery was observed within 3–6 months after initiation of early and intensive multidisciplinary rehabilitation [30]. In an 11 year follow up cohort study, the physical impairments remained substantial, and only a few subjects progressed to the point where they could manipulate an object. None of the patients could speak in sentences, and most could not speak a single word consistently. In the same cohort, the use of tracheostomies and feeding tubes decreased eight- and four-fold, respectively, over time [31].

Once a patient is medically stable for more than a year, the 5-year and 10-year survival rates are 83 %, and the 20 year survival rate is 40 % [31]. According to data from 250 patients in the ALIS database, the mean duration of LIS is 6 years, with a range from 14 days to 27 years [6].

Prevalence is influenced by mortality, which is high in acute LIS. 87 % of acute LIS patients die within the first 4 months of onset [4]. Common causes of death are pneumonia (40 % of cases), brain stem stroke (25 %), recurrent brain stem stroke (10 %), refusal of artificial nutrition and hydration (10 %) and other causes including cardiac arrest, cardiac failure, and hepatitis [6].

In chronic LIS, the level of patient care remains extensive, complex, multidisciplinary and primarily long-term. In a study of 50 surveyed patients, most (28) received nursing care two times a day, 66 % had physical therapy at least five times a week, and speech therapy was performed at least three times a week for 55 % of the patients [6]. Nursing homes in the Netherlands, especially the somatic ones, specialise in this type of complex long-term care, which makes them suitable participants for a survey.

Special circumstances in the Netherlands provide an excellent opportunity for a prevalence study, as there are more than 180 long-term care organisations spread throughout the country that serve a population of 16.7 million people. These organisations provide long-term care in more than 480 nursing homes, with an estimated 72,000 total beds [32]. These nursing homes are specialised in

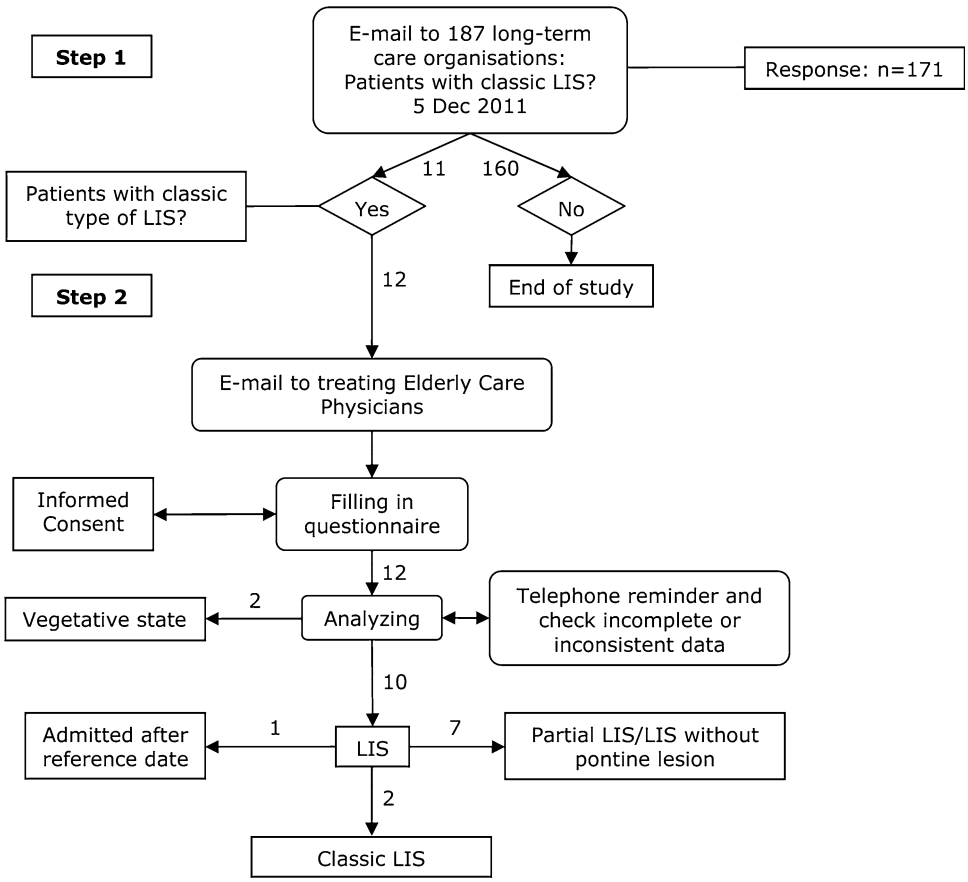

Fig. 1 Flow chart of research design

somatic (41.6 %) or psychogeriatric (58.4 %) long-term care [33]. Patients with chronic somatic or psychogeriatric conditions who require intensive care and who are unable to live at home are admitted to the somatic wards of nursing homes or to the dementia special care units. Professional care is provided by multidisciplinary teams, which are led by an elderly care physician (ECP). Elderly Care Physicians are nursing home physician specialists who are trained in a 3-year academic specialist training program. This training program only exists in the Netherlands [34].

Because the prevalence of LIS, and of the classic type in particular, is unknown in nursing homes, this study aims to establish the prevalence and characteristics of patients with classic LIS in Dutch nursing homes.

Methods

We conducted a cross-sectional survey in all Dutch somatic nursing homes that covered a total of approximately 30,000 beds (Fig. 1). December 5, 2011 was the reference date for establishing the point-prevalence.

Classic LIS was defined according to the criteria of the American Congress of Rehabilitation Medicine (1995).

Inclusion criteria were quadriplegia, anarthria, vertical eye movements on request, eye blinking on request, and a pontine lesion detectable by magnetic resonance imaging (MRI) or computed tomography (CT). Exclusion criteria were the presence of voluntary movements beyond vertical eye movements or eye blinking, total absence of vertical eye movements, or eye blinking and the absence of a pontine lesion detectable by MRI or CT.

Using a national address list, an e-mail addressed to the ECPs was sent to all long-term care organisations ($n = 187$) to inform them about the study and to ask them if they had any patients with classic LIS in their nursing homes. A letter was attached with the criteria for classic LIS.

The treating ECPs were asked to complete a questionnaire consisting of 18 items (Table 1) if they reported a patient with LIS. The diagnosis was based on a clinical consensus and was established by neurologic examination in the hospital and in the nursing home. The ECPs were contacted by telephone if the questionnaire was not returned, or if the data they provided was incomplete or inconsistent. Returned questionnaires were assessed according to the inclusion and exclusion criteria.

The study did not require ethical approval because no medical scientific research was involved, in accordance with the criteria of the Dutch Medical Research Involving

Table 1 The items from the questionnaire

Date of birth
Sex
Marital status
Cause of LIS
Date of brain incident
Neurological examination in hospital including magnetic resonance imaging (MRI)/computed tomography (CT)
Hospital diagnosis at discharge
Date of discharge from hospital
Place of residence before admission
Date of admission in nursing home
Physical examination by the elderly care physician related to LIS
Means of communication
Recovery of voluntary movement in addition to vertical eye movements or eye blinking during admission
The use of a nasogastric feeding tube
The use of a percutaneous endoscopic gastrostomy (PEG)
The use of tracheal cannula
The use of mechanical ventilation if a tracheal cannula was used
The use of a tracheostomy

Human Subjects Act, and as assessed by the local Research Ethics Committee at Radboud University Medical Centre Nijmegen. The questionnaire survey was carried out with the informed consent of the patients, which was non-verbally expressed in the presence of a family member or the treating ECP. The questionnaires were rendered anonymous.

Results

The majority of long-term care organisations, 171 (91.4 %), responded. Eleven care organisations reported a total of 12 LIS patients (Fig. 1), for which all questionnaires were returned. After assessment of the questionnaires, only two patients met the criteria for classic LIS.

Both patients were female and were admitted from a rehabilitation centre. The cause of LIS in the first patient was an ischemic stroke. A vertebral dissection with secondary basilar thrombosis was found in the second patient. The LIS durations were 50 days and 5.7 years, respectively, and both patients had a percutaneous endoscopic gastrostomy.

One patient used a letter board for communication on which letters are listed, and through vertical eye movements or blinking, she indicated a particular letter. The other patient communicated by blinking, only responding with "yes" or "no", without technical aid. Both patients communicated via vertical eye movements.

The other LIS patients had partial LIS ($n = 5$) or LIS without a pontine lesion detectable by MRI or CT ($n = 2$). The patients without a pontine lesion were clinically partial LIS patients. The characteristics of these patients are listed in Table 2.

One LIS patient was admitted after the reference date, and two patients were in a vegetative state, according to the hospital discharge diagnosis. As the total number of somatic nursing home beds was approximately 30,000, the prevalence of classic LIS was 0.7/10,000 in all Dutch long-term care organisations.

Discussion

This is the first study on the prevalence of LIS, and classic LIS in nursing home patients in particular. The general prevalence of LIS is unknown in the Netherlands, and because of substantial impairments of LIS patients, with as a result a higher risk for institutionalisation, we conducted this first national prevalence study in nursing homes. We expected to find most patients there, but we found a low prevalence of 0.7/10,000 beds in all somatic wards. Moreover, a national study aimed at establishing the prevalence of all community dwelling patients with LIS is not feasible, because we have to address all Dutch general practitioners to get a representative sample. Because of the lack of prevalence data in the literature, comparison is not possible.

We found two female patients with classic LIS. A review of 139 LIS patients reported 85 males and 52 females and two studies of 27 and 29 patients with a male/female ratio of 2:1 [4, 35, 36]. In a more recent survey (2002) of 44 LIS patients, LIS was equally frequent in men (51.2 %) and women (48.1 %) [7]. Comparison with these figures is difficult because of our small sample size. Furthermore, we only included classic LIS, while the other studies apparently included partial LIS as well, and in the review of 139 LIS patients, 89 were in classic, 46 in partial and 3 in total LIS [4].

A remarkable finding was vertebral dissection as a cause of LIS, which was potentially caused by neck manipulation after treatment by a manual therapist a few days prior to the event. Ischemic stroke secondary to vertebral artery dissection following chiropractic manipulation of the cervical spine has been previously reported, leading to persistent LIS in one case [37]. LIS after cervical/spinal manipulation was also documented in three case reports [38–40]. The occurrence of stroke after cervical spine treatment is rare and is estimated to comprise one case for every 1.3 million cervical treatments and one case for every 0.9 million upper cervical treatment sessions [41]. In the case of vertebral dissection, it is estimated that for every 100,000 persons aged <45 years receiving chiropractic care,

Table 2 Characteristics of the reported locked-in syndrome (LIS) patients

N	Age	M/F	Marital status	Admitted from	Cause of LIS	LIS duration	Feeding Tube	Duration (FT)[a]	Airway management	Duration (AM)[a]	Means of communication	Recovery of voluntary movement
Classic LIS												
1	35	F	Not married	Rehabilitation centre	Ischemic stroke	50 days	PEG	4 days	–		Blinking, eye movements	–
2	53	F	Divorced	Rehabilitation centre	Vertebral dissection with secondary basilar thrombosis	5.7 years	PEG	4 years	–		Eye movements, letter board	–
Partial LIS												
3	68	M	Widowed	Hospital	Ischemic stroke	16.9 years	PEG	16.5 years	Tracheal cannula	72 days[b]	Blinking, eye movements, letter board, computer	Head
4	34	F	Not married	Rehabilitation centre	Ischemic stroke	7.4 years	PEG	6.3 years	–		Blinking, sounds, letter board, computer	Head
5	62	M	Not married	Hospital	Ischemic stroke	2.5 years	PEG	1.9 years	Tracheostomy	1.9 years	Blinking, nod yes, shake no	Head, thumbs, fingers, arms, legs
6	53	F	Married	Nursing home	Ischemic stroke	1.7 years	PEG	0.2 years	–	–	Blinking, sounds, letter board	Head, thumbs, fingers, legs
7	69	M	Divorced	Nursing home	Ischemic stroke	1.05 years	PEG	0.2 years	–		Blinking, sounds	Head, thumb
LIS without pontine lesion detectable by magnetic resonance imaging/computed tomography												
8	54	F	Divorced	Hospital	Exacerbation of multiple sclerosis	3.6 years	PEG	3.4 years	Tracheal cannula	3.4 years	Blinking, eye movements	Thumb (minimal)
9	50	F	Married	Nursing home	Ischemic stroke	9.9 years	PEG	9.2 years	–		Blinking, sounds, laughing, crying	–

[a] Calculated for present nursing home stay

[b] Removed before reference date

approximately 1.3 cases would be observed within 1 week after manipulation [42].

In this study, the duration of LIS was 50 days and 5.7 years in the two patients with classic LIS. This is similar to previous literature, where the duration ranged from 14 days to 27 years [6]. There was no recovery of any type in either patient as of the reference date, which makes comparison with the recovery literature impossible. Considering the duration of LIS in these patients, the probability of motor recovery in patient 1 is higher than in patient 2. The same likelihood applies to recovery of some speech production and removal of the PEG. At this point, it is unclear if and how much improvement will occur in these two patients.

We also identified five patients with partial LIS and two patients without a pontine lesion detectable by MRI/CT who were clinically partial. One of these patients (patient 8 in Table 2) had LIS because of an exacerbation of multiple sclerosis. LIS has been previously reported in a male patient with multiple sclerosis [43]. These patients were described because, prior to this study, the general characteristics of LIS were largely undefined in the Netherlands.

Because the care required for LIS patients is intensive, due to their substantial impairments, we expected to find more than two LIS patients in somatic nursing homes. However, the prevalence appeared to be very low. We have two hypotheses for this low prevalence.

One hypothesis is that LIS patients may live outside nursing homes and receive home care. Since 1995, a personal budget allows patients to choose who their care provider is and how their care is delivered [44]. In the French ALIS database, 44 % of the 245 LIS patients live at home [6]. These statistics are unknown in the Netherlands.

Another hypothesis is that the Dutch practice of end-of-life decision-making, such as euthanasia or withholding or withdrawing artificial nutrition and hydration, may lead to a low prevalence in general. Previously, the low prevalence of patients in a vegetative state in Dutch nursing homes was discussed in the context of these end-of-life decisions [45]. However, in contrast to patients in a vegetative/unresponsive state, LIS patients are conscious, legally competent and have the right and capacity to make health care decisions themselves, including a request for euthanasia or refusal of life-sustaining treatment [46]. In a French study ($n = 65$) 58 % of the patients declared they did not wish to be resuscitated in case of cardiac arrest and 7 % expressed a wish for euthanasia [47]. It must be taken into account that in France, euthanasia is legally not allowed and it is assumable that the small percentage of patients that expressed a request for euthanasia could be influenced by the fact that it cannot be met. In the Netherlands, however, there is the possibility of euthanasia, which is strictly regulated by law and is only performed if certain due care criteria are met [48]. The reality that LIS might be a cause of suffering that could ultimately lead to a request for euthanasia was recently highlighted worldwide by the rejected request by the English patient Tony Nicklinson [49]. Further research is necessary to study the relationship of LIS to end-of life decisions.

The strength of this study is that it was carried out for the first time in all nursing homes in a country with a high response rate of 91.4 % and the use of uniform definitions and strict criteria. Another strength is that we addressed all ECPs. Although patients were not clinically assessed by a researcher to confirm the diagnosis, we consider establishing the diagnosis via a neurologist and a treating ECP as adequate.

We found such a small group of patients that treating ECPs are unlikely to be able to establish expertise in long-term care for LIS. Nevertheless, the concentration of such patients far away from their families in specialised centres is not recommended. An alternative may be the provision of a central team of experts for questions and consultations, creating a network of expertise to be utilised by care providers. We recommend further research to establish the prevalence of LIS outside nursing homes and to investigate the relationship between LIS prevalence, end-of-life issues and quality of life. Living with LIS can be described as being locked inside a diving bell on the bottom of the ocean, as depicted in the movie "The Diving Bell and the Butterfly", which is based upon the book by Jean-Dominique Bauby [50, 51]. This graphic illustration makes it clear that LIS has an immense impact on patients, families and caregivers, despite the low numbers we have found.

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Conflicts of interest The authors declare that they have no conflict of interest.

Ethical standard This study has been approved by the local ethics committee and has been performed in accordance with the ethical standards.

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