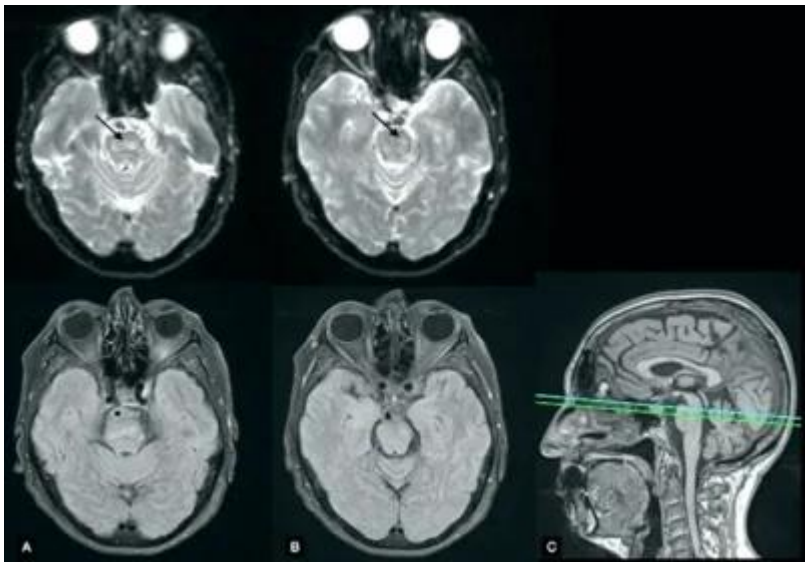
Locked-in syndrome (LIS) is caused by a ventral pontine lesion. The most common cause is vascular (typically an ischemic stroke), while rare causes include trauma, infection, and inflammatory demyelination. LIS is classified into three categories, based on neurological deficits and clinical presentation, “classic”, “total”, and “incomplete”.In this study, the authors from Norway investigated the complexity of the course and outcomes of long-term LIS in a national cohort of patients. They examined the functional status of patients over time and the potential importance of different localization of lesions inside and outside the brainstem on LIS outcome.

“Classic LIS” refers to a neurological condition characterized by quadriplegia and mutism, but intact consciousness and cognitive functions. The patients communicate through eye movements, vertical gazing, and/or blinking. In “total” LIS, patients are unable to communicate through their eyes. Various criteria were used for “incomplete” LIS, such as voluntary motion beyond vertical gazing and/or blinking, moving any limb against gravity, or walking a few steps with assistance. However, the patients are completely dependent in their activities of daily living (ADL).



About the study

The authors used the register of the Norwegian National Unit for Rehabilitation of Locked-in Syndrome to collect demographic, medical, and follow-up data for the period between 2012 and 2022. The register included all patients with LIS as long as they met all the

following criteria: severe communication impairment, paralysis or paresis in all four extremities, complete dependence in ADL, and normal or close-to-normal cognition. If one or more of the four criteria were no longer met, the patient was considered not in the LIS state.

The localization of the lesion was determined by magnetic resonance imaging (MRI) and a computerized tomography (CT) scan. Verbal communication, motor function, and dependence in ADL were evaluated using the modified Rankin scale and LIS motor recovery scale during annual follow-up visits. The LIS motor recovery scale by Patterson et al. measures functional motor status in five categories, ranging from “no recovery” to “no neurologic deficit.” The modified Rankin’s scale measures the degree of disability or dependence in ADL.

Results

This population-based sample included 51 patients, and follow-up data were available for 43 of them. Most of the patients were men (n=36), which is consistent with previous studies. The mean age at onset of LIS was 55.7 years. Hypertension was the most prevalent risk factor. Three patients had a history of drug abuse. Seven patients were unable to work due to a previous stroke or other chronic illness.

The etiology of LIS was ischemic stroke in 35 patients, and hemorrhagic stroke in 14 patients. In two cases LIS was caused by a hemorrhage in the brainstem, in one case after invasive treatment of an ischemic stroke, and in another case by septic infarction and subsequent hemorrhage. In five cases, stroke was associated with dissection, and in three patients with infection.

The localization of lesions

Most of the patients (n = 44) underwent MRI, and these findings were combined with CT scan reports. MRI and CT findings showed numerous combinations of lesions inside and outside the brainstem.

Only 10% of the patients had an isolated pontine lesion. The majority of patients (80%) had various lesions outside the brainstem, most commonly localized in the cerebellum (n = 30) and occipital lobe (n = 8). Three patients had LIS with mesencephalic localization and another three patients had isolated injury of the medulla oblongata (n = 3) without any

other brainstem lesions.

Six patients had a primary hemorrhage in the cerebellum or posterior cranial fossa, suggesting that the brainstem lesion was secondary. That mechanism is known as the "pseudo-LIS."

The functional outcome

Out of 51 patients, 15 died, at a median age of 3.5 years after disease onset. The cumulative survival rates at three, five, and 10-years were 87%, 79%, and 73%, respectively. 3 of the 15 patients who died came out of the LIS state before death, and 12 patients remained in the LIS state until death (one patient with classic LIS, and 11 with incomplete LIS). The median age of patients who died was 65.4 years, and they were older at the onset of LIS compared to those who survived.

Of 51 patients, 23 came out of the LIS state. Importantly, patients who emerged from the LIS state had a lower prevalence of multiple lesions outside the brain stem than patients who remained in the LIS state.

At the final follow-up, all but one patient diagnosed with LIS achieved some motor improvement. Three patients had achieved full motor recovery. However, most patients (n = 27) had achieved "minimal recovery" according to scores on the LIS motor recovery scale by Patterson et al. and were fully dependent in ADL. Seven patients could not respond verbally, 12 could not make sounds, and 16 had dysarthric speech.

Three patients who achieved full motor recovery emerged from the LIS relatively quickly, between 6 weeks and 6 months. They had residual neurological deficits and could not return to work.

The authors also discussed the LIS criteria and complex trajectories of LIS motor outcomes, dependence, and verbal communication.

Conclusion

This Norwegian National Study showed that most of the patients diagnosed with locked-in syndrome remain severely disabled. The MRI and CT results demonstrated that additional lesions outside the brainstem are common in long-term LIS and may have prognostic value for patients who remain in the LIS state.

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Journal Reference

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