

Screening Power of Short Tau Inversion Recovery Muscle Magnetic Resonance Imaging in Critical Illness Myoneuropathy and Guillain–Barre Syndrome in the Intensive Care Unit

Boby Varkey Maramattom 

ABSTRACT

Introduction: Critical illness myoneuropathy (CIMN) or intensive care unit (ICU)-acquired weakness (AW) is a common cause of weakness in ICU patients. Guillain–Barre syndrome (GBS) is also a common cause of acute neurological weakness in the ICU. It is diagnosed by clinical features, nerve conduction studies (NCS), and muscle/nerve biopsies.

Methods: The short tau inversion recovery (STIR) muscle magnetic resonance (MR) images of seven patients with suspected CIMN and seven GBS patients over a 5-year period from February 2015 till May 2020 were analyzed.

Results: All seven patients with CIMN showed diffuse muscle edema, predominating in the lower limbs. Only one patient with GBS showed abnormal magnetic resonance imaging (MRI) changes (14%) and MRI was normal in 86%. The sensitivity of MRI to detect CIMN was 100%, whereas the specificity was 85.7%. Thus, the positive predictive value (PPV) of MRI in this situation was 87.5% and the negative predictive value (NPV) was 100%.

Conclusion: Muscle STIR imaging may help to differentiate between CIMN and GBS.

Keywords: Critical illness myoneuropathy, Critical illness myoneuropathy and magnetic resonance imaging, Critical illness myopathy, Magnetic resonance imaging, Magnetic resonance imaging critical illness polyneuropathy, Magnetic resonance imaging muscle imaging, Magnetic resonance imaging muscle in intensive care unit.

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INTRODUCTION

Weakness in critically ill patients is one of the leading causes of ventilator dependence in the intensive care unit (ICU). Important categories of weakness in the ICU are critical illness myopathy (CIM), critical illness polyneuropathy (CIP) notwithstanding that most patients have a mixture of the two conditions: a critical illness myoneuropathy (CIMN) and Guillain–Barre syndrome (GBS). It is also termed ICU-acquired weakness (ICU-AW). Risk factors for CIMN include the severity and duration of critical illness, hyperglycemia, use of neuromuscular blockers or steroids as well as circulatory factors in sepsis that reduce muscle membrane or nerve excitability. CIMN is suspected when ventilator weaning becomes problematic. Neurological examination discloses flaccid quadriplegia and areflexia. The cranial musculature and facial expressions are relatively spared. Sensory impairment is difficult to determine clinically as patients can be encephalopathic secondary to multiple underlying issues.¹ CIMN can develop within 3–5 days of admission to the ICU.²

Current diagnostic modalities include a combination of clinical scoring; Medical Research Council (MRC) muscle strength grading, nerve conduction studies (NCS), electromyography (EMG) studies, direct muscle stimulation (DMS), muscle ultrasound, and muscle/nerve biopsies. MRC grading assigns a power score between 0 and 5 for 12 muscle groups (six on either side—shoulder abduction, elbow flexion, wrist extension, hip flexion, knee extension, and ankle dorsiflexion). The sum score ranges between 0 and 60 and CIMN is diagnosed when the total is <48.

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DMS provides a “nerve/muscle ratio” (nerve stimulation/muscle stimulation compound muscle action potential (CMAP) amplitudes) with a ratio of >0.5 indicating a neuropathic process (CIP), whereas a ratio <0.5 suggests a myopathic disorder (CIM).³ The early diagnosis of CIMN in patients is hampered by a number of factors such as alteration in sensorium, poor patient cooperation, ICU-associated electrical artifacts, anasarca, necessity for specialized equipment, trained electrophysiologists, and invasive tests. We have previously published an algorithm for the evaluation of a weak patient in the ICU.^{4,5} Diagnostic criteria for CIMN are also available.⁶

Guillain–Barre syndrome (GBS) is a close differential diagnosis of CIMN. It may be difficult at times to differentiate between GBS

and CIMN. Some patients with CIMN undergo neuroimaging, an encephalopathy or doubt of spinal cord dysfunction exists. However, MRI has not been systematically used to assess muscle involvement in CIMN or GBS. In some cases, patients develop GBS while in hospital or during ICU admissions for other conditions. The differentiation between GBS and CIMN can be difficult as many of the acute examination findings and electrophysiological changes can be very similar in both the conditions. We sought to assess the screening power of muscle STIR MRI and determine whether whole-body muscle STIR MRI findings were different between CIMN and GBS.

MATERIALS AND METHODS

The medical records of all patients with a diagnosis of ICUAW, CIM, or CIP or GBS in Aster Medcity over a 5-year period from February 2015 till May 2020 were retrospectively analyzed. Institutional review board approval was obtained. All patients with a suspected diagnosis of CIMN had been seen by the lead author. Out of 20 patients with confirmed CIMN, 8 patients underwent whole-body muscle STIR MR imaging [short tau inversion recovery (TR/TE, 3000–3665 ms/15–35 ms; inversion time, 150 ms) sequence] along with routine cranio-spinal imaging. When possible, axial STIR images of the pelvis and thighs were obtained. Out of 77 patients with confirmed GBS, 7 patients underwent whole-body STIR muscle MRI and these images were also procured and analyzed. The images were reviewed by a radiologist with a specialization in musculoskeletal imaging. The clinical records of all 15 patients and histopathological slides were collected. Institutional ethics committee approval was obtained. All patients underwent a standardized evaluation of muscle strength assessment, NCS, EMG, and lumbar puncture after 7 days. Five of seven patients with CIMN underwent a muscle biopsy. Standard criteria for ICU-AW and the Brighton criteria for GBS were used for diagnosis.⁷

Representative Case

A 74-year-old female with hypertension, type 2 diabetes mellitus, and coronary artery disease was admitted with altered sensorium and intubated. Troponin I (Trop I) was elevated and low molecular weight heparin was started. On day 7, she was conscious, quadriparetic (UL 1/5 power, LL 0/5), and areflexic and had severe muscle tenderness in both thigh muscles. Her C-reactive protein (CRP) was 33 mg/dL, creatine phosphokinase (CPK) was 266, and cerebrospinal fluid (CSF) showed 3 cells with elevated protein (75 mg%). MRI brain revealed sulcal subarachnoid hemorrhage (SAH). Her upper limb power improved to grade IV; however, she had persistent thigh pain and paraparesis. NCS showed a sensory-motor axonopathy. MRI thigh on day 12 showed extensive muscle changes (Fig. 1). Muscle biopsy showed diffuse atrophy of muscle fibers with angulated and shrunken fibers with peripheral nuclei with scattered foci of endomysial and perivascular chronic inflammatory infiltrate and vacuolization, consistent with CIM (non-necrotizing cachectic type) (Figs 2 to 4).

RESULTS

Seven cases of CIMN (male:female ratio 4:3) with a median age range of 59 years (range 36–74 years) and seven cases of GBS with a median age range of 57 years (age range 47–72 years) (male:female ratio 4:3) underwent whole-body STIR MRI at a median range of 16 days (11–28 days) for CIMN and 17 days (12–24 days) for GBS. Subcutaneous edema was found in five out of seven patients (71%).

All patients with CIMN showed STIR muscle hyperintensities (100%) by the 3rd week of illness, whereas only one patient with GBS (14%) showed muscle hyperintensities. The MRI changes in the GBS patient were restricted to the proximal lower limbs and occurred in an acute motor axonal neuropathy (AMAN) variant.

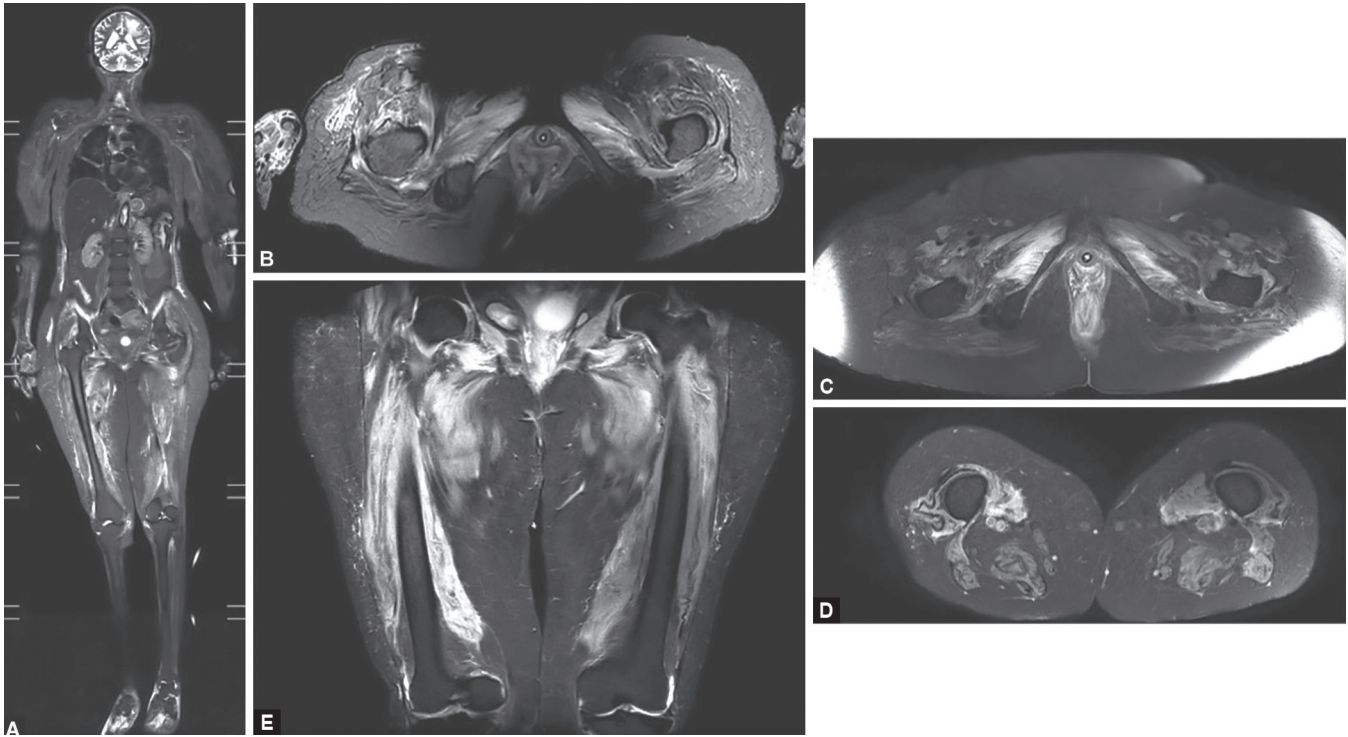
Albumino-cytological dissociation was noted in all seven GBS patients and none of the CIMN patients. Muscle biopsy in all five patients with CIM showed findings consistent with CIM. The sensitivity of MRI to detect CIMN was 100%, whereas the specificity was 85.7%. Thus, the positive predictive value (PPV) of MRI in this situation was 87.5% and the negative predictive value (NPV) was 100%.

DISCUSSION

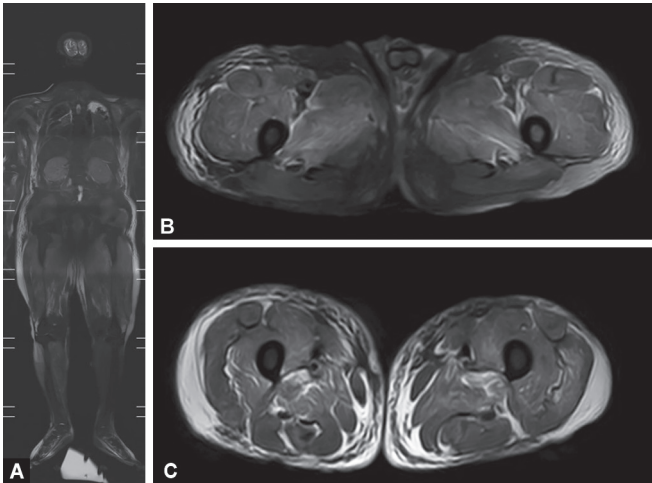
Our patients with CIMN demonstrated extensive muscle edema on MRI which was more florid in the lower limbs and pelvic muscles. Edematous muscles show hyperintensity on STIR MRI sequences. Deep muscles (obturator muscles and iliopsoas) which are difficult to assess by conventional techniques such as EMG or muscle biopsy also showed edema on MRI. Our patients showed a lesser extent of involvement in the upper limbs—this may be due to a smaller volume of muscles in the upper extremity as well as MRI limitations when a whole-body STIR imaging is performed.

Subcutaneous edema was commonly found in CIMN patients (71%) reflecting fluid shifts in the underlying critical illness. Our groups were comparable in terms of age and time to MRI. With the use of targeted MRI sequences, we could demonstrate striking muscle abnormalities in all cases of CIMN by the 3rd week of illness. The majority of GBS patients (86%) did not have any changes on muscle MRI. Only the patient with a severe AMAN variant showed proximal lower limb changes due to severe denervation. We found a high sensitivity and PPV of MRI in detecting CIMN. Accordingly, we propose the incorporation of MRI muscle imaging in the diagnostic evaluation of weakness in the ICU (Flowchart 1). Sixty percent of patients with sepsis develop early neuromuscular and cardiac electrophysiological abnormalities on NCS and EKG (low sensory nerve action potentials (SNAPs) and CMAPs, reduced QRS complex on ECG (QRS) complex amplitudes, and increased QRS duration) within 72 hours of ICU admission. Of this cohort, approximately half progresses to frank CIMN and the others show rapid improvement in electrophysiological parameters. This reversibility reflects temporary impairment of skeletal/cardiac muscle membranes and nerve excitability and is attributed to circulatory factors in sepsis (such as nitric oxide) which induce a nodopathy or paranodopathy.^{8–10} These inflammatory mediators inhibit mitochondrial activity and disrupt Na⁺/K⁺ ion channel pump function, resulting in Na⁺ influx, axonal depolarization, and conduction failure. Later, secondary Ca²⁺-mediated axonal degeneration supervenes. Accordingly, NCS may take up to 1–3 weeks to confirm CIMN and serial testing demonstrates progressive electrophysiological abnormalities.^{1,11,12} Conversely, clinical and electrophysiological improvement occurs over several months.¹³

Critically ill patients may undergo neuroimaging with MRI, especially when an encephalopathy is present. Hence, whole-body or regional muscle MRI in critically ill patients is a logical extension of this diagnostic modality. Muscle changes in neuromuscular disease broadly show up as muscle edema, mass lesions, fatty replacement, or atrophy on MRI. The first two occur in subacute processes, whereas fibrosis and atrophy suggest chronic muscle



Figs 1A to E: (A) MRI coronal STIR; (B) Axial STIR image of patient 1; (C and D) Axial STIR images of thighs (patient 2); (E) Coronal STIR image of thigh



Figs 2A to C: Coronal and axial STIR images of patient 3

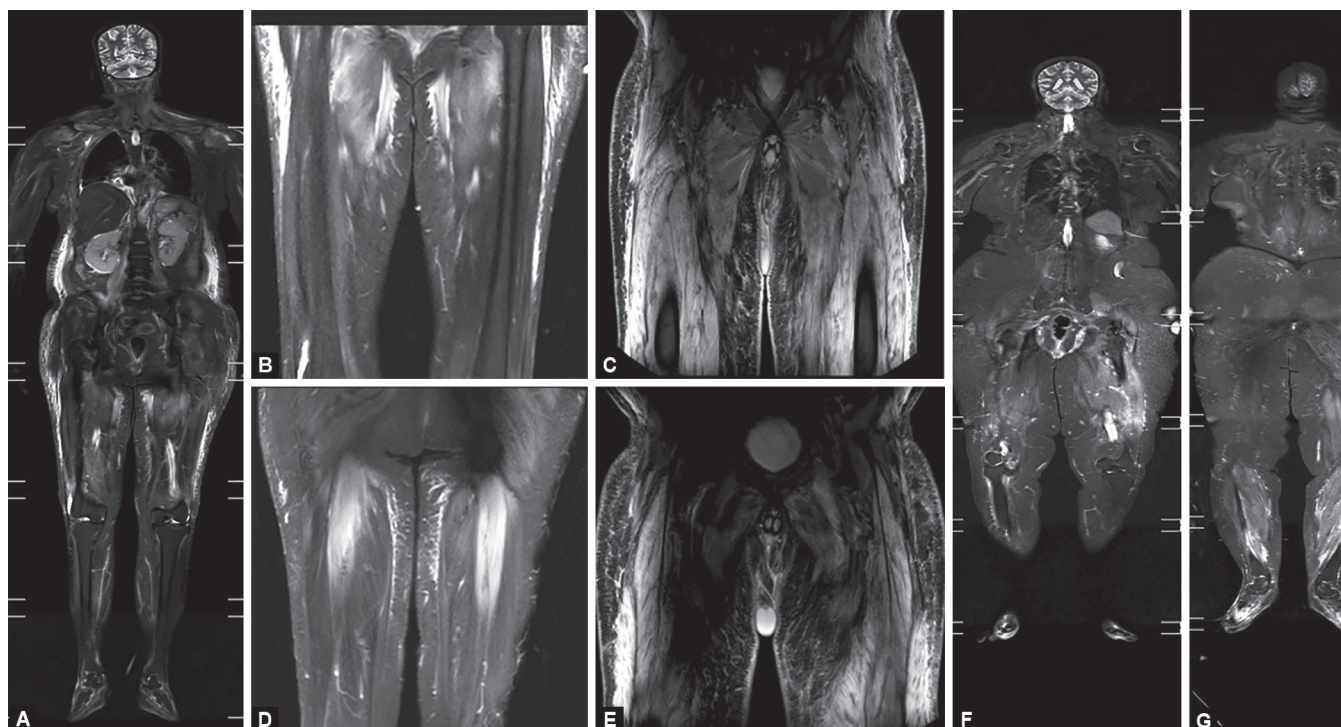
disease. Muscle edema is seen in inflammatory myopathies, infectious myositis, radiation therapy, subacute denervation, and many other muscle diseases.^{14–16} Of these, inflammatory myopathies, rhabdomyolysis, or vasculitis results in extensive and generalized muscle edema on MRI. Muscle edema is thought to be caused by intramuscular fluid shift, vascular congestion, or perfusion alterations related to denervation or muscle inflammation. Following nerve injury, muscles innervated by that nerve undergo denervation and uniform edema. Although it may be evident as early as 2–4 days after denervation, 2–4 weeks are often required for MRI abnormalities to manifest.^{17,18} If effective re-innervation occurs, the MRI changes normalize. Otherwise, it progresses to muscle atrophy with fatty infiltration in about

6 months.¹⁹ Unlike restricted muscle denervation following focal nerve injury, CIMN is a unique entity characterized by diffuse denervation and muscle injury and scattered changes on MRI. Nevertheless, the timing of MRI muscle imaging in CIM is crucial to pick up acute changes.

Neuromuscular imaging now incorporates multiple MRI sequences including T1W, T2W, STIR sequences, chemical shift imaging (CSI), diffusion-weighted and diffusion tensor imaging (DWI/DTI), perfusion imaging, contrast imaging, and MR neurography to differentiate muscle pathology.¹⁸ Ideally, all these sequences are required for proper interpretation. However, this adds a considerable amount of time of imaging in a critically ill patient. Therefore, we used only STIR sequences to shorten MR imaging times as patients were undergoing concurrent cranio-spinal imaging.

Limitations of our study include a small sample size and the timing of MRI. Our patients could undergo an MRI only by the 3rd week. The timing of muscle MRI is crucial to pick up acute changes and we could not obtain MRI early in the course of the illness to see whether it could contribute to therapeutic decisions.

The diagnosis of CIMN is often delayed until a neurologic specialist's opinion is obtained. Muscle MRI complements electrophysiological testing and helps in targeting muscles for biopsy. Moreover, muscles that are not amenable to conventional EMG or biopsy such as the pelvic or deep muscles can be easily imaged by MRI. Therefore, the addition of a STIR muscle MRI protocol in critically ill patients can expedite the diagnosis of CIMN. Furthermore, STIR MRI might permit a more objective diagnostic tool that is easier to interpret, for all physicians involved in the care of critically ill patients. The incorporation of muscle MRI in the diagnostic evaluation of weakness in the ICU may be useful (Flowchart 1).



Figs 3A to G: (A to C) Patient 4: (A) STIR coronal whole body, (B) Coronal anterior thigh, (C) Posterior thigh; (D and E) Patient 5: Coronal images through anterior and mid-thigh; (F and G) Patient 6: (F) Coronal STIR images through anterior and (G) Posterior planes

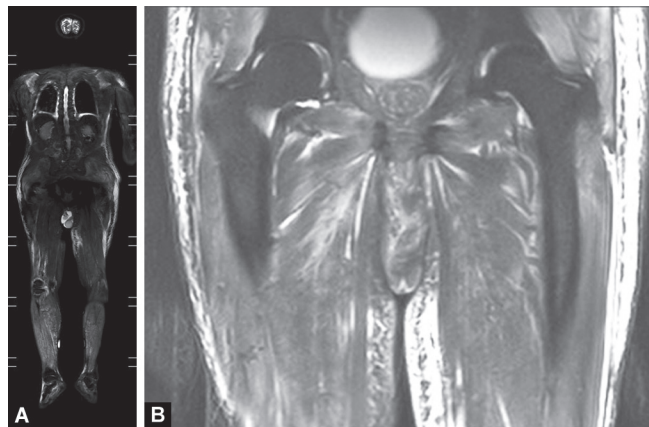
Table 1: MRI abnormalities in patients with CIMN and GBS

S. No	Age/ gender	Diagnosis	Time to MRI	NCS findings	MRI muscle hyperintensities	MRI muscle atrophy	MRI extramuscular changes	Recovery at 60 days
1	72/female	CIMN	13 days	Sensory-motor axonopathy EMG-myopathic potentials, fibrillations	Quadriceps, adductor muscles of thigh, pelvic muscles (obturator muscles)	None	Minimal subcutaneous edema	mRS-4
2	74/female	CIMN	12 days	Sensory-motor axonopathy EMG-myopathic potentials	Quadriceps, adductor muscles of thigh, pelvic muscles (obturator muscles)	Quadriceps muscles	None	mRS-3
3	52/male	CIMN	17 days	Sensory-motor axonopathy EMG-myopathic potentials	B/l thigh adductor, pelvic (obturator) and right tibialis anterior	None	Extensive subcutaneous edema	mRS-5
4	57/female	CIMN	11 days	Sensory-motor axonopathy EMG-myopathic potentials, fibrillations	Vastus lateralis, posterior compartment of calf, shoulder rotator cuff muscles	None	Extensive subcutaneous edema	mRS-4
5	36/male	CIMN	21 days	Sensory-motor axonopathy EMG-myopathic potentials	Bilateral thigh and left > right calf muscles	None	None	mRS-5
6	67/male	CIMN	12 days	Sensory-motor axonopathy EMG-myopathic potentials, fibrillations	Bilateral thigh, calf muscles, infraspinatus	None	Extensive subcutaneous edema	mRS-4
7	57/male	CIMN	28 days	Sensory-motor axonopathy EMG-myopathic potentials	Bilateral thigh, pelvic, calf muscles >> UL muscles	None	Extensive subcutaneous edema	mRS-5

(Contd...)

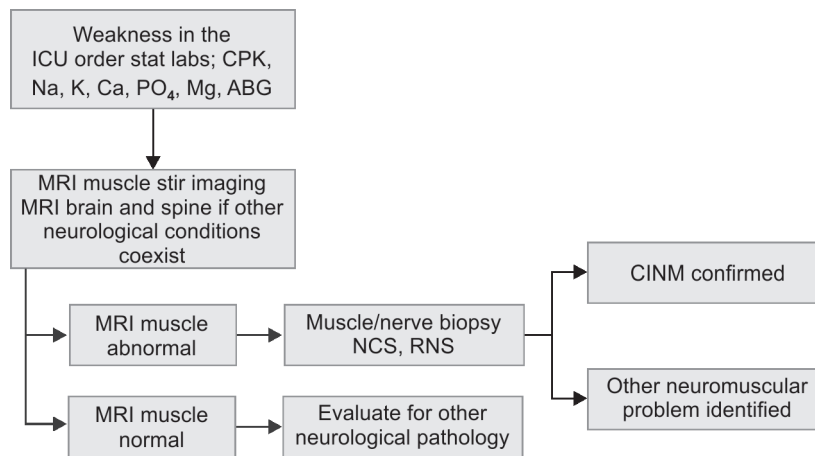
Table 1: (Contd...)

S. No	Age/ gender	Diagnosis	Time to MRI	NCS findings	MRI muscle hyperintensities	MRI muscle atrophy	MRI extramuscular changes	Recovery at 60 days
8	50/male	GBS	15 days	Demyelinating neuropathy	None	None	None	mRS-0
9	47/male	GBS	18 days	Motor-sensory axonopathy	None	None	None	mRS-1
10	72/male	GBS	14 days	Demyelinating neuropathy	None	None	None	mRS-1
11	65/female	GBS	24 days	Mixed axonal-demyelinating neuropathy	None	None	None	mRS-1
12	62/female	GBS	21 days	Demyelinating neuropathy	None	None	None	mRS-1
13	52/female	GBS	12 days	Motor axonal neuropathy	Bilateral thigh muscles	None	None	mRS-3
14	56/male	GBS	18 days	Demyelinating neuropathy	None	None	None	mRS-1



Figs 4A and B: (A) Coronal STIR MR image; (B) Coronal STIR image through the thigh

Flowchart 1: Algorithm for the evaluation of a weak patient in the ICU



MRI * Disease Crosstabulation					
			Disease		Total
			CIMN	GBS	
MRI	Negative	Count	0	6	6
		% within Disease	0.0%	85.7%	42.9%
	Positive	Count	7	1	8
		% within Disease	100.0%	14.3%	57.1%
Total	Count	7	7	14	
	% within Disease	100.0%	100.0%	100.0%	

	CIMN	GBS			
MRI+	7	1	8	Sensitivity	100
MRI-	0	6	6	Specificity	85.7
	7	7		PPV	87.5
				PPV	100

Future directions include the use of newer MRI sequences to differentiate CIMN subtypes as well as the use of MR neurography and DTI to assess concurrent CIP (Table 1).

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