



Sural-sparing pattern: A study against electrodiagnostic subtypes of Guillain–Barre syndrome



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ABSTRACT

Objective: To study sural-sparing pattern in Guillain–Barre syndrome (GBS) and compare it among GBS's electrodiagnostic subtypes, classified by two recent criteria.

Methods: This study retrospectively reviewed clinical data and electrodiagnostic studies (EDXs) of 88 GBS patients diagnosed in a tertiary care hospital (2010–2019).

Results: Overall, 79/88 (89.8%) and 36/45 (80%) patients had bilateral sensory nerve conduction studies (NCS) in the first EDX and follow-up EDX, respectively. Sural-sparing occurred in all subtypes (50% overall occurrence rate), most commonly in demyelination. There was no statistically significant difference in sural-sparing occurrence rates between demyelinating and axonal GBS; however, sural-sparing in axonal GBS tended to show a lower number of abnormal upper-limb sensory nerve action potentials (SNAPs) than demyelinating GBS. Shifting between sural-sparing and no sural-sparing occurred in approximately one-fourth of patients receiving serial studies. Follow-up EDX additionally discovered 20% of all sural-sparing. Unilateral EDX could have omitted up to 30% of sural-sparing.

Conclusions: Sural-sparing is less obviously manifested in axonal than demyelinating GBS, with respect to the number of affected upper-limb SNAPs. Extended sensory NCS is worth in detecting sural-sparing as a supportive electrodiagnostic GBS feature.

Significance: This report showed one different character of sural-sparing (number of affected upper-limb SNAPs) between demyelinating and axonal GBS.

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1. Introduction

Electrodiagnostic study (EDX) has played a major role in the diagnosis and subtype classification of Guillain–Barre syndrome (GBS). The proposed electrodiagnostic criteria sets for subtype classification are different, mainly in terms of diagnostic stringency (e.g., demyelination cutpoints) and number of EDXs (single vs serial) (Shahrizaila et al., 2013; Rajabally et al., 2015; Uncini and Kuwabara, 2018). These criteria generally rely on motor nerve conduction study (NCS) findings. “Sural-sparing” pattern detected during sensory NCS is a well-recognized electrodiagnostic feature in demyelinating GBS (Freiha et al., 2021), and facilitates in discrim-

inating against GBS mimics (Derksen et al., 2014). During the past decade, a few studies have also demonstrated sural-sparing in axonal GBS (Capasso et al., 2011; Umapathi et al., 2015; Hiew and Rajabally, 2016); however, this information is still limited compared with that available on sural-sparing in demyelinating GBS.

Sural-sparing presence has facilitated GBS diagnosis in clinical practice for years; nevertheless, definitions of sural-sparing are heterogeneous across studies (Hiew and Rajabally, 2016; Freiha et al., 2021). Abnormalities in at least two upper-limb sensory nerves with normal or relatively normal sural response(s) were widely acknowledged for sural-sparing to ensure the exclusion of preexisting entrapment neuropathy (Al-Shekhlee et al., 2007); however, many studies also accepted only one abnormal upper-limb sensory nerve (e.g., “abnormal median normal sural” or “abnormal ulnar normal sural”) (Bromberg and Albers, 1993; Taly et al., 1997; Hiew and Rajabally, 2016). Another defined it as a greater percentage reduction in the median or ulnar sensory nerve action potential (SNAP) compared with percentage reduction in

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sural SNAP (Umaphathi et al., 2015). The severity (absent or abnormal) of SNAP abnormality was also considered (Hiew and Rajabally, 2016; Surpur and Govindarajan, 2017). Additionally, a study showed that the abnormal amplitude of the response was more sensitive in detecting sural-sparing than the slow conduction velocity (Chanson and Echaniz-Laguna, 2014).

This study aimed to describe sural-sparing in a GBS cohort, which received extensive sensory NCS. The authors compared the two categories of “sural-sparing” based on the number of abnormal upper-limb SNAPs among the electrodiagnostic GBS subtypes and demonstrated the evolution of sural-sparing during the acute period.

2. Methods

2.1. Patients

The electronic medical records of GBS-diagnosed patients during 2010–2019 at the King Chulalongkorn Memorial Hospital were retrospectively reviewed. Patients who 1) met the Asbury's diagnostic criteria for GBS (Asbury and Cornblath, 1990) and 2) at least had one EDX done at the neuromuscular electrodiagnostic laboratory within 2 weeks after onset were included. GBS treatment-related fluctuation and patients with a history of preexisting entrapment neuropathy or polyneuropathy and normal EDX were excluded. Epidemiological data, clinical presentation, physical and laboratory findings, treatment, and clinical outcomes were collected. This study was approved by the IRB.

2.2. Electrophysiological studies

All patients must have undergone at least one EDX (EDX1). The most informative follow-up EDX (EDX2) of patients involved in serial studies within weeks 3–8 following clinical onset were also analyzed. Each EDX must include at least three motor nerves in one upper and lower limb, three sensory nerves (median, ulnar, radial) in at least one upper limb, and bilateral sural nerves.

All EDXs were conducted via Nicolet EDX (Viking software) using the standard NCS technique. Median and ulnar SNAPs were antidromically recorded with ring electrodes on the second and fifth digits, respectively, following stimulation 14 cm proximally at the wrist. Superficial radial and sural SNAPs were recorded with surface electrodes on the wrist (snuffbox) and ankle, respectively, following stimulation 14 cm proximally. The bandpass was set at 2 Hz–10 kHz for motor NCS and 20 Hz–3 kHz for sensory NCS. Signal averaging of at least 10 responses was routinely performed for sensory NCS to improve the signal-to-noise ratio. F wave study was routinely conducted when the measured compound muscle action potential (CMAP) was at least 10 % lower limit of normal (LLN). Studies were done in a warm room. Skin temperature was kept at 32–34 °C during the study. A heating lamp was used to warm the limbs if needed.

All EDX waveforms were reviewed. The distal motor latencies, negative peak amplitudes, and durations of CMAPs, conduction velocities, and minimal F-wave latencies were measured for motor nerves. The distal latencies and onset-to-peak amplitudes of SNAPs, and conduction velocities were measured for sensory nerves. All parameters were calculated to be within the upper limit of normal/LLN percentages using our laboratory reference values.

2.3. Electrodiagnostic classification

Four electrodiagnostic subtypes of GBS (demyelinating, axonal, equivocal, inexcitable) were classified according to 1) Rajabally's criteria with temporal dispersion (Rajabally et al., 2015; Van den Bergh et al., 2018) and 2) Uncini's criteria (Uncini et al., 2017).

For Rajabally's criteria with temporal dispersion, subtypes were classified by EDX1 as the first classification; the classification might change in patients having EDX2 to the final classification. Subtypes were classified by serial studies (EDX1 + EDX2) or EDX1 (whichever applicable) for Uncini's criteria (Uncini and Kuwabara, 2018), thus each patient would have only one subtype (final classification).

2.4. Sensory NCS parameters and sural-sparing

Sensory NCS parameters were categorized based on the cross-sectional analysis of any single EDX into three patterns: (1) sural-sparing pattern A (normal or relatively normal bilateral sural responses with absent or abnormal SNAP in at least two nerves in the upper limb[s]); (2) sural-sparing pattern B (normal or relatively normal bilateral sural responses with absent or abnormal SNAP in one upper-limb nerve); and (3) no sural-sparing pattern (C) ([i] normal all SNAPs, [ii] absent all SNAPs, and [iii] abnormal SNAPs that did not qualify the above categories). Relatively normal sural SNAP was defined as the reduced mean sural SNAP amplitude percentage being lesser than the reduced upper-limb nerve SNAP amplitude percentage (Umaphathi et al., 2015).

2.5. Analysis

The number of patients with and without “sural-sparing” in all electrodiagnostic GBS subtypes was counted and analyzed. This was also analyzed in the subgroup having concordant final classifications by two criteria. Fisher's exact test was used to determine the difference in frequencies of sural-sparing patterns between demyelinating and axonal GBS. Statistical significance was set at $p < 0.05$.

3. Results

3.1. Patient characteristics

This study included 88 patients, of which 55 (62.5 %) were male (male: female, 1.67:1). The mean age of onset was 51.8 years (range: 16–83), mean time from clinical onset to first presentation was 5.2 days (standard deviation (SD): 3.6), and the median GBS disability score was 3 (interquartile range [IQR]: 3–5). Antecedent events were reported in 28/88 (31.8 %) patients (22 infections, 4 vaccinations, and 2 diarrhea). The CSF study was performed on 85 patients, which revealed CSF protein elevation in 70 (82.4 %), with the mean CSF protein being 96.9 mg/dl (SD: 75, normal < 45 mg/dl). Antiganglioside immunoglobulin (Ig)G antibody test in 30 patients revealed positivity in 6 (3 axonal, 2 inexcitable, and 1 equivocal). Intravenous Ig was given to 85 patients, 1 received plasmapheresis. All achieved favorable outcome. One patient (inexcitable subtype), who had GBS six years ago, still requires walking aid.

3.2. Electrodiagnostic studies and classifications

The mean time from clinical onset to EDX1 and EDX2 was 7.9 (SD: 3.5) and 27.5 (SD: 8.8) days, respectively. Forty-five patients (51.1 %) underwent serial EDXs. The mean time interval between EDX1 and EDX2 was 21 days (SD: 8.1). Additionally, 79/88 (89.8 %) and 36/45 (80 %) patients received bilateral upper-limb sensory NCS in EDX1 and EDX2, respectively. Electrodiagnostic GBS classifications are shown in Table 1.

Classification changes in EDX2 were found in 11 of 45 (24.4 %) patients for Rajabally's criteria with temporal dispersion (Supplementary data, Figure 1). Concordant results of final classification

Table 1
Occurrence rates of sural-sparing pattern against electrodiagnostic subtypes of Guillain-Barre syndrome (left: all patients, right: patients having bilateral sensory NCS of the upper limbs).

GBS subtype/Number	All					GBS subtype/ Number	Bilateral sensory NCS\$								
	Sural sparing		P value (A vS B)	No sural sparing (Pattern C)	P value (A vS B + C)		P value (A + B vS C)	N	Sural sparing		P value (A vS B)	No sural sparing (Pattern C)	P value (A vS B + C)	P value (A + B vS C)	N
	Pattern A	Pattern B							Pattern A	Pattern B					
Rajabally's criteria with temporal dispersion															
First classification vs first sensory NCS															
De 49	19 (38.8%)	5 (10.2%)	0.0581	25 (51%)	0.0451	0.3496	88	De 45	19 (42.2%)	2 (4.4%)	0.0049	24 (53.3%)	0.0104	0.4856	79
Ax 13	1 (7.7%)	3 (23.1%)		9 (69.2%)				Ax 10	0	3 (30%)		7 (70%)			
Eq 22	4 (18.2%)	6 (27.3%)		12 (54.5%)				Eq 20	4 (20%)	4 (20%)		12 (60%)			
In 4	0	0		4 (100%)				In 4	0	0		4 (100%)			
Final classification vS any sensory NCS\$\$															
De 55	26 (47.3%)	6 (10.9%)	0.0406	23 (41.8%)	0.0211	0.2058	88	De 52	25 (48.1%)	4 (7.7%)	0.0231	23 (44.2%)	0.0198	0.3247	84
Ax 11	1 (9.1%)	3 (27.3%)		7 (63.6%)				Ax 11	1 (9.1%)	3 (27.3%)		7 (63.6%)			
Eq 18	5 (27.8%)	3 (16.7%)		10 (55.6%)				Eq 17	4 (23.5%)	3 (17.6%)		10 (58.8%)			
In 4	0	0		4 (100%)				In 4	0	0		4 (100%)			
Uncini's criteria															
Final classification vs first sensory NCS															
De 57	20 (35.1%)	8 (14%)	0.1034	29 (50.9%)	0.048	0.1659	88	De 50	19 (38%)	4 (8%)	0.05	27 (54%)	0.0437	0.4452	79
Ax 9	0	2 (22.2%)		7 (77.8%)				Ax 8	0	2 (25%)		6 (75%)			
Eq 18	4 (22.2%)	4 (22.2%)		10 (55.6%)				Eq 17	4 (23.5%)	3 (17.6%)		10 (58.8%)			
In 4	0	0		4 (100%)				In 4	0	0		4 (100%)			
Final classification vs any sensory NCS\$\$															
De 57	26 (45.6%)	7 (12.3%)	0.0605	24 (42.1%)	0.0092	0.0719	88	De 54	25 (46.3%)	5 (9.3%)	0.0423	24 (44.4%)	0.0087	0.0816	84
Ax 9	0	2 (22.2%)		7 (77.8%)				Ax 9	0	2 (22.2%)		7 (77.8%)			
Eq 18	6 (33.3%)	3 (16.7%)		9 (50%)				Eq 17	5 (29.4%)	3 (17.6%)		9 (52.9%)			
In 4	0	0		4 (100%)				In 4	0	0		4 (100%)			
Concordance by two criteria															
Final classification vs any sensory NCS\$\$															
De 54	25 (46.3%)	6 (11.1%)	0.053	23 (42.6%)	0.0348	0.231	79	De 51	24 (47.1%)	4 (7.8%)	0.0345	23 (45.1%)	0.0343	0.2458	75
Ax 7	0	2 (28.6%)		5 (71.4%)				Ax 7	0	2 (28.6%)		5 (71.4%)			
Eq 14	4 (28.6%)	3 (21.4%)		7 (50%)				Eq 13	3 (23.1%)	3 (23.1%)		7 (53.8%)			
In 4	0	0		4 (100%)				In 4	0	0		4 (100%)			

GBS, Guillain Barre syndrome; De, demyelinating; Ax, axonal; Eq, equivocal; In, inexcitable; NCS, nerve conduction study; N, number of patients; Parentheses showed percentages of sural-sparing and no sural-sparing in each electrodiagnostic subtype;

\$including bilateral median, bilateral ulnar and bilateral radial nerves;

\$\$ any sensory NCS in first or follow-up electrodiagnostic study that showed sural-sparing patterns; Statistically significance between demyelinating and axonal subtypes are indicated in bold.

by two criteria were found in 79/88 (89.8 %) patients (Supplementary data, Figure 2). “Abnormal ulnar normal sural” (sural-sparing pattern B) is included for demyelination in Uncini’s criteria, which can inflate the false discovery of independence between the interest conditions. However, in this study, no patient required “abnormal ulnar normal sural” as a supportive parameter to reach demyelination diagnosis using the Uncini’s criteria (all patients were classified as demyelinating GBS via fulfilling the motor criteria diagnosis).

3.3. Sural-sparing pattern

The overall occurrence rate of sural-sparing (EDX1 + EDX2) in GBS was 50 % (44/88), which dropped to 36.4 % (32/88) after considering at least two abnormal upper-limb SNAPs (pattern A). The occurrence rates of sural-sparing patterns in all electrodiagnostic GBS subtypes are shown in Table 1. It was most frequent in demyelinating GBS (46 %–58.2 %), followed by the equivocal (40 %–50 %) and axonal (22.2 %–36.4 %) subtypes. The occurrence rates varied depending on the electrodiagnostic criteria, sensory NCS protocols, and EDX timings.

No statistically significant difference was found in the occurrence rates of sural-sparing between demyelinating and axonal GBS (Table 1, A + B vs C). However, statistically significant differences were found for frequencies of sural-sparing pattern A, regardless of the electrodiagnostic criteria, sensory NCS protocols, or EDX timings (Table 1, A vs B + C). Additionally, demyelinating GBS showed a trend toward sural-sparing pattern A, whereas axonal GBS showed a trend toward pattern B (Table 2); statistically significant differences in the sural-sparing patterns A versus B frequencies between these two GBS subtypes were also present in patients with bilateral sensory NCS (except for final Uncini’s classification vs first sensory NCS) (Table 1, A vs B).

In “sural-sparing”, the median SNAP was most predominantly affected in terms of frequency and severity in all GBS subtypes and in both EDX1 and EDX2. This was followed by abnormality

of ulnar SNAP, whereas radial SNAP was remarkably preserved (Table 3). The abnormality of upper limb SNAPs was mostly presented as absent or reduced amplitude. Isolated slow conduction velocity with normal SNAP amplitude was found in two median nerves and one ulnar nerve (all were in equivocal subtype). No patient with spared sural responses had isolated abnormal radial SNAP.

3.3.1. Serial sensory NCS

Sural-sparing occurrence rates in EDX1 and EDX2 were comparable (43.2 % vs 42.2 %). In patients who underwent serial studies (EDX1 + EDX2), the overall occurrence of any sural-sparing increased to 57.8 % (26/45 patients). A shifting pattern between “sural-sparing” and “no sural-sparing” was found in 13/45 (28.9 %) and in 9/31 (29 %) patients with bilateral sensory NCS (Table 4). Sural-sparing found in EDX1 could become absent in EDX2 or vice versa. Sural-sparing pattern disappearance in EDX2 was due to either 1) progressive reduction of sural SNAPs or 2) recovery of upper-limb SNAPs (e.g., reversible conduction failure (RCF)). All delayed sural-sparing pattern detection in EDX2 was because of late amplitude reduction of upper-limb SNAPs.

3.3.2. Bilateral sensory NCS in the upper limbs

In patients receiving bilateral upper-limb sensory NCS, 32/79 (EDX1) and 17/36 (EDX2) patients showed a sural-sparing (patterns A or B). Abnormal SNAPs were confined to the unilateral upper limb in 11/32 (34.4 %) and 5/17 (29.4 %) patients in EDX1 and EDX2, respectively. No selective preference was observed on sensory NCS of the right or left hands in detecting sural-sparing patterns.

Sural-sparing pattern A was detected in 23 (EDX1) and 13 (EDX2) patients. Among 23 patients (EDX1), 9 had abnormal SNAPs (≥2 nerves) in both upper limbs, 11 had abnormal SNAPs (≥2 nerves) in one upper limb, and 3 had one abnormal SNAP in each upper limb. Among 13 patients (EDX2), five had abnormal SNAPs (≥2 nerves) in both upper limbs, five had abnormal SNAPs (≥2

Table 2
Number of abnormal upper-limb SNAP in demyelinating and axonal GBS with sural-sparing in patients receiving bilateral sensory NCS of the upper limbs.

GBS subtypes (N)	Bilateral sensory NCS\$	Number of abnormal upper limb SNAP					
		6	5	4	3	2	1
Rajabally’s criteria with temporal dispersion							
First classification vs first sensory NCS							
De (45)	21	2	1	7	5	4	2
Ax (10)	3	0	0	0	0	0	3
Eq (20)	8	0	0	2	0	2	4
Final classification vs any sensory NCS\$\$							
De (52)	29	2	2	9	7	5	4
Ax (11)	4	0	0	0	0	1	3
Eq (17)	7	0	0	2	1	1	3
Uncini’s criteria							
Final classification vs first sensory NCS							
De (50)	23	2	1	6	5	5	4
Ax (8)	2	0	0	0	0	0	2
Eq (17)	7	0	0	3	0	1	3
Final classification vs any sensory NCS \$\$							
De (54)	30	2	2	9	7	5	5
Ax (9)	2	0	0	0	0	0	2
Eq (17)	8	0	0	3	0	2	3
Concordance by two criteria							
Final classification vs any sensory NCS\$\$							
De (51)	28	2	2	9	6	5	4
Ax (7)	2	0	0	0	0	0	2
Eq (13)	6	0	0	2	0	1	3

SNAP, sensory nerve action potential; GBS, Guillain Barre syndrome; NCS, nerve conduction study; N, number; De, demyelinating; Ax, axonal; Eq, equivocal; \$Including bilateral median, bilateral ulnar and bilateral radial nerves;

\$\$Any sensory NCS in first or follow-up electrodiagnostic study that showed sural-sparing patterns.

Table 3
Affected upper-limb SNAPs and their severity in all patients with “sural-sparing” pattern.

	N of tested upper limbs	SNAP	Nerve		
			Median#	Ulnar	Radial\$
EDX1 (38* patients)	70	Absent	21	14	1
		Abnormal	29\$\$	22\$\$	9
		Normal	20	34	60
		% Absent + abnormal	71.4 % (50/70)	51.4 % (36/70)	14.3 % (10/70)
EDX2 (19** patients)	36	Absent	14	10	1
		Abnormal	12	11	2
		Normal	10	15	33
		% Absent + abnormal	72.2 % (26/36)	58.3 % (21/36)	8.3 % (3/36)

SNAP, sensory nerve action potential; N, number; EDX1, first electrodiagnostic study; EDX2, follow-up electrodiagnostic study; NCS, nerve conduction study.
 *In EDX1, 38/88 patients had sural-sparing. [32/38 patients had sensory NCS in both upper limbs. 6/88 patients had sensory NCS in an upper limb.].
 **In EDX2, 19/45 patients had sural-sparing. [17/19 patients had sensory NCS in both upper limbs. 2/19 patients had sensory NCS in an upper limb.].
 #Median SNAP (absent or abnormal) abnormality was the most predominantly affected upper limb SNAP in all subtypes. It was found in 90%, 100% and 100% of sural-sparing patients with demyelinating, axonal and equivocal subtypes (concordant classification by two criteria), respectively.
 \$Radial SNAP was remarkably preserved in all electrodiagnostic subtypes. No patient with sural-sparing had isolated abnormality of radial SNAP.
 \$\$Two median nerves and one ulnar nerve had isolated slow conduction velocity.

Table 4
Number of patients with changes between “sural sparing” and “no sural sparing” in EDX1 and EDX2\$ (left, all patients receiving serial studies; right, patients receiving serial and bilateral sensory NCS).

N = 45			EDX1			N = 31			EDX1		
			Sural sparing		No sural sparing				Sural sparing		No sural sparing
			Pattern A	Pattern B					Pattern A	Pattern B	
EDX2*	Sural sparing	Pattern A	7	4	4	EDX2**	Sural Sparing	Pattern A	6	1	3
		Pattern B	1	1	2			Pattern B	1	1	1
	No sural sparing	4	3	19	No sural sparing		2	3	13		

NCS, nerve conduction study; N, number of patients; EDX1, first electrodiagnostic study; EDX2, follow-up electrodiagnostic study.
 *Among all patients receiving serial studies (left), 6/26 (23.1%) of sural-sparing patients were additionally detected by EDX2.
 **Among patients receiving serial and bilateral sensory NCS (right), 4/18(22.2%) of sural-sparing patients were additionally detected by EDX2.
 \$Changes between “sural sparing” and “no sural sparing” were found in 13/45 (28.9%) and 9/31(29%) patients. Changes were found in all subtypes.

nerves) in one upper limb, and three had one abnormal SNAP in each limb.

4. Discussion

According to Rajabally’s criteria with temporal dispersion and Uncini’s criteria, demyelination was the most common GBS subtype in our study, accounting for 62.5 % and 64.8 %, respectively. High concordance between the final classifications of the two criteria might reflect some similarity in their contents. Axonal GBS proportion was slightly low compared with several Asian studies (Bae et al., 2014). However, our result was similar to that of a recent study from Thailand and those from Western countries (Kulkantrakorn and Sukphullopapat, 2017). Antecedent diarrhea from *Campylobacter jejuni* infection was suggested as an underlying pathogenesis of axonal GBS. This was also the least frequently reported event in this study. Furthermore, adding “temporal dispersion,” an electrodiagnostic sign of demyelination, to the criteria set would cause a shift of classification from axonal or equivocal subtype to demyelination (Uncini et al., 2017; Van den Bergh et al., 2018). Moreover, allocating patients to the inexcitable group instead of lumping them with the axonal group decreased the proportion of axonal GBS. Subgroup analysis in patients having concordant final classifications by two criteria was also performed in our study to increase electrodiagnostic subtype classification reliability.

Our results were comparable with previous literature and contributed further to it. (1) We confirmed that sural-sparing occurred in all electrodiagnostic GBS subtypes (except inexcitable) with different occurrence rates, with the highest in demyelination. (2) The median SNAP was most affected in all subtypes, followed by ulnar

SNAPs, whereas the radial SNAP was remarkably preserved. (3) Sural-sparing in demyelinating GBS is more prominent than axonal GBS based on the number of abnormal upper-limb SNAPs. Moreover, (4) changing between “sural-sparing” and “no sural-sparing” in serial EDXs could occur in all subtypes.

Sural-sparing occurrence rates in GBS are highly variable, depending on sural-sparing definitions, electrodiagnostic criteria, sensory NCS protocol (e.g., number of tested nerves), and EDX timing. Increasing the strictness from at least one to two abnormal upper-limb SNAPs reduced the detection rate from 39 % to 83 % to 19.1 %–65 % in demyelinating GBS (Bromberg and Albers, 1993; Al-Shekhlee et al., 2005; Al-Shekhlee et al., 2007; Chanson and Echaniz-Laguna, 2014; Umapathi et al., 2015; Hiew and Rajabally, 2016; Surpur and Govindarajan, 2017; Wali et al., 2017; Al-Hillali et al., 2020). Sural-sparing occurrence rates in axonal GBS were 18.7 %–38.5 % and 0 %–9.5 %, considering at least one and two abnormal upper-limb SNAPs, respectively (Capasso et al., 2011; Umapathi et al., 2015; Hiew and Rajabally, 2016). These abovementioned comparative data were derived from studies conducted in separate groups with various numbers of tested upper-limb sensory NCS. Our study was distinctive because we explored two categories of sural-sparing patterns in the same group, mostly having a similarly extensive sensory NCS protocol. Thus, assessing the number of affected upper-limb SNAPs was less biased for our patients. Moreover, this decreased the possibility of underdetection of sural-sparing.

As postulated, nerve roots, terminal nerves, and common entrapment sites where the blood–nerve barriers are vulnerable are predisposed to immune-mediated injuries in GBS (Bromberg and Albers, 1993; Capasso et al., 2011; Bae et al., 2014; Umapathi et al., 2015). Sural sensory NCS is usually tested proxi-

mally at the distal calf, potentially explaining sural-sparing response, as opposed to the median and ulnar SNAPs, which are usually tested distally. This could be applicable for the spared antidromic radial SNAP, recorded proximally over the snuffbox. Radial sparing was another finding described in GBS, despite its limited diagnostic value (Freiha et al., 2021). Al-Shekhlee A et al. reported 29.5 % radial sparing in all demyelinating GBS patients (including patients without sural-sparing) (Al-Shekhlee et al., 2007). Our study showed the remarkably preserved radial SNAP in all GBS subtypes with sural-sparing pattern. Whether radial SNAP recording at the first digit is also remarkably preserved warrants further studies (Umamathi et al., 2015). The median SNAP was most severely affected. Dual predisposing factors of being not only the terminal nerve but also the common entrapment site probably explain this.

Hiew et al. showed the “extreme” pattern by “absent median and preserved sural” as a hint point to diagnose demyelinating GBS (Hiew and Rajabally, 2016). Our study showed that sural-sparing also manifested more obviously in demyelinating than axonal GBS, as the former tended to have a higher number of affected upper-limb SNAPs (Tables 1 and 2). In addition, our study showed statistically significant difference in frequencies of sural-sparing pattern A (A vs B + C) between demyelinating and axonal GBS. Contrastingly, Hiew et al. did not find statistical difference in frequencies of “present sural with two abnormal upper-limb SNAPs” between demyelinating and axonal GBS (Hiew and Rajabally, 2016). It was possible conducting bilateral and serial sensory NCS in most patients led to positive results in our study. Extended sensory NCS could further enhance the detection of abnormal upper-limb SNAPs hidden in demyelinating GBS, however, its role might be restricted in axonal GBS. Alternatively, abnormal upper-limb SNAPs in axonal GBS with sural-sparing were too scant or limited to be detected via the routine sensory NCS.

Acute motor axonal neuropathy (AMAN) is a pure motor neuropathy; however, a study revealed SNAP involvement in 69 % of patients, declared by SNAP amplitude alterations in the serial NCS (Capasso et al., 2011). The pathology of axonal GBS includes length-dependent Wallerian-like degeneration and RCF (Umamathi et al., 2015). RCF could affect motor and sensory nerves, and “the occurrence of early conduction failure” in any upper-limb sensory nerves more than in sural nerve might explain sural-sparing in axonal GBS (Freiha et al., 2021). However, reasons why sural-sparing in axonal GBS showed lower number of affected upper-limb SNAP than demyelinating GBS might be as follows: (1) because part of axonal GBS is AMAN, wherein sensory nerves are less prominently affected than in demyelinating GBS, a sensorimotor syndrome, and (2) the attack site of the nerves in axonal GBS may not be necessary at the distal segments (Hiew and Rajabally, 2016); thus, detecting abnormality is limited.

Changes between “sural-sparing” and “no sural-sparing” were found in approximately-one-fourth of all patients. Furthermore, EDX2 additionally discovered approximately 20 % of all “sural-sparing” (Table 4). Thus, serial EDXs modestly increase sural-sparing detection yield. Delayed detection might not have a significant influence on the treatment decision but could increase GBS’s diagnostic confidence. Moreover, it might provide an extension to identify the pathophysiological mechanism and GBS prognosis.

NCS protocol in GBS (e.g., number of tested nerves) varies broadly worldwide with no minimum standard for EDX (Arends et al., 2022). The range of sensory NCS is 0–10 sensory nerves (median: 4, IQR: 3–5) in GBS (Arends et al., 2022). Since abnormal SNAPs were confined in one upper limb in approximately 30 % of sural-sparing, it could be missed if sensory NCS was conducted in one upper limb, despite a complete study of the three nerves. We suggested that extended upper-limb sensory NCS will be worth

in clinical practice to additionally search for this supportively GBS electrodiagnostic feature. Though abnormal radial SNAP was detected in limited number of sural-sparing patients and always occurred with abnormal median and/or abnormal ulnar SNAPs, its detection could enhance the diagnostic certainty of sural-sparing.

This study has the following limitations: (1) all patients did not undergo the same NCS protocol due to the retrospective nature. Nevertheless, most patients received bilateral and serial sensory NCS, which is advantageous for sensory NCS analysis. (2) Our sural-sparing definition allowed inclusion of varying degrees of abnormal upper-limb SNAPs (from mild abnormality to an absent response). This was potentially affected by preexisting neuropathy (e.g., asymptomatic carpal tunnel syndrome), which was hard to exclude in retrospective study. (3) Not all patients received EDX2 because of practicality. However, applying EDX1 with the first study Uncini’s criteria has been recommended in clinical practice (Uncini and Kuwabara, 2018). Finally, (4) although this study showed a different character of sural-sparing between the two major GBS subtypes, the sample number in the axonal arm was low. Hence, to confirm our findings, further studies are warranted.

5. Conclusions

This study reappraised the sural-sparing pattern and its evolution in the GBS acute phase in a cohort that underwent extensive sensory NCS. Furthermore, we confirmed that the sural-sparing pattern occurring across all electrodiagnostic subtypes is most frequently present in demyelinating GBS. In axonal GBS, sural-sparing was less obvious and tended to manifest with a lesser number of abnormal upper-limb SNAPs. Sural-sparing pattern might be changeable in the acute period. Nevertheless, the diagnostic value of “sural-sparing” in GBS was emphasized in both early and delayed EDXs. Extended NCS (bilateral and serial) will be worth in detecting sural-sparing as a supportive electrodiagnostic GBS feature.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.cnp.2022.09.001>.

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