



## Decision-making on radiologically isolated syndrome among Argentinean neurologists: A survey based on clinical experience



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### ABSTRACT

**Background:** Although management of radiologically isolated syndrome (RIS) is still a challenge in clinical practice, in the absence of evidence-based guidelines, the report of survey results might give neurologists some guidance to optimize clinical decision-making. Our aim was to investigate the current RIS management approach of Argentinean neurologists based on their clinical experience.

**Methods:** An anonymous voluntary cross-sectional web-based survey was performed by Argentinean neurologists. We developed questions based on a hypothetical patient with RIS. General agreement was defined as at least 75% of concordance in the answer to each particular question.

**Results:** Sixty-six out of 91 (72%) neurologists completed the survey. There was general agreement on following up patients, performing further examinations and not treating RIS patients at presentation. In addition, participants agreed to perform a lumbar puncture to evaluate the presence of oligoclonal bands (OCB, 82%) and to order a spinal cord MRI (75.4%). During follow-up, there was agreement to perform brain (100%) and spinal (80%) MRI. A few participants would prescribe treatment to RIS patients with both Gd-negative and Gd-positive lesions on spinal MRI. In addition, if a brain Gd-positive lesion is observed at onset, 43.6% would prescribe treatment. During the follow-up, only 15.4% would initiate treatment in the absence of clinical symptoms, regardless of the examinations' results. In those cases in which a treatment was prescribed, there was agreement in using injectable drugs (78.7%).

**Conclusion:** These findings give us a first idea about Argentinean neurologists' decision-making on this entity and may help in the development of a practice guideline.

### 1. Introduction

The advances in brain magnetic resonance imaging (MRI) techniques and the widespread use of this diagnostic test lead to the discovery of incidental white matter T2 lesions within the central nervous system (CNS). These incidentally identified findings may have different etiologies and are rarely (0.1%) due to inflammatory or demyelinating abnormalities (Granberg et al., 2013; Forslin et al., 2016). However, some lesions, because of their size and topography as well as morphology and distribution, could be suggestive of multiple sclerosis (MS) and will fulfill dissemination in space (DIS) criteria (Granberg et al., 2013; Forslin et al., 2016; Okuda et al., 2009; Polman et al., 2005). In 2009, Okuda et al. defined the radiologically isolated syndrome (RIS) as white matter T2 lesions suggestive of MS in asymptomatic people lacking history or previous symptomatology of demyelinating events. Although the Okuda criteria for RIS diagnosis (Okuda et al., 2009) were based on DIS according to the Barkhof/Tintore criteria, the recently published

MAGNIMS consensus recommendations (De Stefano et al., 2018) for diagnosis and management of RIS used DIS as described in the 2017 McDonald criteria (which increased the sensitivity by defining DIS for MS with only 2 lesions in specific areas) proposing that identical MRI criteria for DIS should be applied for the diagnosis of RIS and MS (Thompson et al., 2018; De Stefano et al., 2018). While the RIS criteria (based on expert opinion) have been initially described in 2009 (Okuda et al., 2009), it is currently still discussed which people have low risk of developing MS and who present a preclinical stage of MS (with a high risk of developing MS) (De Stefano et al., 2018). Therefore, starting disease modifying therapies (DMTs) in asymptomatic people is widely discussed and even not recommended by consensus opinions and MS experts' recommendations, which were recently published in North America (Tornatore et al., 2012 and 2016) and Europe (Fernandez et al., 2017). So far, MS expert opinion of Latin American neurologists based on the results of a national survey (clinical practices) has not been published yet. Although these results are not themselves a

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consensus practice parameter or a treatment guideline currently, they were compared with MS experts' recommendations from North America and Europe.

Given that the management of people with RIS is still a challenge in everyday clinical practice, reports of survey results based on MS experts' opinion might give neurologists some guidance in order to optimize clinical and therapeutic decision-making for patients of this region. These results could also help develop future practice guidelines for the investigation and treatment of people with RIS.

For this reason, the aim of this study was to investigate current RIS management opinion of Argentinean MS expert neurologists based on their clinical experience.

## 2. Methods

A cross-sectional study was performed. An anonymous, voluntary web-based survey, which was proposed by the coordinating center of the study (Hospital Alemán de Buenos Aires), was designed in order to investigate clinical and therapeutic decision-making by Argentinean neurologists, based on a hypothetical patient with RIS. No individual responses were known by the coordinating center (E.C.C., J.P.P., A.C. and P.A.L.) and survey results were analyzed using excel software. A total of 91 Argentinean neurologists were invited to participate and 66 (72%) of them (MS experts) completed the survey. The survey was sent via email to potential responders and administered from February 2018 to April 2018 (details about the whole survey is shown in supplementary data). Responders were identified from the Demyelinating Disease Working Group (DDWG) of the Argentinean Neurological Society (ANS) and/or Multiple Sclerosis Centers (MSC) with expertise in demyelinating diseases. This DDWG joins the main Argentinean neurologists with expertise in MS and is dedicated to coordinate national research and treatment guidelines on MS. This survey was developed independently of any DDWG or ANS input. We developed questions on clinical and therapeutic decision-making based on a hypothetical patient with RIS, and reported survey results with degree of agreement based on current practice patterns of Argentinean MS experts. Treatment decision-making based on modifications of this hypothetical case was also investigated.

The hypothetical case was described as follows: "A 32-year-old woman underwent a brain MRI for evaluation of migraine. She has no prior history of demyelinating events. Neurological examination was

normal. The brain MRI showed white matter non-enhancing (gadolinium negative [Gd-]), hyperintense T2 lesions in the CNS suggestive of MS, fulfilling DIS criterion according to the 2017 McDonald MS diagnostic criteria (Thompson et al., 2018) (4 periventricular lesions and 1 juxtacortical lesion)". Thus, this hypothetical patient fulfilled the MAGNIMS consensus recommendations (De Stefano et al., 2018) for RIS diagnosis. However, it would be cautious to wait for the MAGNIMS recommendations validation for their utilization in everyday clinical practice.

General agreement was defined as at least 75% of concordance in the answer to each particular question, and majority agreement ( $\geq 50\%$ ) was also reported (Tornatore et al., 2012 and 2016; Fernandez et al., 2017). This study was approved by the ethics committee of the Hospital Alemán de Buenos Aires, Argentina and all participants signed an electronic informed consent form before data collection. Descriptive statistics (proportions and percents) were reported based on the survey results.

## 3. Results

A total of 66 MS experts from 13 Argentinean provinces who are dedicated to the diagnosis and treatment of patients with MS completed the survey. More than half of the responders had been treating patients with MS for at least 10 years (10–15 years: 19.7%, 15–20 years: 16.1% and  $> 20$  years: 18.2%). The majority of responders belong to Buenos Aires city (59.1%), followed by responders from Buenos Aires province (9.1%). Neurologists from Catamarca, San Luis, Jujuy, Córdoba, Misiones, Neuquén, San Juan, Santa Fe and Santiago del Estero provinces also answered the survey. As for the two previously described organizations, 62.1% of neurologists come from the DDWG and 37.9% from MSC non-DDWG. In addition, these participants carry out their main clinical practice at: public hospitals (general hospitals: 10.3% and university hospitals: 12.1%), private hospitals (general hospitals: 16.1% and university hospitals: 20.7%), mixed practice (33.3% [private and public hospitals]) or private office (7.5%).

### 3.1. General and majority agreement

There was general agreement (93.9%) on following up the hypothetical patient with RIS, performing further examinations and not treating at presentation. As shown in Table 1, participants agreed to

**Table 1**  
Recommendations of both US and European MS experts compared to survey results from Argentinean neurologists\*.

Major areas of agreement amongst Argentinian neurologists (MS experts)	Argentinean MS experts* 2018	US MS experts 2011–2016	European MS experts 2017
<i>At presentation</i>			
• Follow-up and further examinations should be performed in people with RIS (pwRIS)	93.9%	94%	80%
• Both LP and spinal MRI would be performed as part of the diagnostic testing for RIS	82% and 75.4%	67% and 94%	78% and 80%
• If results of LP and spinal MRI are normal pwRIS should not be treated with DMT	65.5% and 86.9%	79%**	96% and 77%
• No prescription of DMT if the brain MRI showed only non-enhancing lesions	98.5%	72%	64%
• If brain Gd+ MRI lesions were observed, treatment should <b>not</b> be prescribed	54.2%	$\leq 2$ : 30% and $\geq 3$ : 20%	71%
• If spinal Gd+ or Gd- MRI lesions were observed, treatment should <b>not</b> be prescribed	56.3% and 86.9%	NR	70%
<i>At follow-up</i>			
• Both brain and spinal MRI should be performed in pwRIS (in those who decided not to prescribe treatment)	100% and 80%	100%	94%
• First follow-up MRI would be performed within 3–6 or 12 months	93.5% and 4.9%	NR, 84%	73%, NR
• If brain Gd+ MRI lesions were observed, treatment should <b>not</b> be prescribed	39%	$\leq 2$ : 30% and $\geq 3$ : 20%	44%
• If new or enlarging brain MRI lesion were observed, treatment should <b>not</b> be prescribed	52.5%	NR	49%
• If spinal Gd+ or Gd- MRI lesions were observed, treatment should <b>not</b> be prescribed	39% and 86.9%	NR	47%

LP: lumbar puncture, MRI: magnetic resonance imaging, Gd + : positive gadolinium-enhancing, Gd - : negative gadolinium-enhancing, NR: not reported, DMT: disease modifying therapies.

\* These items were major areas of agreement amongst Argentinian neurologists in the survey and not general recommendations or consensus opinion on management and treatment, as described in both US and European studies. However, although our survey results are not a formal guidance, we found several similarities with both US and European studies.

\*\* Only described for MRI.

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