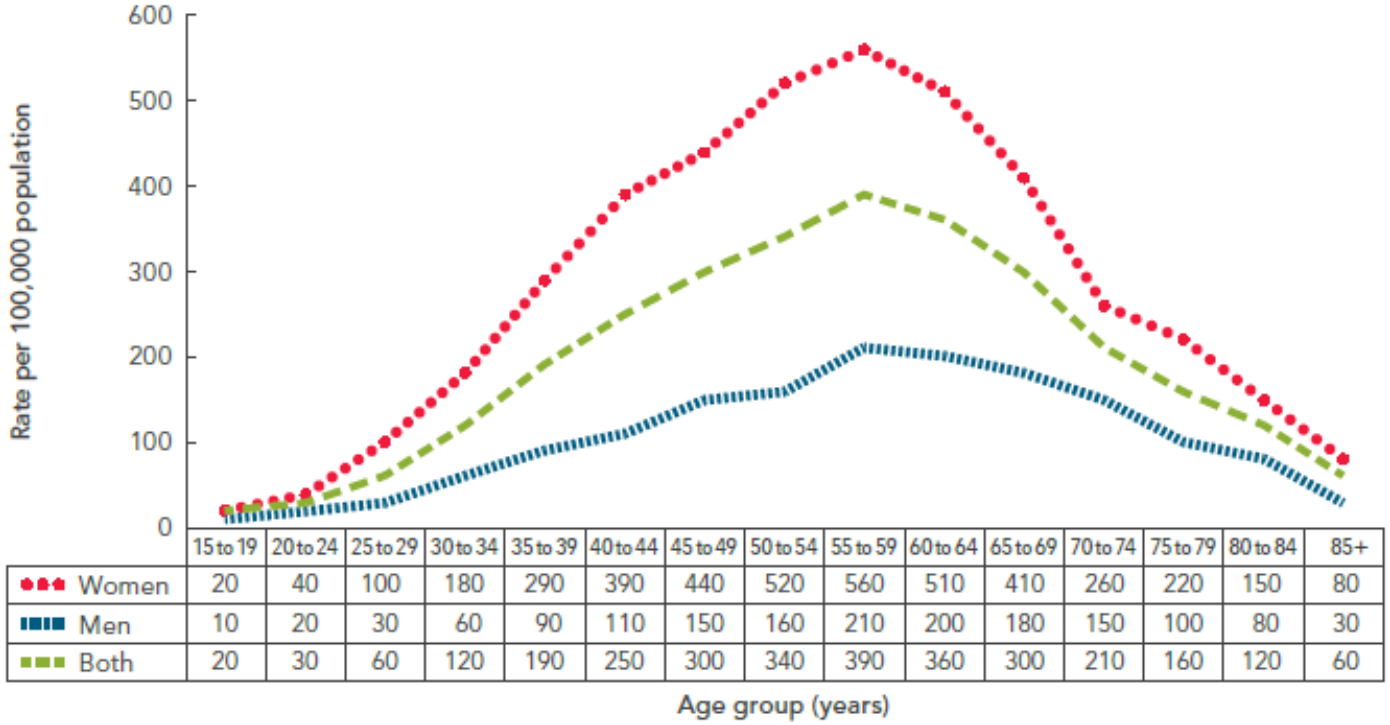
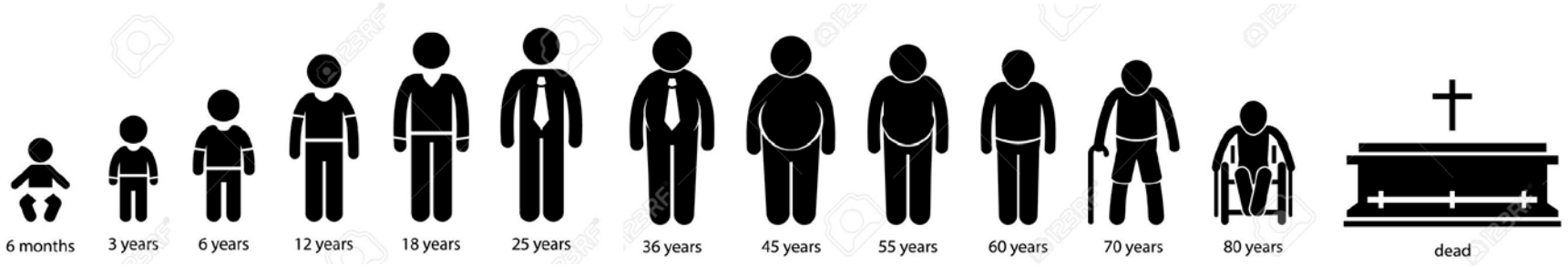
RADYOLOJİK İZOLE SENDROM
VE
TANI KRİTERLERİ

Dr Serpil DEMİRCİ
SDÜTF-NR
2019

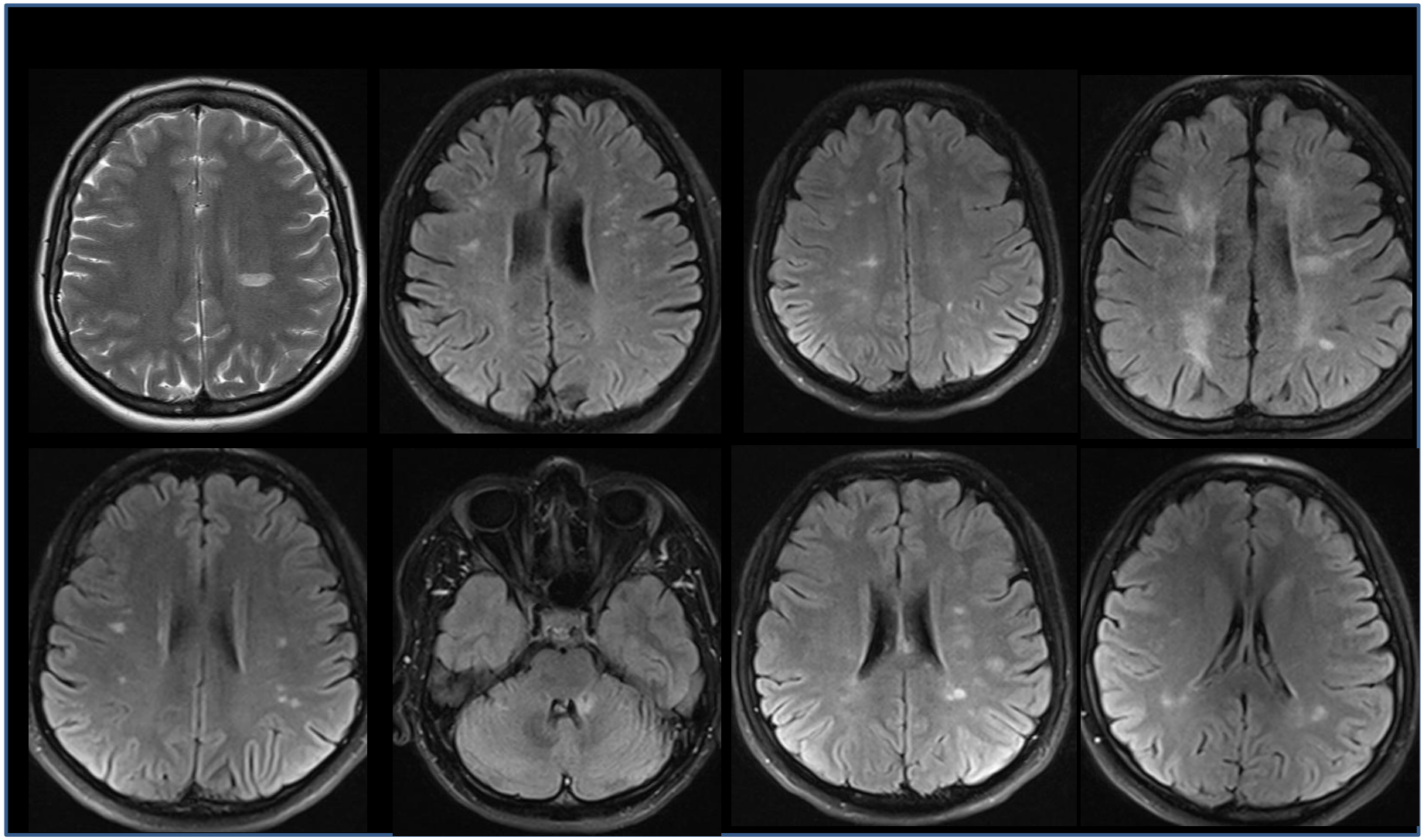


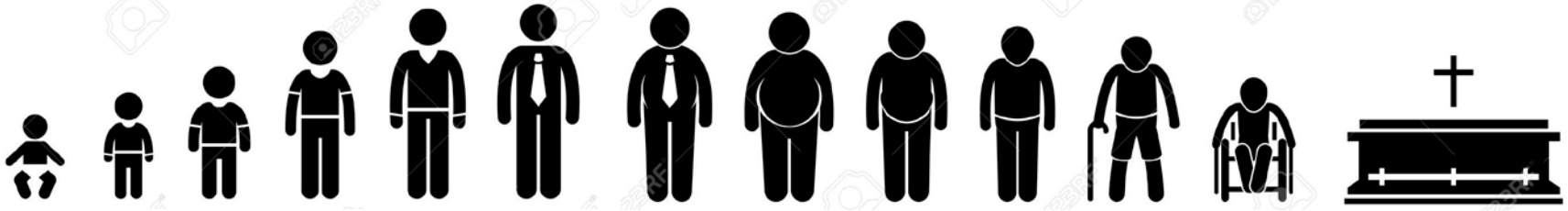
	15 to 19	20 to 24	25 to 29	30 to 34	35 to 39	40 to 44	45 to 49	50 to 54	55 to 59	60 to 64	65 to 69	70 to 74	75 to 79	80 to 84	85+
Women	20	40	100	180	290	390	440	520	560	510	410	260	220	150	80
Men	10	20	30	60	90	110	150	160	210	200	180	150	100	80	30
Both	20	30	60	120	190	250	300	340	390	360	300	210	160	120	60

Age group (years)



Prevalence of multiple sclerosis, by sex and age group, British Columbia, 2009/2010, BC Administrative Data Project
Marrie RA. The rising prevalence and changing age distribution of multiple sclerosis in Manitoba. Neurology 2010; 74 (6)





Klinik öykü ve tanı yok - patoloji MS !

	Toplam	MS	%
Georgi; 1961	15 644	12	0.08
Gilbert JJ, Sadler M; 1983	2450	5	0.2
Engell TA; 1989	16 100	13	0.08

MS klinik olarak sessiz olabilir

Familial multiple sclerosis: MRI findings in clinically affected and unaffected siblings

P J Tienari, O Salonen, J Wikström, L Valan

Journal of Neurology, Neurosurgery, and Psychiatry 19

Ima

Nicola
Andrea
Maria L. Strom

2

Abstract

Subclinical demyel occur in the brains viduals, and the fir multiple sclerosis particular risk. Clin ations were perfor from families with MS. These included cally definite MS, clinically probable tomatic siblings. Sy applied to MRI inter their specificity for the 17 patients wit suggesting MS. Lesi six (38%) of the 16 under age 50 and in over age 50. Judged the lesions of only asymptomatic siblin be due to demyelina onstrate the occur demyelination in asy MS patients and str clinical follow up a

Objective: Our obje familial multiple sclerosis (MS). *Methods:* As gree relatives of sporadic (sMS, n = 152) and familial MS (fMS, n = 88) and healthy volunteers (NC, n derwent brain MRI and magnetization transfer (MT) imaging on a mobile MR scan. On MR examinations, we visually assessed white matter (WM) lesions and quantified WM lesion volumes, brain volumes, and MT ratio (MTr) in lesions and normal-appearing WM (NAWM). *Results:* A lesional MR pattern similar to that of MS patients was found in 4% sMS and 10% fMS. In these WM lesions, MTr was lower ($p < 0.0001$) than in the WM of NC. In contrast, there was no difference in NAWM-MTr and brain volume values between the three groups. *Interpretation:* Focal brain abnormalities indistinguishable from those of MS occur in asymptomatic first-degree relatives of MS patients. These are twice more frequent in fMS than in sMS but do not lead to the widespread tissue damage commonly found in MS patients. Although there is a genetic susceptibility to develop brain abnormalities suggestive of focal demyelination in first-degree relatives of MS patients, other factors are probably critical for the development of a diffuse, clinically relevant, pathology.

Ann Neurol 2006;59:6

Non-MS popülasyonu → 15,559 sağlıklı kontrol
9 kesin demiyelinizan → %0.06
4 olası demiyelinizan → %0.03

MS'lilerin asemptomatik aile üyelerinde %4
Familial MS asemptomatik aile üyeleri %10

Case report

Clinical presentation of primary progressive multiple sclerosis 10 years after the incidental finding of typical magnetic resonance imaging brain lesions

The subclinical stage of primary progressive multiple sclerosis may last 10 years

Sequential magnetic resonance imaging follow-up of multiple sclerosis before the clinical phase

J de Seze and P Vermersch*
Department of Neurology, University of Lille, Lille, France

There is much evidence of the importance of the preclinical phase of multiple sclerosis (MS). However, apart from a recent report of the incidental discovery of a case of primary progressive MS, there are no data on the sequential magnetic resonance imaging (MRI) follow-up of patients before the clinical phase. We report the incidental discovery of white matter changes on MRI and their follow-up in a patient three years before the first neurological event (optic neuritis). A 34-year-old woman presented with headaches and depression after her young daughter had been involved in a car accident and spent two weeks in intensive care. The woman's general practitioner performed a brain MRI, which revealed multiple T2-weighted hypersignals suggesting MS. During the next three years, clinical examination remained normal but we observed new T2 lesions and/or new enhanced T1 lesions after gadolinium infusion on the four successive MRIs. Thirty-seven months after the first MRI, the patient developed a right optic neuritis. The diagnosis of MS was made according to space and time dissemination on MRI criteria. We proposed a treatment with Interferon Beta 1a (Avonex).

Multiple Sclerosis *(2005)* **11,** 395–397

3 yıl sonra

P357

Clinically unsuspected multiple sclerosis: report of 22 cases and review of the literature

M. Eraksoy, M. Kurtuncu, G. Akman-Demir, Z. Yapici, M. Mutlu, B. Topcular, A. Tumac, U. Tuzun, M. Calay, H. Durmus, H. Ozcan
Istanbul University (Istanbul, TR)

Magnetic resonance imaging (MRI)and cerebrospinal fluid (CSF)analysis reduce the number of undiagnosed cases of multiple sclerosis, but there has been some reports about the cases with multiple sclerosis discovered unexpectedly at necropsy. In this report, we describe twenty-two cases with the ages between 13 and 74 years in which multiple sclerosis was discovered unexpectedly at MRI.There were 13 girls/women and 9 boys/men in the group. Nine of the cases had history of vascular/tension headache, three of the cases were admitted because of epilepsy, and the rest of the cases had panick attacks (2), cervical pain (2), head trauma (2), pubertas precox (1), paroxysmal positional vertigo (1), neck trauma(1), and drop attack (1). Family history of multiple sclerosis was positive in 4 cases. Five of the cases had slight neurological findings. Oligoclonal bands were detected in CSF in 10 cases, but not in 2 cases in which lumbar puncture was performed. Median duration of follow-up was 3 years. Eleven patients developed new and contrast enhanced lesions, but only 10 cases converted to definite multiple sclerosis according to McDonald's criteria within 3 years. Diagnostic and treatment approaches to unsuspected multiple sclerosis and management of the cases in the preclinical period are important and controversial. In this presentation, diagnostic problems and management strategies of the unsuspected multiple sclerosis will be discussed in the light of the literature.

22 olgu; 13 kadın, 9 erkek

Yaş: 13-74 yıl

MS aile öyküsü → 4 /22

BOS OKB + → 10/12

3 yıl izlem

DIT → 11/22

KKMS → 10/22

P358

The diagnosis of multiple sclerosis in China

Z. Xinghu, W. Zhangwei, L. Yun, Z. Heng, L. Jun, L. Penju, H. Ming, W. Yongjun
Beijing Tiantan Hospital (Beijing, CHN)

Unexpected multiple sclerosis: follow-up of 30 patients with magnetic resonance imaging and clinical conversion profil

C Lebrun,[1] C Bensa,[2] M Debouverie,[3]
P Clavelou,[7] D Brassat,[8] P Labauge,[9] E

The concept of preclinical multiple sclerosis is now well recognised, and a diagnosis of silent brain T2 lesions is frequent because of the ease of performing MRI. Nevertheless, patients with incidental brain MRI fulfilling Barkhof– Tintoré criteria are more rare. We report a descriptive retrospective study of clinical and 5 year MRI follow-up in patients with subclinical demyelinating lesions fulfilling MRI Barkhof–Tintoré criteria with a normal neurological examination. 30 patients were identified and the first brain MRI was performed for various medical events: headaches (n = 14), migraine with (n = 2) or without (n = 4) aura, craniocerebral trauma (n = 3), depression (n = 3), dysmenorrhoea (n = 2), epilepsy (n = 1) and cognitive changes (n = 1). Mean time for the sensitive sy (n = 2) and cognitive deterioration (n = 1). Eight (72%) already had criteria of dissemination to space and time before the clinical event. Mean time between the first brain MRI and clinically isolated syndrome (CIS) was 2.3 years. To our knowledge, this is the first cohort of CIS with preclinical follow-up. Early treatment should be discussed in view of the predictive value on conversion of the MRI burden of the disease.

26 kadın, 4 erkek ; Ort yaş: 29 yıl

- MS aile öyküsü → 5/30
- BOS OKB+ → 9/25; IgG+ → 25/24
- VEP → 8/30
- DIT → 25/30
- CIS → 11/30 (ort 2.3 yıl

J Neurol Neurosurg Psychiatry 2008;**79**:195–198.

RESEARCH PAPER *Multiple Sclerosis* 2009; 15: 918–927

Multiple sclerosis risk in radiologically uncovered asymptomatic possible inflammatory-demyelinating disease

A Siva[1], S Saip[1], A Altintas[1], A Jacob[2,], BM Keegan[3] and OH Kantarci[3]*

Background Natural history of patients with incidentally discovered lesions that fulfill magnetic resonance imaging (MRI) criteria for multiple sclerosis (MS) in the absence of objective clinical symptoms suggestive of central nervous system (CNS) inflammatory-demyelinating disease is not well defined.

Objective We evaluated the risk of developing symptomatic MS in patients with radiologically uncovered asymptomatic possible inflammatory-demyelinating disease (RAPIDD).

Methods We identified and longitudinally followed a cohort of 22 patients from two tertiary care MS centers: Istanbul University, Cerrahpasa School of Medicine, Istanbul, Turkey, and Mayo Clinic, Rochester, Minnesota, after an initial MRI study fulfilling the Barkhof–Tintore MRI criteria completed for other reasons unrelated to MS.

Results Eight of 22 patients developed an objective clinical symptom consistent with a CNS inflammatory-demyelinating syndrome and fulfilled dissemination in space and time criteria for definite MS. Median age at the time of diagnosis of MS was 44.8 years (range 28.3–71.4 years). Time taken for the development of definite MS was studied by survival analysis. Cumulative event rates were; 12 months: 9%, 24 months: 15%, 36 months: 30.4%, and 60 months: 44.6%. Six of 22 patients were followed beyond 60 months. Two of these six patients developed MS later (at 66 and 112 months, respectively). Three patients remained asymptomatic despite follow-up of 10 years.

- MS trait
- Asemptomatik MS
- Umulmadık/beklenmeyen MS
- Radyolojik olarak ortaya çıkan asemptomatik olası inflamatuar demiyelinizan hastalık (RAPIDD)
- Tip 5 CIS : demiyelinizan hastalığı düşündüren klinik yok, MR düşündürüyor
- Radyolojik İzole Sendrom

Incidental MRI anomalies suggestive of multiple sclerosis

The radiologically isolated syndrome

D.T. Okuda, MD
E.M. Mowry, M
A. Beheshtian, M
E. Waubant, MI
S.E. Baranzini, P
D.S. Goodin, M
S.L. Hauser, MD
D. Pelletier, MD

44 olgu, 41 K-3 E, median yaş: 38.5 yıl

- 10 → CIS/MS (median 2.7 yıl)
- DIT → 24 (%59)
- İlk MRI Gd+ → dönüşüm için risk

Address correspondence and reprint requests to Dr. Darin T. Okuda, University of California, San Francisco, Department of Neurology, UCSF Multiple Sclerosis Center, 350 Parnassus Avenue, Suite 908, San Francisco, CA 94117
darin.okuda@ucsf.edu

ion of MRI in medicine has led to an increased
ntal white matter pathology in the CNS. Routinely
ry or evolution of such individuals with respect to
unclear.
patients who exhibit incidental imaging findings

were obtained from asymptomatic patients with

and 3 male subjects (median age = 38.5, range: 16.2 .1). Clinical evaluations were performed in 44 patients at the time of initial imaging; longitudinal clinical follow-up occurred for 30 patients, and longitudinal MRI data were acquired for 41 patients. Neurologic examination at the time of the initial MRI scans was normal in nearly all cases. While radiologic progression was identified in 59% of cases, only 10 patients converted to either clinically isolated syndrome or definite MS. The presence of contrast-enhancing lesions on the initial MRI was predictive of dissemination in time on repeat imaging of the brain (hazard ratio [HR] = 3.4, 95% confidence interval [1.3, 8.7], $p = 0.01$).

Conclusion: Individuals with MRI anomalies highly suggestive of demyelinating pathology, not better accounted for by another disease process, are very likely to experience subsequent radiologic or clinical events related to multiple sclerosis. Additional studies will be necessary to fully define this risk. *Neurology*® 2009;72:800–805

Rastlantısal olarak saptanan SSS beyaz cevher lezyonları

- Ovoid, sınırları belirli ve homojen lezyon, ± korpus kallosum tutulumu
- T2↑ lezyon >3 mm,
  DIS ← Barkhof kriterleri (+) (en az ¾)
- Vasküler paternde olmayacak

Barkhof kriterleri (DIS)	
T2 lezyon	≥9 T2 hiperintens ya da ≥1 Gd+
Infratentorial lezyonlar	≥1
Jukstakortikal lezyonlar	≥1
Periventriküler lezyonlar	≥4

RIS tanı ölçütleri

Öyküde nörolojik bozuklukla ilişkili düzelen klinik belirti olmaması
MRG bulgularının klinik, sosyal ya da işlevsel bir bozukluğa neden olmaması
MRG bulgularının başka nedenlerin direkt etkisi ile açıklanamaması (madde bağımlılığı, toksin, başka tıbbi durum)
Korpus kallozum tutulumu göstermeyen yaygın beyaz cevher lezyonu ya da lökoariozis gibi patolojilerin dışlanması
MRG bulgularını açıklayabilecek başka bir hastalık süreci olmaması

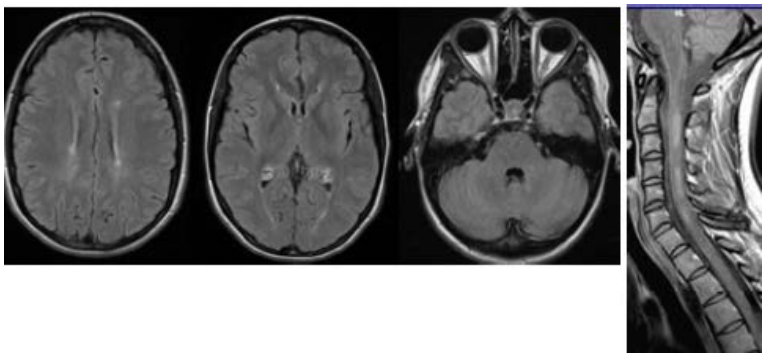
MRI criteria for multiple sclerosis in patients presenting with clinically isolated syndromes: a multicentre retrospective study

Josephine K Swanton, Alex Rovira, Mar Tintoré, Daniel R Altmann, Frederik Barkhof, Massimo Filippi, Elena Huerga, Katherine A Miszkiel, Gordon T Plant, Chris Polman, Marco Rovaris, Alan J Thompson, Xavier Montalban, David H Miller

Lancet Neurology 2007

≥2 karakteristik bölgede ≥ 1 T2 lezyon :

- Periventriküler
- Jukstakortikal
- İnfratentorial
- Spinal kord



DIS y DIT	Sensitivity (95% C.I)	Specificity (95% C.I)	Accuracy (95% C.I)	PPV (95% C.I)
McDonald 2001	47.1% (36-58%)	91.1% (85-95%)	73.1% (67-79%)	78.4% (65-89%)
McDonald 2005	60.0% (49-70%)	87.8% (81-93%)	76.4% (70-82%)	77.3% (65-87%)
Swanton 2006	71.8% (61-81%)	87.0% (80-92%)	80.8% (75-86%)	79.2% (68-88%)

Multiple Sclerosis and Related Disorders 24 (2018) 48–54

Contents lists available at ScienceDirect

Multiple Sclerosis and Related Disorders

journal homepage: www.elsevier.com/locate/msard

Review article

2017 McDonald diagnostic criteria: A review of the evidence

N McNicholas[a,*], M Hutchinson[a], C McGuigan[a], J Chataway[b]

Evolution of MRI criteria for dissemination in space and time, McDonald criteria.

	McDonald 2001	McDonald 2005	McDonald 2010	McDonald 2017
DIS	≥3 of the following:	≥3 of the following:	≥1 lesion in each of ≥2 characteristic locations:	**≥1 lesion in each of ≥2 characteristic locations:**
	9 T2 lesions or 1 Gd-enhancing lesion	9 T2 lesions or 1 Gd-enhancing lesion	PV	**PV**
	3 or more PV lesions	3 or more PV lesions	Juxtacortical	**JC/Cortical**
	1 or more JC lesions	1 or more JC lesions	Infratentorial	**Infratentorial**
	1 or more infratentorial lesions	1 or more infratentorial lesions	Cord	**Cord**
	A cord lesion may replace one brain lesion	A cord lesion can replace an infratentorial lesion Any number of cord lesions can be included in the total lesion count	All lesions in symptomatic regions **excluded** in BS and cord syndromes	**All lesions in symptomatic regions included**
DIT	A Gd-enhancing lesion at least 3 months after CIS onset A new T2 lesion relative to a prior scan, at least 3 months after CIS onset	A Gd-enhancing lesion at least 3 months after CIS onset A new T2 lesion relative to a baseline scan, obtained at least 30 days after CIS onset	A new T2 lesion on follow-up MRI regardless of timing of baseline scan Concomitant enhancing and non-enhancing **asymptomatic** lesions	**A new T2 lesion on follow-up MRI regardless of timing of baseline scan** **Concomitant enhancing and non-enhancing lesions – symptomatic or asymptomatic. Optic nerve lesions are an exception**

Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria

Alan J Thompson, Brenda L Banwell, Frederik Barkhof, William M Carroll, Timothy Coetzee, Giancarlo Comi, Jorge Correale, Franz Fazekas, Massimo Filippi, Mark S Freedman, Kazuo Fujihara, Steven L Galetta, Hans Peter Hartung, Ludwig Kappos, Fred D Lublin, Ruth Ann Marrie, Aaron E Miller, David H Miller, Xavier Montalban, Ellen M Mowry, Per Soelberg Sorensen, Mar Tintoré, Anthony L Traboulsee, Maria Trojano, Bernard M J Uitdehaag, Sandra Vukusic, Emmanuelle Waubant, Brian G Weinshenker, Stephen C Reingold, Jeffrey A Cohen

↑ MS olasılığı
MS özellikleri + (yorgunluk, kognitif bozukluk, talamik atrofi)
MS tanısı ve tedavi gecikmesi → özürlülük riski ↑

Yanlış tanı riski ↑
2/3'ü 5 yıl içinde MS tanısı almıyor

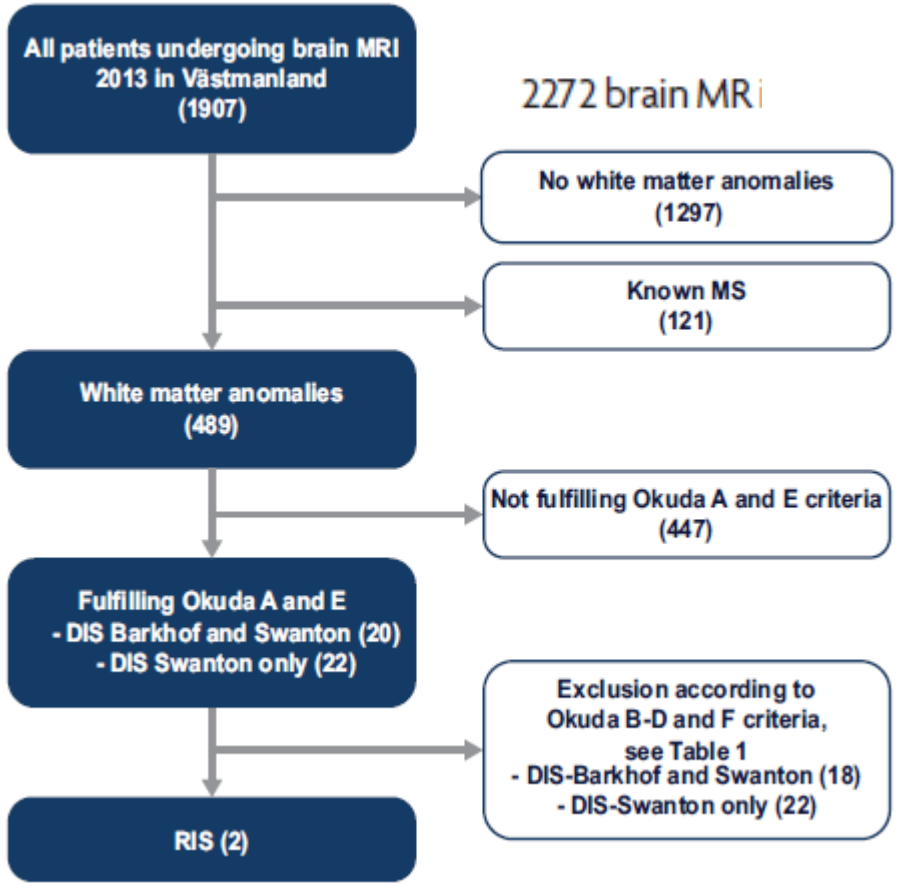
MS tanısı için **Klinik belirtiler** olmalı
CIS gelişenlerde MS tanısı için DIS ve DIT (2010) ölçütleri kullanılmalı

Incidence of Radiologically Isolated Syndrome: A Population-Based Study

Y. Forslin, T. Granberg, A. Antwan Jumah, S. Shams, P. Aspelin, M. Kristoffersen-Wiberg, J. Martola, and S. Fredrikson

DIS Barkhof Classification[4]	DIS Swanton Classification[3]
At least 3 of ≥3 Periventricular lesion ≥1 Juxtacortical lesion ≥1 Infratentorial or spinal cord lesion ≥1 Contrast-enhancing or ≥9 T2 lesions	At least 2 of ≥1 Periventricular lesion ≥1 Juxtacortical lesion ≥1 Infratentorial lesion ≥1 Spinal cord lesion

RESULTS: The cumulative incidence of radiologically isolated syndrome was 2 patients (0.1%), equaling an incidence rate of 0.8 cases per 100,000 person-years, in a region with an incidence rate of MS of 10.2 cases per 100,000 person-years. There was no difference in radiologically isolated syndrome incidence rate when applying a modified version of the Okuda criteria by using the newer Swanton classification for dissemination in space.



Radiologically isolated syndrome or subclinical multiple sclerosis: MAGNIMS consensus recommendations

Nicola De Stefano, Antonio Giorgio, Mar Tintoré, Maria Pia Amato, Ludwig Kappos, Jacqueline Palace, Tarek Yousry, Maria A Rocca, Olga Ciccarelli, Christian Enzinger, Jette Frederiksen, Massimo Filippi, Hugo Vrenken and Àlex Rovira ; on behalf of the MAGNIMS study group

Multiple Sclerosis Journal
2018, Vol. 24(2) 214–221
DOI: 10.1177/1352458517717808

Dahil etme kriterleri (DIS : Swanton kriterleri)

DIS için en az 2 topografik bölgede ≥1 T2-hiperintens lezyon

- Periventriküler beyaz cevher
- Kortikal/juktakortikal
- İnfratentorial
- Spinal kord

Dışlama kriterleri

- Öykü/muayenede MS'u düşündürecek işlev bozukluğuna ait klinik kanıt
- MR bulguları başka hastalık süreçleri ile açıklanabilir; yaşlanma, vasküler nedenli ve toksin-madde maruziyeti

BMJ Open

Radiologically isolated syndrome: an uncommon finding at a university clinic in a high-prevalence region for multiple sclerosis

Granberg T, Martola J, Aspelin P, *et al.* Radiologically isolated syndrome: an uncommon finding at a university clinic in a high-prevalence region for multiple sclerosis. *BMJ Open* 2013;**3**:e003531. doi:10.1136/bmjopen-2013-003531

2105 kişi → 1 RIS
Prevalans → %0.05
15 -40 yaş arası → %0.15

Incidence of Radiologically Isolated Syndrome: A Population-Based Study

AJNR Am J Neuroradiol 37:1017–22 Jun 2016

Y. Forslin, T. Granberg, A. Antwan Jumah, S. Shams, P. Aspelin, M. Kristoffersen-Wiberg, J. Martola, and S. Fredrikson

2272 MRI → 2 RIS
RIS insidans: 0.8/100.000
MS insidans : 10.2 /100.000

Review

MULTIPLE SCLEROSIS JOURNAL | MSJ

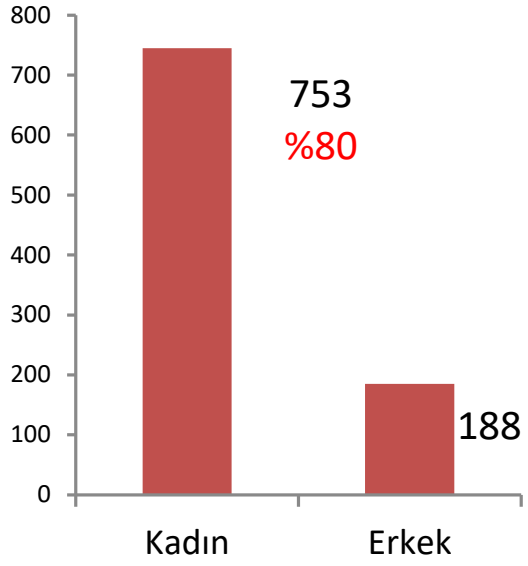
Multiple Sclerosis Journal
19(3) 271–280

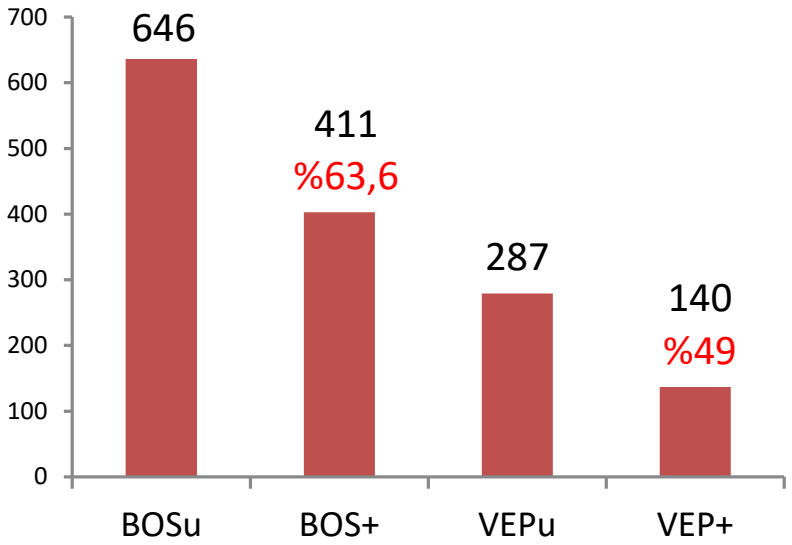
DOI: 10.1177/1352458512451943
msj.sagepub.com
SAGE

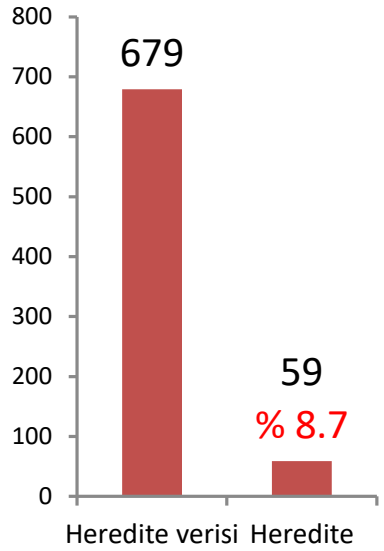
Radiologically isolated syndrome – incidental magnetic resonance imaging findings suggestive of multiple sclerosis, a systematic review

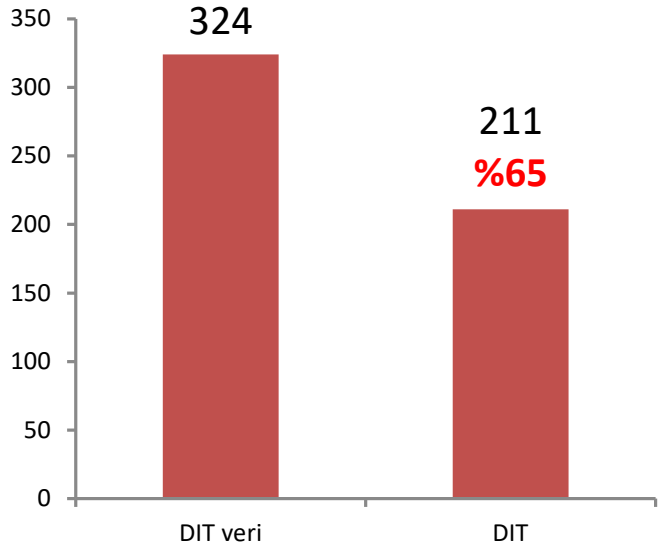
Tobias Granberg[1], Juha Martola[1], Maria Kristoffersen-Wiberg[1], Peter Aspelin[1] and Sten Fredrikson[2]

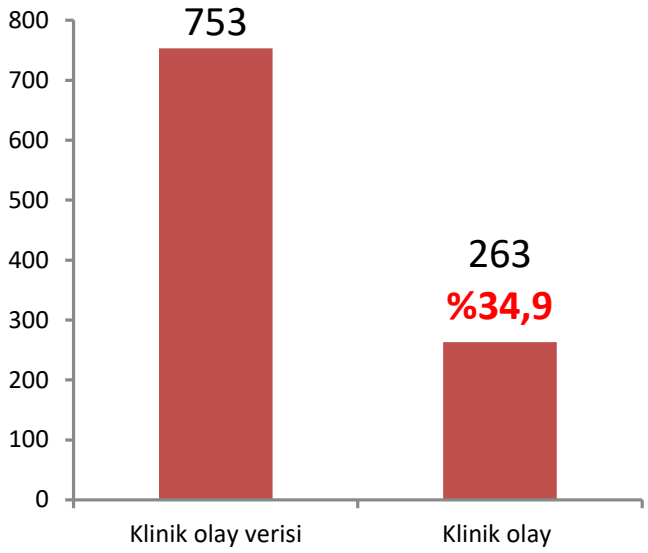
RIS 941, yaş 13-74 yıl





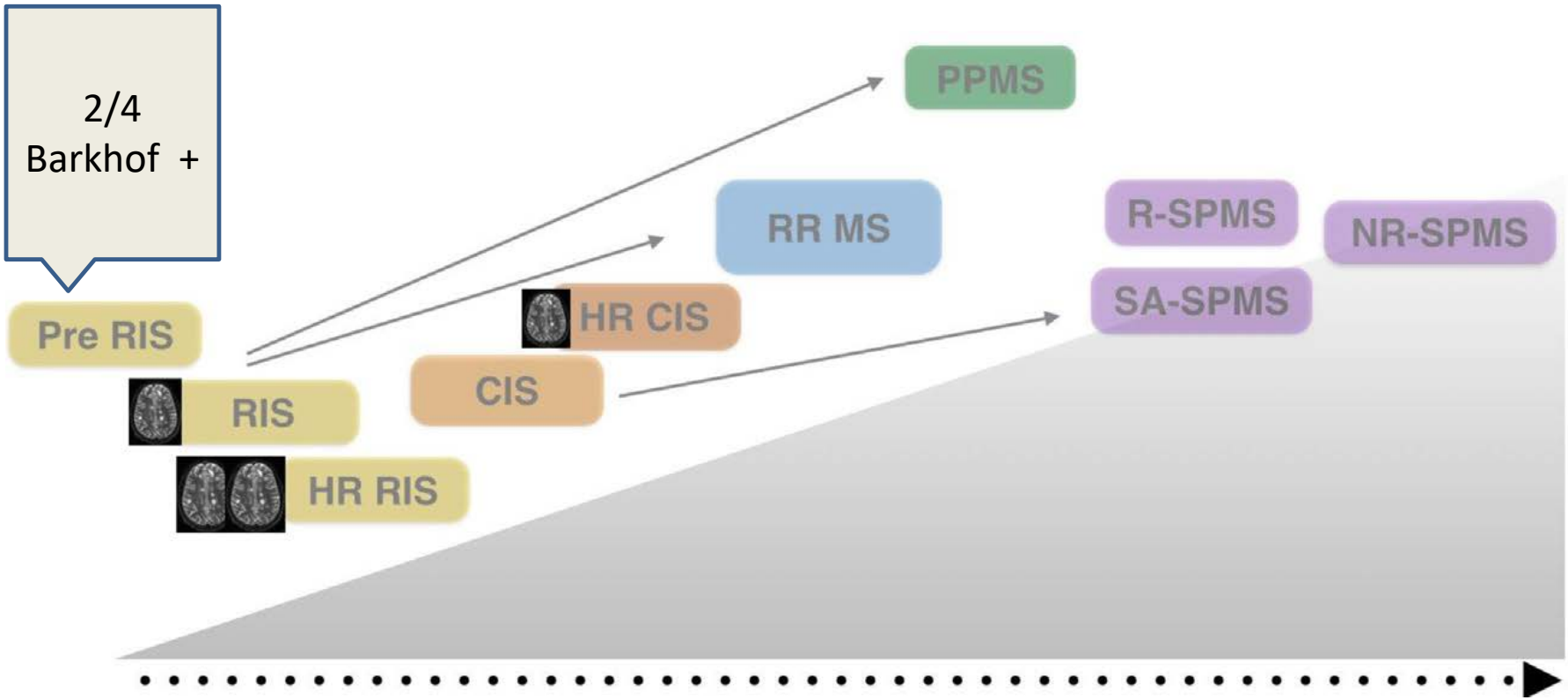






CIS/MS
PPMS

Ortalama 2-5 yıl



Revue Neurologique 2015; 171: 698-706

OPEN ACCESS Freely available online

PLOS ONE

Radiologically Isolated Syndrome: 5-Year Risk for an Initial Clinical Event

Darin T. Okuda[1*], Aksel Siva[2], Orhun Kantarci[3], Matilde Inglese[4], Ilana Katz[4], Melih Tutuncu[2], B. Mark Keegan[3], Stacy Donlon[5], Le H. Hua[6], Angela Vidal-Jordana[7], Xavier Montalban[7], Alex Rovira[7], Mar Tintoré[7], Maria Pia Amato[8], Bruno Brochet[9], Jérôme de Seze[10], David Brassat[11], Patrick Vermersch[12], Nicola De Stefano[13], Maria Pia Sormani[14☯], Daniel Pelletier[15☯], Christine Lebrun[16☯], on behalf of the Radiologically Isolated Syndrome Consortium (RISC) and Club Francophone de la Sclérose en Plaques (CFSEP)[¶]

451 olgu

- 354 (78.5) Kadın
- Yaş: 37.2 yıl
- MS aile öyküsü : %10
- Ortalama izlem süresi : 4.4 yıl (0.01 -21.1 yıl)

- BOS bulgusu : % 64.7
- DMT : %17

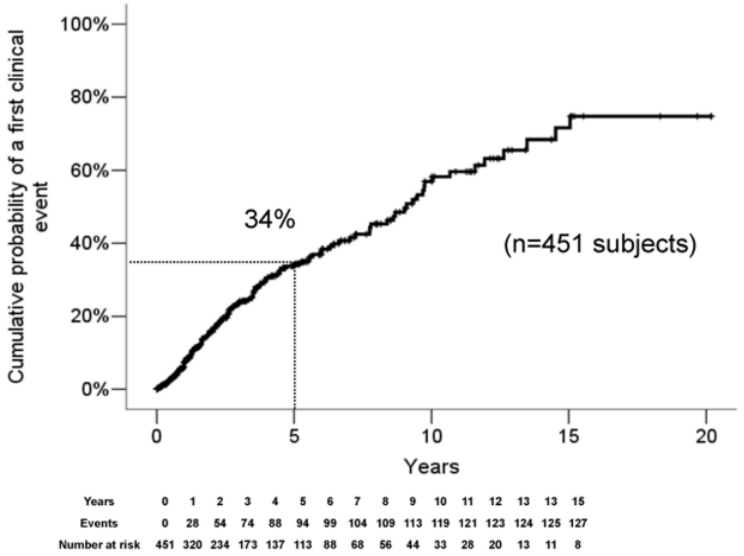
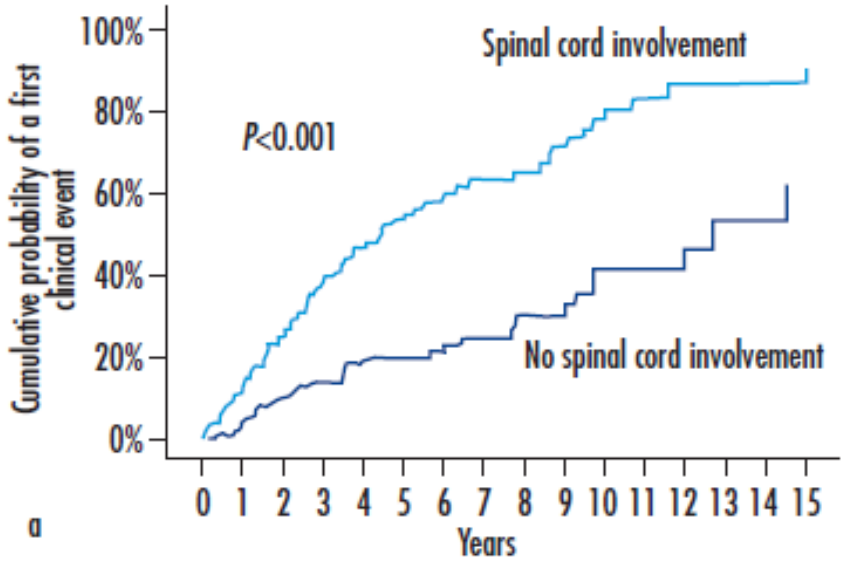


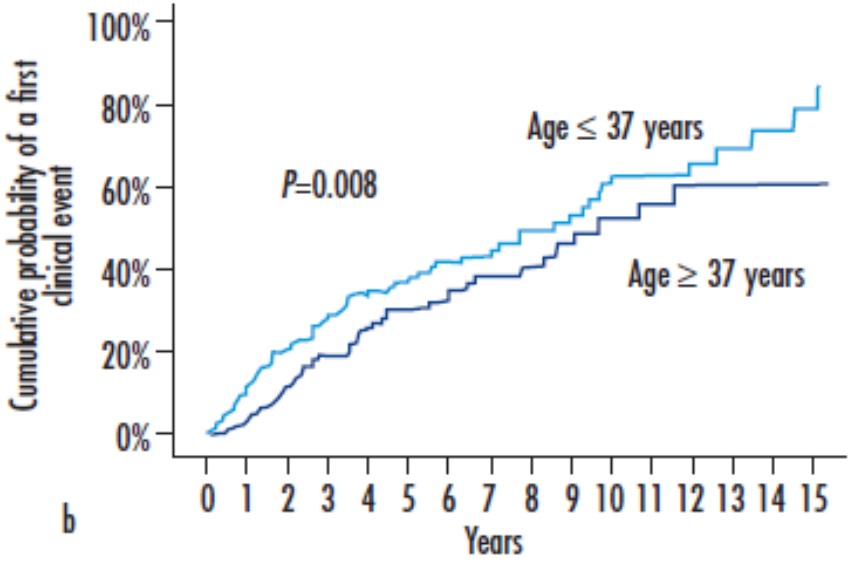
Table 4. Cox regression models containing univariate and multivariate analyses of factors related to time to the first acute or progressive clinical event.

Variable	n	Univariate Analysis* HR (95% C.I.)	*p*	Multivariate Analysis* HR (95% C.I.)	*p*
Age	451	0.97 (0.96–0.99)	<0.001	0.98 (0.96–0.99)	0.009
Sex (Male)	451	1.64 (1.10–2.44)	0.015	1.93 (1.24–2.99)	0.004
Positive Family MS History	451	2.20 (1.31–3.70)	0.003		
Ethnicity	451		0.99		
Abnormal CSF[§]	300	1.78 (1.11–2.87)	0.017		
Periventricular lesions presence	446	0.84 (0.21–3.90)	0.8		
Infratentorial lesions presence	446	1.26 (0.88–1.83)	0.2		
Juxtacortical lesions presence	444	0.94 (0.50–1.77)	0.84		
Cervical or thoracic spinal cord lesion	383	3.26 (2.18–4.86)	<0.001	3.09 (2.06–4.62)	<0.001
Contrast enhancement on RIS MRI	381	1.09 (0.70–1.69)	0.70		

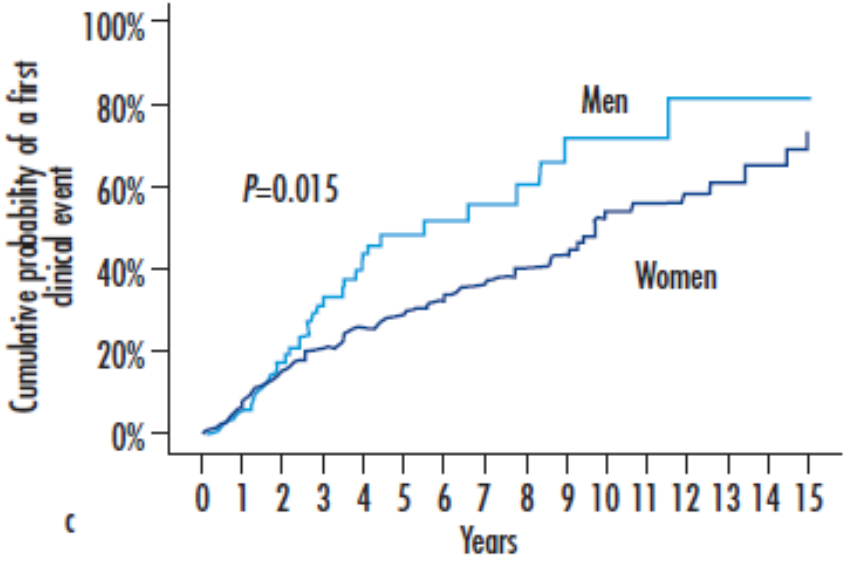
*Adjusted for Center and date of RIS diagnosis.
HR = hazard ratio; CSF = cerebrospinal fluid.
[§]= IgG index >0.7 or the presence of >2 unique oligoclonal bands within the CNS.


Cumulative probability of a first clinical event
100%
80%
60%
40%
20%
0%
Spinal cord involvement
P<0.001
No spinal cord involvement
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Years

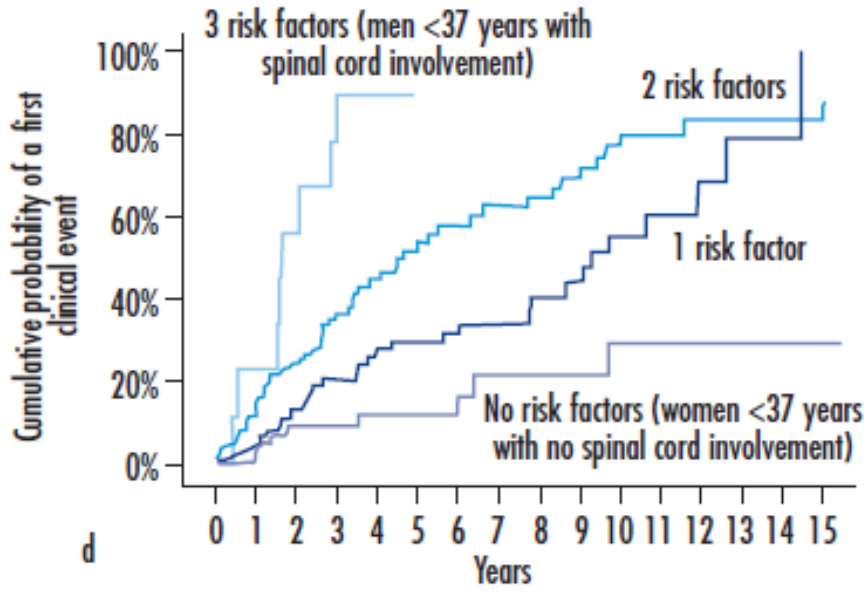
a


Cumulative probability of a first clinical event
100%
80%
60%
40%
20%
0%
Age ≤ 37 years
P=0.008
Age ≥ 37 years
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Years

b


Cumulative probability of a first clinical event
100%
80%
60%
40%
20%
0%
Men
P=0.015
Women
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Years

c


3 risk factors (men <37 years with spinal cord involvement)
2 risk factors
1 risk factor
No risk factors (women <37 years with no spinal cord involvement)
Cumulative probability of a first clinical event
100%
80%
60%
40%
20%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Years

d

Association Between Clinical Con
Sclerosis in Radiologically Isolate
Magnetic Resonance Imaging, Cer
and Visual Evoked Potential

Arch Neurol. 2009;66(7):841-846

Follow-up of 70 Patients

Christine Lebrun, MD; Caroline Bensa, MD; Marc Debouverie, MD; Sandrine

70 olgu

- 53 Kadın, 35.6 yaş (16-48 yıl)
- MS aile öyküsü : 5
- İzlem süresi : 3-6 yıl
- BOS bulgusu : 30 OKB+, 28 IgG Indeksi ↑
- VEP : 45 bozuk

- DIT : 64/70 (20 Gd+, 47 yeni T2 lezyon)
- CIS: 23/70

MRI	n(%)
Gd+	17
>9 T2	58
İnfratentorial	45

Table 3. Prognostic Factors for Developing a Clinically Isolated Syndrome

Prognostic Factor	No. of Patients by Presence or Absence of Prognostic Factor: Present	Absent	*P* Value
First MRI			
Gadolinium enhancement	17	53	.46
≥9 T2-hyperintense signals	58	12	.50
Infratentorial lesions	45	25	.47
Barkhof/Tintoré criteria	56	14	.08
Second MRI			
Gadolinium enhancement	20	50	.01
≥9 T2-hyperintense signals	63	7	.18
Infratentorial lesions	45	25	.57
Dissemination	64	6	.07
CSF			
>4 Cells/mm^3	28	42	.61
Oligoclonal bands	30	40	.69
Increased IgG index	28	42	.26
1 Abnormal result in CSF	51	19	.66
VEP			
Abnormal	45	25	.04
1 Abnormal result in CSF and ≥9 T2-hyperintense lesions on first MRI	48	22	.02
Abnormal VEP and ≥9 T2-hyperintense lesions on first MRI	38	32	.12

Primary Progressive Multiple Sclerosis Evolving From Radiologically Isolated Syndrome

453 RIS
- 113 CIS/MS
- 15 PPMS (%11.7)
  - ort 3.5 yıl
  - erkek
  - ileri yaş
  - spinal kord lezyonu daha fazla

ebrun, MD, PhD,[2] Aksel Siva, MD,[3]
edo, MD, MPH,[4] Matilde Inglese, MD,[5]

gressive phase in subjects with radiologically isolated syn-
rosis (PPMS).
ed. Demographic, clinical, and radiological characteristics
compared to those that developed a relapsing disease
ally isolated syndrome [CIS] or relapsing-remitting MS) and were also compared to two other
population- and clinic-based PPMS cohorts.
Results: Of the 453 subjects with RIS, 128 evolved to symptomatic MS during the follow-up (113 developed a first acute clinical event consistent with CIS/MS, 15 evolved to PPMS). PPMS prevalence (11.7%) and onset age (mean ± standard deviation; 49.1 ± 12.1) in the RIS group were comparable to other PPMS populations ($p > 0.05$). Median time to PPMS was 3.5 years (range, 1.6–5.4). RIS evolved to PPMS more commonly in men ($p = 0.005$) and at an older age ($p < 0.001$) when compared to CIS/MS, independent of follow-up duration. Subjects who evolved to PPMS had more spinal cord lesions (100%) before symptomatic evolution than those that developed CIS/MS (64%) and those that remained asymptomatic (23%) within the follow-up period ($P = 0.005$). Other MRI characteristics in the preprogressive phase of PPMS were indistinguishable from CIS/MS.
Interpretation: Subjects with RIS evolve to PPMS at the same frequency as expected from general MS populations in an age-dependent manner. Besides age, unequivocal presence of spinal cord lesions and being male predicted evolution to PPMS. Our findings further suggest that RIS is biologically part of the MS spectrum.

ANN NEUROL 2016;79:288–294

Impact of pregnancy on conversion to clinically isolated syndrome in a radiologically isolated syndrome cohort

Multiple Sclerosis Journal
18(9) 1297–1302

DOI: 10.1177/1352458511435931
msj.sagepub.com
SAGE

Results: A total of 60 women with RIS were followed for up to seven years. Among them, seven became pregnant and were compared with 53 age-matched control women with RIS who did not become pregnant during the observation period. A significantly shorter time of conversion to the first neurological event was observed in the pregnant group [15.3 months (10–18)] compared with the non-pregnant controls [35.7 months (8–76)], yielding an absolute difference of 20.4 months ($p<0.05$). The mean (SD) number of active lesions on a subsequent brain MRI scan was significantly higher in the pregnant group [3.2 (±1.7)] compared with the control group [1.8 (±0.6)].

RIS patients	Pregnant		Non-pregnant		*p*-value
Number	7 Remaining RIS: 3 Developing MS: 4		53 Remaining RIS: 31 Developing MS: 22		–
Mean age, years (range) at RIS diagnosis	28.5 (24–36)		31.9 (22–46)		0.3
	First MRI	**Second MRI**	**First MRI**	**Second MRI**	
Mean number of T2 lesions	13.1	17.8	14.2	16.3	0.49/0.6
Mean volume of T2 lesions (mm^3)	8.9	13.5	10	11	0.39/0.7
Number of patients with enhancing lesions (%)	1 (14.2)	3 (42.8)	12 (22.6)	21 (39.6)	0.7/0.6
Number of patients with infra-tentorial lesions	1	2	16	20	0.7/0.8
Mean number of active lesions (new T2 or enhancing lesions)	3.2 [± 1.7]		1.8 [± 0.6]		0.043
Number of patients with new T2 lesions (%)	7/7 (100%)		41/53 (77.3%)		0.038

Klinik ilerleme riskini artıran etkenler
Servikal **Torakal spinal kord lezyonları;** ↑sensitivite, spesifite ve pozitif kestirim değeri
Erkek cinsiyet
Genç yaş
İnfratentorial lezyonlar
Lezyon sayısının çok olması
VEP anormalliği
İlk MRG'de >9 T2 lezyonla birlikte OKB ve/veya IgG indeksinde artış
Gebelik; MS gelişenlerde gebelik klinik dönüşüm zamanını azaltmakta

De Stefano, 2011	19 RIS 20 RRMS 20 SK	10/1918 SK DIT+ 10/15 BOS+ 3/15 VEP+
Giorgio, 2011	15 RIS	9/15 DIT+ 8/13 BOS+
Stromillo, 2013	23 RIS 20 SK	9/23 DIT+ 14/19 BOS+
Rojas,2015	10 RIS 43 CIS 29 ISC	
Giorgio,2015	18 RIS 20 RRMS 20 SK	13/18 DIS+ 11/16 BOS+
Azevedo, 2016	21 RIS 42 SK	
Labiano-Fontcuberta, 2016	17 RIS 17 CIS 17 SK	6/17 DIT+ 4/9 BOS+
	18 RIS 18 SK	5/18 DIT+

- **Kortikal lezyon**
  - %40; Fronto - temporal
  - BOS+, spinal lezyon ile ilişkili; klinik kestirimci!
- **İşlevsel bağlantılar korunmuş**
  - (SM ve WM network)
  - Maladaptif plastisite
  - Fonksiyonel reorganizasyona gerek olmaması
- **Mikroyapısal bütünlük korunmuş**: DTI, MTr, Voxel
  - Kontrollerle aynı NAWM
  - Lezyon bölgelerinde myelin/aksonal hasarı
  - Etkin onarım mekanizmaları
- **Atrofi**
  - Tüm beyin, Kortikal ve **Talamik**
- **NAA/Cr oranı ↓ /≈**
  - **aksonal hasar,**
  - %10 ile MS'dekinden fazla
  - Diğer MR ölçütleri ile ilişkili değil
  - Klinik dönüşüm riski olanlarda düşme eğiliminde

	Olgu	RIS özellik	Amaç	Sonuç
Şehitoğlu, 2014	13 RIS 23 MS 50 SK	4/13→ MS	Serum Sorcin Ab (ic Ca homeostazı)	RIS+MS-↓ **RIS+MS+↑**(%75) RRMS↑(%56)
Rossi, 2015	18 RIS, 39 CIS 108 MS 18 NMS, 76 SK	10/18 → RRMS	BOS İnterlökin-8 (IL-8)	RIS ≈RRMS; **RIS+MS+ ↑** **↑ IL-8 klinik dönüşüm için risk**
Lebrun, 2016	1417 olgu 35 RIS	11/35 →DIT 3/35 → CIS	BOS /Serum IL-17	RIS, CIS, MS fark Ø Dönüşüm için Kestirim değeri yok
Thouvenot, 2018	71 RIS 48 CIS 50 MS 42 SK	20/71→ RRMS 64/71 BOS+	BOS CHI3L1	RIS≈ SK < RRMS **RIS+MS+ ↑** +BOS, spinal lord lezyonu,4 Barkhof krit. dönüşüm zamanı ↓
Pawlitzki, 2018	23 RIS 30 CIS/MS 30 SK	19/23 BOS+	BOS NfL, progranulin	NfL : RIS, SK < CIS/MS Progranulin : RIS, CIS/MS > SK
Matute-Blanch, 2018	75 RIS 65 CIS/MS	23/75 →CIS MS 53/75 BOS+	BOS CHI3L1 NfL OKB	CHI3L1 : RIS < CIS/MS RIS+MS- /RIS+MS+ Ø NfL : RIS≈ CIS-MS **RIS+MS+ ↑** NfL, OKB klinik dönüşüm için risk

Optical coherence tomography indicat
disease activity prior to clinical onset o
nervous system demyelination

Ben… …k, Paul Schmidt, Claus Zimme…
…rn

20 RIS, 18 CIS,18 NSWML, 19 SK
RNFL ↓ , T2 lezyon yükü ile ilişkili

Retinal nörodejenerasyon erken evrelerden itibaren saptanabilir

Bulgular beyindeki yaygın/genel hastalık sürecini yansıtır

…orial lesions i…
…drome are a…
…nglion cell/in…

30 RIS, 60 SK
RNFL kontrollerle aynı
Spinal/infratentorial lezyon+
→ GCIPL ↓

…Esch, Madiha Qutab, Natalia Gonzalez-Caldito,
…Shiv Saidha and Elias S Sotirchos

Retinal degeneration is associated wi…
brain volume reduction and prognosi…
radiologically isolated syndrome

15 RIS, 15 SK
4/15 → MS
RNFL, GCIPL kalınlığı↓
Atrofi ile ilişkili
MS'e dönüşenlerde peripapiller RNFL kalınlığı ↓

Atay Vural, Serhat Okar, Aslı Kurne, Güliz Sayat-Gürel, Nazire Pınar A…
Erdem Karabulut, Kader Karlı Oğuz, Sibel Kadayıfçılar and Rana Karabuda…

RIS tanısı : Öykü/muayenede MS'u düşündürecek işlev bozukluğuna ait klinik kanıt Ø

OPEN ACCESS Freely available online

PLOS ONE

Radiologically Isolated Syndrome: 5-Year Risk for an Initial Clinical Event

Darin T. Okuda[1]*, Aksel Siva[2], Orhun Kantarci[3], Matilde Inglese[4], Ilana Katz[4], Melih Tutuncu[2], B. Mark Keegan[3],

EDSS Score (%)	
0	420 (93.1)
1	23 (5.1)
1.5	6 (1.3)
2	2 (0.4)

31 olguda EDSS >0
Optik disk solukluğu
Görme keskinliği değişiklikleri
Hafif vibrasyon duyusu bozukluğu
Hafif üriner yakınmalar/ kabızlık
Depresyon
Yorgunluk
Piramidal sistem puanları > 0
periferik nedenli

Multiple Sclerosis

Cognitive function in radiologically isolated syndrome

Christine Lebrun[1], Frederic Blanc[2], David Brassat[3], Hélène Zephir[4] and Jerome de Seze[2] on behalf of CFSEP

26 RIS, 26 MS, 26 SK
Kognitif işlev MS< RIS < SK

Her olguya
Kognitif değerlendirme yapılmalı mı?
Kognitif bozukluk varsa RIS mı?

MRI metr
radiologic

29 RIS, 26 RRMS
RIS → Kognitif bozukluk %27.6
T1 lezyon hacmi ve
Kortikal atrofi ile ilişkili
MS → %34.6

M.P. Amato, MD
B. Hakiki, MD
B. Goretti, PhD

ABSTRACT

Objective: To evaluate cognitive changes in a cohort of radiologically isolated syndromes (RIS) suggestive of multiple sclerosis (MS) and to assess th

A comparison study of cognitive def radiologically and clinically isolated

Andrés Labiano-Fontcuberta, Mª Luisa Martínez-Ginés, Yolanda Aladro, Mitchell, Verónica Puertas-Martín, Marta Cerezo, Yolanda Higueras and

28 RIS, 25 CIS, 22 SK
RIS → en az 1 test ↓ : %50
Kognitif bozukluk %21.4
CIS→ en az 1 test ↓ : %48
Kognitif bozukluk % 20

Psychiatric disturbances in radiologically isolated syndrome

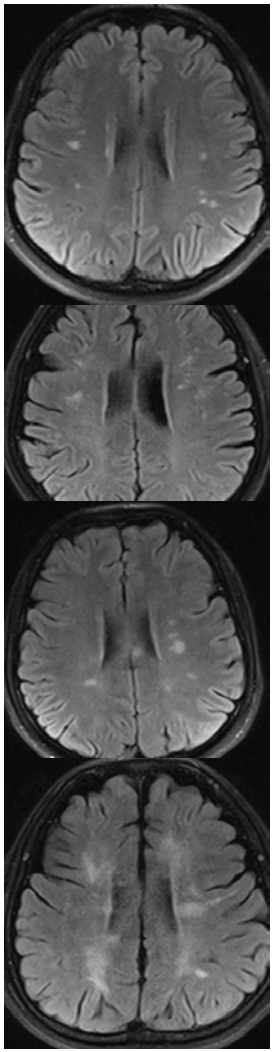
Andrés Labiano-Fontcuberta [a], Yolanda Aladro [b], Mª Luisa Martínez-Ginés [c], Lucía Ayuso [d], Alex J. Mitchell [e], Verónica Puertas [a], Marta Cerezo [b], Yolanda Higueras [c], Julián Benito-León [a, f, g, *]

Journal of Psychiatric Research 68 (2015) 309–315

	RIS patients (N = 28)[1]	CIS patients (N = 25)[2]	Healthy controls (N = 22)[3]	Group differences F or H[a]/p[b]
HAMD-17 total score	9.9 ± 6.8 (7.5)[3]	10.2 ± 7.0 (9.0)[3]	3.8 ± 4.6 (1.5)[1,2]	6.90/0.02
Anxiety*	4.5 ± 2.9 (4.5)[3]	3.2 ± 2.6 (3.0)	1.2 ± 1.8 (0.0)[1]	10.63/<0.001
HAMD subtotal score**	5.4 ± 4.4 (5.0)	7.0 ± 5.5 (5.0)[3]	2.4 ± 2.7 (2. 0)[2]	5.82/0.05
Clinical depression				
Mild (8–16)	6 (21.4%)	8 (32.0%)	4 (20.0%)	0.16/0.92
Moderate (17–23)	8 (28.6%)[3]	6 (24.0%)[3]	0[1,2]	6.91/0.03
Anxious Depression***	11 (39.3%)[2,3]	3 (12.0%)[1]	0[1,2]	13.68/0.001
Personality structure				
Negative impression	51.9 ± 9.2 (49.0)	48.1 ± 4.5 (45.0)	51.1 ± 9.6 (49.0)	2.18/0.14
Somatic complaints	60.9 ± 14.9 (57.0)[2,3]	52.2 ± 11.5 (50.0)[3]	49.1 ± 11.7 (49.0)[1]	6.35/0.003
Obsessive–compulsiveness	54.9 ± 11.4 (50.0)[2]	47.2 ± 6.2 (46.0)[3]	49.3 ± 9.6 (46.5)	4.18/0.02
Mania	46.9 ± 9.1 (46.0)[2]	41.0 ± 11.8 (38.0)[1]	44.4 ± 6.8 (42.0)	2.96/0.05
Paranoia	49.8 ± 10.2 (49.0)	47.7 ± 11.8 (46.0)	44.9 ± 7.2 (48.0)	1.70/0.19
Schizophrenia	49.1 ± 8.0 (51.0)[3]	48.7 ± 8.1 (49.0)[3]	43.1 ± 4.9 (43.5)[1,2]	3.66/0.035
Borderline features	49.1 ± 9.4 (46.0)	48.6 ± 9.8 (46.0)	45.1 ± 6.8 (46.0)	1.31/0.27
Antisocial features	45.7 ± 6.7 (43.0)	44.9 ± 4.4 (43.0)	47.9 ± 6.7 (48.0)	1.42/0.25
Alcohol problems	47.7 ± 5.6 (46.0)	46.9 ± 4.5 (46.0)	48.0 ± 4.7 (46.0)	0.25/0.77
Aggression	49.2 ± 8.6 (50.0)	47.1 ± 8.3 (47.0)	50.7 ± 7.8 (50.0)	1.01/0.37
Suicidal ideation	48. 9 ± 2.1 (46.0)	48.6 ± 4.9 (46.0)	48.6 ± 6.4 (46.0)	0.84/0.48
Stress	48.9 ± 10.1 (49.0)	49.8 ± 10.1 (49.0)	50.7 ± 10.9 (49.0)	0.22/0.80
Fatigue (D-FIS)	11.7 ± 10.7 (7.00)[2,3]	8.4 ± 1.8 (4.0)[1,3]	5.1 ± 5.1 (4.0)[1,2]	3.54/0.03
EQ-5D				
EQ- descriptive scores	0.77 ± 0.2 (0.79)[3]	0.85 ± 0.17 (0.79)	0.91 ± 0.1 (1.0)[1]	3.49/0.04
EQ VAS	65.0 ± 19 (70.0)[2,3]	77.73 ± 14.61 (80.0)[1]	83.25 ± 9.8 (85.0)[1]	8.77/<0.001

Her fokal beyaz cevher lezyonu RIS mi?

RIS: MRG bulgularını açıklayabilecek başka patolojilerin bulunmaması



Rastlantısal
- Migren
- Normal popülasyon

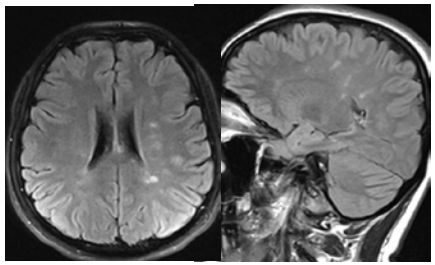
Hipoksik-iskemik vaskülopatiler
- Küçük damar hastalığı
- CADASIL

Demiyelinizan
- Multipl skleroz
- RIS

Vaskülitler /bağ doku hastalıkları
- Primer, Lupus, Sjögren

Metabolik
- Fabry, Lökodistrofiler, B12 eksikliği

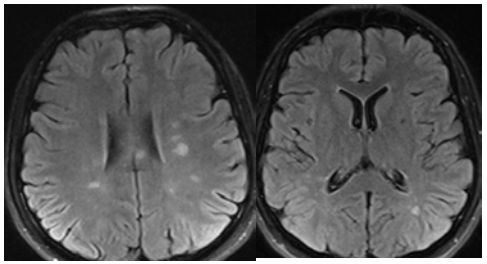
İnfratentorial Ø
Gd Ø, Spinal Ø
≥9 T2, ≥ 3 PV, 1 Juks-Cor
≥ 2 bölgede ≥1 T2



5/2016

8/2016
NM: Normal
MRI:
DIT Ø
Gd+ Ø
Spinal lezyon Ø

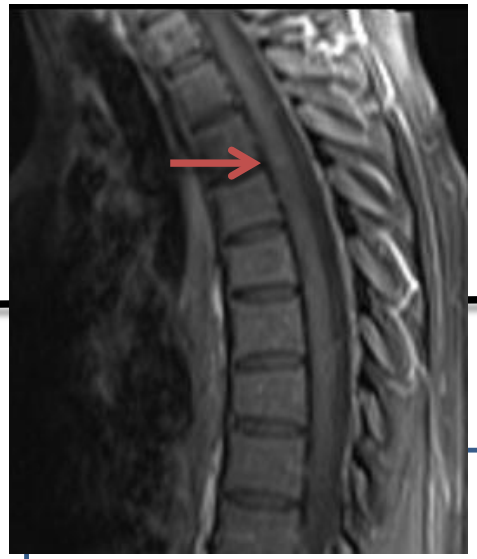
L Görme bulanıklığı
V L:0,6
R:Tam



4/2017

Gd+ Ø
Spinal lezyon Ø
VEP: L iletim gecikmesi
BOS: OKB Tip II
Ig G indeksi: 0.75
Ccs
Tedavi: Kabul etmiyor

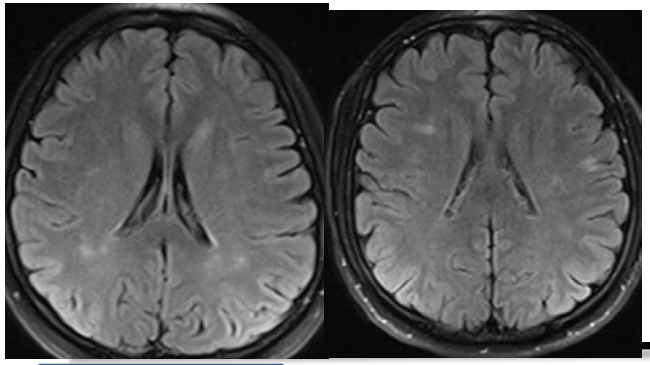
Bacaklarda uyuşma, 2 gün



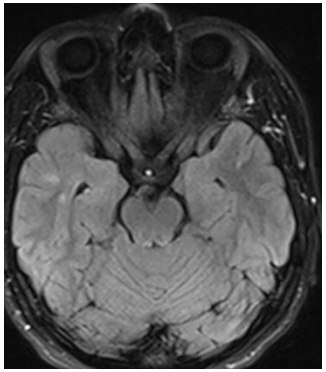
Sağ alt ektremite kas gücü 4/5
Ccs: 5 gün

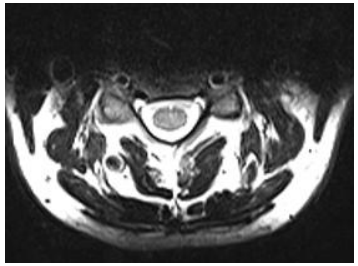
DMT başlandı

30y, K,
MRI→
Başağrısı
NM: Normal



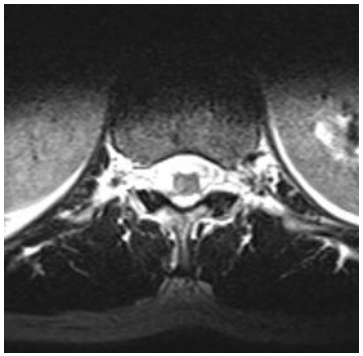
6/2013



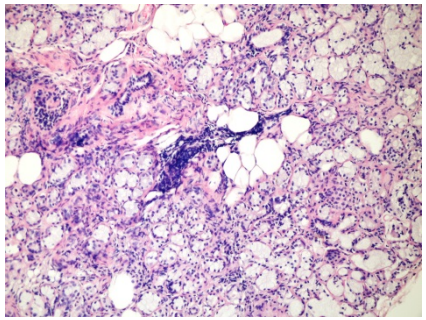


Klinik yakınma yok
NM: Normal
İnceleme kabul etmiyor

11/2015



Baş dönmesi, 1ay önce, parestezi



10/2016

BOS: OKB Tip I
Ig G indeksi: 0.60
ANA +
Anti-Ro ++
Anti-La ++
ENMG: PNP

Neurol Ther (2014) 3:123–132
DOI 10.1007/s40120-014-0024-7

ORIGINAL RESEARCH

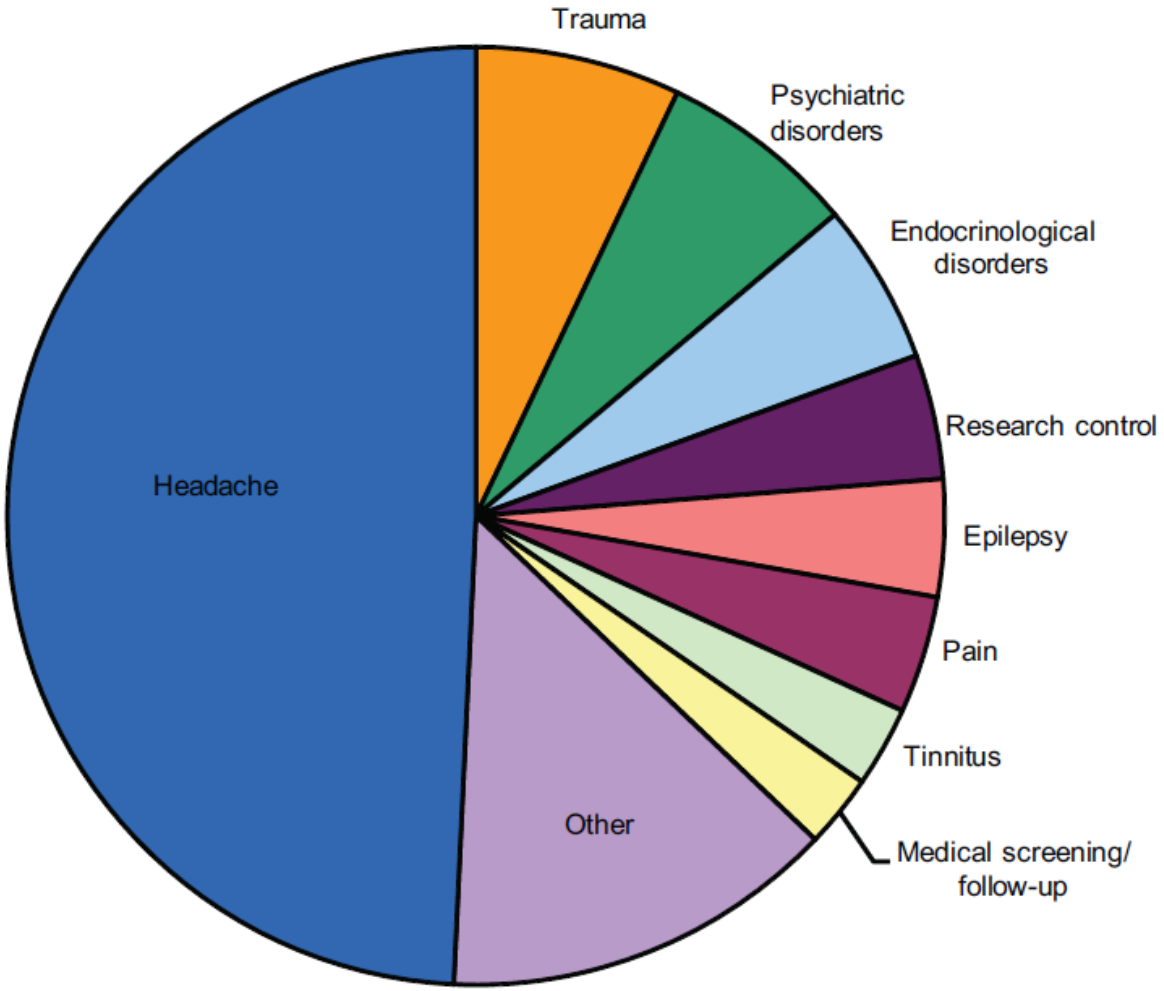
A Prospective Study of Patients with Brain MRI Showing Incidental T2 Hyperintensities Addressed as Multiple Sclerosis: a Lot of Work to do Before Treating

Christine Lebrun · Mikael Cohen · Annabelle Chaussenot · Lydiane Mondot · Stephane Chanalet

Table 3 Data (% of patients) on fulfilled MRI criteria according to the final diagnosis

MRI criteria (%)	MS (%)	Other inflammatory diseases (connectivitis) (%)	Vasculopathy (%)	RIS (%)	Non-pathological (%)
3 DS criteria BARKHOF	**85**	**20**	34.6	100	0
PATY	90	50	72.3	71.4	33.3
FAZEKAS	90	20	3.9	14.3	0
SWANTON	90	40	42.3	88.6	6.7
Non-specific T2 hypersignals	**5**	**0**	7.7	28.6	86.7
2 DS criteria + CSF abnormalities	57.8	30	0	42.3	0
DT MRI only (new T2 or gadolinium +)	**82.7**	0	0	36	0
Association of 2 HS + CSF and DT on MRI	**90**	30	**0**	44	**0**

DS dissemination in space, *DT* dissemination in time, *HS* hypersignal, *MS* relapsing remitting multiple sclerosis, *CSF* cerebrospinal spinal fluid



gure 3. Overview of the indications for MRI in published cohorts, n=394.[4,6–12,23,26–33] There are overlaps of the cohorts, whicl ight mean that a patient has been registered more than once. For a complete description of all indications, please see the

Multiple Sclerosis Journal
19(3) 271–280

Journal of Neural Transmission
https://doi.org/10.1007/s00702-018-1959-0

NEUROLOGY AND PRECLINICAL NEUROLOGICAL STUDIES - ORIGINAL ARTICLE

Headache in the course of multiple sclerosis: a prospective study

Marcel Gebhardt[1] · Peter Kropp[2] · Frank Hoffmann[1] · Uwe K. Zettl[3]

	All		CIS		Multiple sclerosis	
	N	%	*N*	%	*N*	%
Patients	150		50		100	
Headache prevalence	101	67.3	39	78	62	62
Headache subtypes[a]						
Migraine-like headache	43	29	23	46	20	40
Migraine	14	9	8	16	6	6
Tension-type headache	30	20	11	22	19	19
Unclassifiable headache	25	17	4	8	21	21
Gender						
Male	45	30	11	22	34	34
With headache	27	60	8	73	19	56
Female	105	70	39	78	66	66
With headache	74	71	31	80	43	65

Radiologically isolated syndrome or subclinical multiple sclerosis: MAGNIMS consensus recommendations

Multiple Sclerosis Journal

2018, Vol. 24(2) 214–221

DOI: 10.1177/1352458517717808

	Migraine	Demyelinating
Lesion size	Punctate (usually <5 mm)	Variable (usually >5 mm)
Lesion number	Low	Variable
Lesion confluency	Rare	Variable
Lesion topography	Anterior, subcortical, juxtacortical, deep white matter	Posterior, periventricular
Infratentorial lesions	≈10%	Frequent
New lesions	Rare	Frequent
Venocentric pattern[a]	Rare	Frequent
Intralesional signal loss[a]	Absent	Frequent
Spinal cord lesions	Absent	Frequent
Gadolinium-enhancing lesions	Absent	Frequent
Corpus callosum lesions	Absent	Frequent

[a]On susceptibility-weighted imaging (SWI).

Radiologically isolated syndrome or subclinical multiple sclerosis: MAGNIMS consensus recommendations

Nicola De Stefano, Antonio Giorgio, Mar Tintoré, Maria Pia Amato, Ludwig Kappos, Jacqueline Palace, Tarek Yousry, Maria A Rocca, Olga Ciccarelli, Christian Enzinger, Jette Frederiksen, Massimo Filippi, Hugo Vrenken and Àlex Rovira ; on behalf of the MAGNIMS study group

Multiple Sclerosis Journal
2018, Vol. 24(2) 214–221
DOI: 10.1177/1352458517717808

Table 4. Stratification of RIS and supporting features for a diagnosis of subclinical MS.

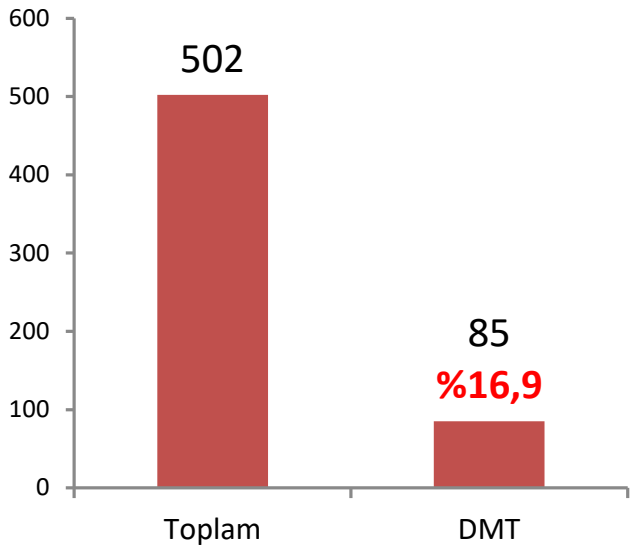
- ✓ Extreme caution should be used in considering RIS subjects with
  - Migraine/chronic headache
  - Seizures
  - Paroxysmal symptoms
  - Psychiatric disturbances
  - Overt cognitive impairment
- ✓ Increased likelihood to be subclinical MS in case of
  - Dissemination in time on MRI (gadolinium-enhancing and/or new T2 lesions)
  - Infratentorial and/or spinal cord lesions on MRI
  - High T2-lesion load on MRI
  - Cortico-juxtacortical lesions on MRI
  - Presence of oligoclonal bands in cerebrospinal fluid
  - Abnormal visual evoked potentials
  - Deficits of specific cognitive functions (information processing speed, complex attention, episodic memory, and executive functions)

RIS: radiologically isolated syndrome; MS: multiple sclerosis; MRI: magnetic resonance imaging.

Yaklaşım

Bekle	Pasif / konservatif	Belirti olursa yeniden değerlendir
İzle	Aktif	Planlı klinik ve radyolojik izlem İlk yıl 6 ayda 2 yıl yılda bir Sonrasında 5. yılda kontrol Spinal kord değerlendirilmeli BOS incelemesi → Radyolojik DIT + →İlk MRI Barkhof kriterleri +
Tedavi et	Tartışmalı	

Lebrun 2008	3/30
Okuda 2009	7/44
Meuth 2009	1/1
Sempere 2009	1/1
Okuda 2014	73/456



Multiple Sclerosis Journal
2017, Vol. 23(14) 1820–1821
DOI: 10.1177/
1352458517726385

Radiologically isolated syndrome should be treated with disease-modifying therapy – No

Andrés Labiano-Fontcuberta and Julián Benito-León

- Mevcut ilaçların Yarar/Zarar oranı
  %30'unda 5 yıl içinde klinik olay gelişiyor
  Etkin onarım mekanizmaları (MRI ile gösterilmiş)
  'number needed to treat to benefit' (NNTB) çok yüksek
  DMT etkinliğini gösteren bir çalışma yok
- Yanlış tanı !
- Klinik ve radyolojik ölçütlerin geçerliliği ??
  İzlem süreleri kısa; klinik olay Ø, hastalık süresi çok daha uzun süreli olabilir
  CIS/MS'de yeni T2 lezyonlar üzerindeki tedavi etkisi relapslar üzerindeki uzun-dönem etkiyi kestirebilir, RIS'de bir ölçüt yok
  EDSS yeterli bir ölçüt değil (RIS olgularında da izlenen kognitif ve psikiyatrik belirtileri yeterince yansıtmıyor)

MULTIPLE SCLEROSIS JOURNAL | MSJ

Controversies in Multiple Sclerosis

Radiologically isolated syndrome should be treated with disease-modifying therapy – Yes

Darin T Okuda

Multiple Sclerosis Journal

2017, Vol. 23(14) 1818–1819

DOI: 10.1177/1352458517729462

SSS demiyelinizasyonu ‘sessiz hırsız’; yavaş yavaş çalıyor, eşik geçilince belirti veriyor

Kronik hastalıklarda amaç asemptomatik iken tedavi etmek

Gd+ lezyonlarda etkilenen akson >11.000 /cm^3

Talamik atrofi → nörodejenerasyon klinik olaydan önce

Risk faktörleri → %34’ünde klinik dönüşüm

Oluşabilecek özürlülüklerin engellenmesi

Neurology®

The most widely read and highly cited peer-reviewed neurology journal

AMERICAN ACADEMY OF NEUROLOGY®

April 06, 2015; 84 (14 Supplement) APRIL 23, 2015

Multi-center, randomized, double-blinded assessment of dimethyl fumarate in extending the time to a first attack in radiologically isolated syndrome (RIS) (ARISE Trial) (P7.207)

Darin Okuda, Christine Lebrun Frenay, Aksel Siva, Christophe Hotermans, Christian Von Hehn, Gina Remington, Braeden Newton, Teresa Frohman, Elliot Frohman, Orhun Kantarci Daniel Pelletier

First published April 8, 2015,

April 18, 2017; 88 (16 Supplement) APRIL 28, 2017

Multi-center, randomized, double-blinded assessment of teriflunomide in extending the time to a first clinical event in radiologically isolated syndrome (RIS) The TERIS study (P6.359)

Christine Lebrun Frenay, Aksel Siva, Orhun Kantarci, Christina Azevedo, Maria Pia Sormani, Daniel Pelletier, Darin Okuda

First published April 17, 2017,