



Gruppo di Ricerca Geriatrica
Journal Club
23 Ottobre 2009

CASI CLINICI IN GERIATRIA

L'ARTRITE REUMATOIDE

Alessandra Marrè

Pz di ... anni (XX), già ricoverata nel nostro Reparto nell'Ottobre-Novembre 2006. Vedova, vive sola.

DIAGNOSI DI DIMISSIONE

- **Recente endoprotesi (17/10/2006) di anca per frattura del collo del femore sx (16/10/2006) complicata da anemia e stato confusionale lieve**
 - **Ipertensione arteriosa stadio I gruppo di rischio cardiovascolare elevato**
 - **Diabete mellito tipo 2 in terapia dietetica**
 - **Artrosi diffusa di grado severo**
 - **Depressione del tono dell'umore**
-

TERAPIA in CORSO ALLA DIMISSIONE

Nome commerciale	Principio attivo	Posologia	Orario
- Efexor 75	<i>venlafaxina</i>	1 c	Ore 8
- Trittico 75	<i>trazodone</i>	2/3 c	Ore 20
- Fraxiparina 0,4	<i>Nadroparina</i>	1 fiala sottocute	Ore 18 fino al 3-12-06
- Paracetamolo 1000	<i>paracetamolo</i>	1 c	Al bisogno

VALUTAZIONE MULTIDIMENSIONALE

		Premorboso	Ingresso	Dimissione
<u>C.A.M.*</u>	<i>Stato confusionale</i>		3/4	0/4
<u>MMSE</u>	<i>Stato cognitivo</i>		23/30	27/30
<u>Geriatric Depression Scale</u>	<i>Tono dell'umore</i>		6/15	--/15
<u>Mini Nutritional Assessment</u>	<i>Stato nutrizionale</i>		9 + 11.5	
<u>IADL (n funzioni perse):</u>	<i>Stato funzionale</i>	2/8		
<u>BARTHEL INDEX</u>	<i>Stato funzionale</i>	87/100	30/100	83/100
<u>TINETTI:</u>	<i>Stato funzionale</i>		1/28	14/28
<u>FIM:</u>	<i>Stato funzionale</i>		42/126	85/126

La paziente è stata poi seguita in ambulatorio. In Dicembre 2006 è funzionalmente migliorata (Tinetti 18/28), deambula ancora con girello (dice che si sente più sicura). Dopo 3 mesi dalla dimissione dal nostro reparto compaiono artrite alle spalle, alle mani ed alle caviglie con indici di flogosi elevati, RA test positivo a basso titolo e Anticorpi anticitrullina (CCP) negativi.

D] ARTRITE REUMATOIDE AD ESORDIO TARDIVO

Viene prescritto steroide (Prednisone 12.5 mg/die) + Ca-Vit D con rapida remissione dell'artrite. Dopo 2 mesi viene scalato progressivamente il dosaggio di steroide fino a 2.5 mg/die (Ottobre 2007); non segni di artrite.

Al successivo tentativo di sospendere la terapia si verifica una recidiva (Dicembre 2007). Riprende 5 mg/die con buon controllo clinico e laboratoristico.

Continua ad utilizzare il girello prescritto; le prestazioni funzionali, in assenza di artrite, sono sovrapponibili alla dimissione dal Reparto (Tinetti 18/28).

In Gennaio 2008 si rileva deficit di attenzione, MMSE 19/30: si consiglia assistenza nelle IADL e si richiede valutazione neuropsicologica.

VALUTAZIONE NEUROPSICOLOGICA: declino cognitivo lieve con disorientamento nel tempo e nello spazio, deficit di attenzione, deficit delle funzioni esecutive (uso di strategie di ricerca, pianificazione e grave deficit di controllo esecutivo), aprassia costruttiva e deficit di critica e giudizio.

La paziente viene seguita a domicilio da un'ex OSS (conoscente della figlia).

Gennaio 2009: si evidenzia calo ponderale (47→43 Kg). L'OSS che accompagna la paziente alle visite riferisce che si alimenta poco, anche in relazione a “paura del diabete”, nonostante i controlli glicemici fossero tutti nella norma e la paziente fosse stata più volte rassicurata.

Si convoca la figlia e si consiglia una soluzione assistenziale diversa.

La paziente, in Aprile 2009, si trasferisce in Casa Albergo.

Nel frattempo il dosaggio di Prednisone resta 2.5 mg a giorni alterni: la sospensione infatti provoca sempre recidiva.

Al controllo di Luglio 2009 la paziente ha recuperato 2 Kg. Riferisce artralgie diffuse e un episodio di caduta. Tinetti 13/28. Si propone il ricovero riabilitativo con l'obiettivo di rivalutare il rischio di caduta.

TERAPIA DOMICILIARE

•Venlafaxina 75 mg	1 cp ore 8
•Enalapril 20 mg	½ cp ore 8
•Trazodone 75 mg	2/3 di cp ore 20
•Ca-vit. D	½ bustina ore 20
•Prednisone 25 mg	¼ di cp ore 8

CASO CLINICO: Epicrisi

Pz di aa..., proveniente dal domicilio. Vedova, vive in Casa Albergo da Aprile. Assistita anche da un'amica. Esce molto raramente, solo accompagnata.

Sindromi Geriatriche : disturbo della deambulazione, deficit cognitivo

Affetta da:

- **Disturbo della deambulazione a genesi multifattoriale**
- **Artrite reumatoide ad esordio tardivo**
- **Artrosi diffusa**
- **Esiti di intervento di endoprotesi per frattura del collo femore sx (10/06) complicato da delirium**
- **Ipertensione arteriosa stadio 1 gruppo di rischio C**
- **Depressione anamnesticca e declino cognitivo lieve**

Epicrisi - 2

Paziente nota per ricovero nel 2006. Dal Febbraio 2007 in terapia con steroide a basso dosaggio a cicli per artrite reumatoide. Riscontrati calo ponderale e deficit delle funzioni esecutive, da Aprile risiede in Casa Albergo. Negli ultimi tempi si sono acutizzate le artralgie (non segni di attività dell'artrite) e la paziente è caduta, con genesi non chiara. Entra per ciclo di FKT.

E.O.: ipotrofia muscolare diffusa, > AAll, con deficit di forza. Deambula con girello/bastone con zopia a dx.

OBIETTIVI CLINICI

- Rivalutazione rischio di caduta
- Controllo dolore
- Rivalutazione tono dell'umore/deficit cognitivo

OBIETTIVI NURSING/FKT

- Controllo dolore
- Incremento autonomia nelle ADL

Valutazione multidimensionale

		Premorboso	Ingresso
<u>C.A.M.</u>	<i>Stato confusionale</i>		0/4
<u>MMSE</u>	<i>Stato cognitivo</i>		21/30
<u>Geriatric Depression Scale</u>	<i>Tono dell'umore</i>		11/15
<u>Mini Nutritional Assessment</u>	<i>Stato nutrizionale</i>	11+9/30	
<u>IADL (n funzioni perse):</u>	<i>Stato funzionale</i>	7/8	
<u>BARTHEL INDEX</u>	<i>Stato funzionale</i>	88/100	85/100
<u>TINETTI:</u>	<i>Stato funzionale</i>		15/28
<u>FIM:</u>	<i>Stato funzionale</i>		87/126

BMI: 20

Diario clinico

Tutta l'équipe nota che la paziente è molto ripetitiva e ansiosa. Dopo qualche giorno di degenza si riduce lievemente l'ansia: si riesce più facilmente ad interagire con la paziente e a tranquillizzarla verbalmente .

È stato gradualmente ridotto il dosaggio steroideo: non segni clinici né bioumorali di artrite alla dimissione. In considerazione della sintomatologia ansiosa (anche in relazione al lieve deficit cognitivo noto, ed al rischio di caduta), in accordo con la paziente, è stata progressivamente sospesa la terapia con venlafaxina: prescritto controllo evolutivo. Per il riscontro di valori di PA elevati è stato aumentato il dosaggio di Enalapril a 20 mg/die; si consiglia controllo frequente della PA.

Colloquio con la figlia: vengono spiegati gli interventi effettuati, viene consigliato di stimolare la paziente ad uscire e si raccomanda una più stretta supervisione nell'assunzione dei farmaci.

ESAMI EMATICI

Esame	Ingresso	Dimissione		Valori normali
GB	5.7		10 ³ /ul	4.00-9.00
GR	4.0		10 ⁶ /ul	4.00-5.50
Ht	35.0		%	38.0-50.0
Hb	11.7		g/dl	11.5-14.5
MCV	87.5		fl	80.0-95.0
PLT	356		10 ³ /ul	150-400
Neutrofili	51.4		% * 10 ³ /ul	40.0-75.0
Linfociti	31.4		% * 10 ³ /ul	20.0-40.0
Monociti	5.1		% * 10 ³ /ul	0.0-12.0
Eosinofili	11.8		% * 10 ³ /ul	0.0-2.5
Basofili	0.3		% * 10 ³ /ul	0.0-0.54
VES	40	42	mm/1° ora	0-20
PCR	3.1	2.5	mg/dl	0.0-1.0
Azotemia	32		mg/dl	10-50
Creatinina	0.7		mg/dl	0.5-1.2
Ac. Urico	3.5		mg/dl	1.5-7.0
Na	140		Mmol/L	136-146
K	4.3		Mmol/L	3.5-5.10
Cl	97		Mmol/L	98-108
Glicemia	81		mg/dl	60-110
Colesterolo tot	193		mg/dl	120-200
GOT	16		U/L	0-40
GPT	10		U/L	0-40
Fosfatasi alc	180		U/L	90-270
γGT	27		UI/L	5-30
Bilirubina tot	0.4		mg/dl	0-1.2
PT (INR)	1.0			0.9-1.1
proteine tot	6.5		g/dl	6.2-8.2
Albumina	51/3.3		%	55.1-66.1
α1	3.1		%	1.7-3.3
α2	12.4		%	8.2-13-0
β	11.1		%	9.5-15-0
γ	22.4		%	10.3-18.3
Sideremia	43		microg/dl	70-150
Transferrina	210		Mg/dl	200-350
Es urine	negativo			
Peso corporeo	45.5 Kg	45 Kg		
altezza	150 cm			
P.A.	170/100 mmHg	140/80 mmHg		

ESAMI STRUMENTALI

ECG (23/9/09): RS. FC 90 b/min. RV nei limiti.

Rx torace (25/9/09): Esame eseguito in unica proiezione a paziente seduto. I campi polmonari sufficientemente espansi. Non lesioni pleuro parenchimali a focolaio in atto.

Lieve rinforzo del disegno broncopolmonare a carattere bronchitico in sede ilo peri ilare di dx con ispessimento della scissura interlobare.

Esiti specifici in sede intercleido ilare e sottoclaveare.

Aortomiocardiosclerosi.

DIAGNOSI DI DIMISSIONE

- **Disturbo dell'equilibrio e della deambulazione**
 - **Artrite reumatoide ad esordio tardivo**
 - **Artrosi diffusa**
 - **Esiti di intervento di endoprotesi per frattura del collo femore sx (10/06) complicato da delirium**
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 - **Depressione anamnesticca e declino cognitivo lieve**
-

TERAPIA ALLA DIMISSIONE

Principio attivo	Posologia	Orario
– Enalapril 20 mg	1 cp	Ore 8
– Calcio-vit D	½ cp	Ore 20
– Prednisone 5 mg	½ cp	Ore 8
– Paracetamolo 1 g	1 cp	Al bisogno
– Macrogol	1 bustina	Alla sera

VALUTAZIONE MULTIDIMENSIONALE

		Premorboso	Ingresso	Dimissione
<u>C.A.M.</u>	<i>Stato confusionale</i>		0/4	/4
<u>MMSE</u>	<i>Stato cognitivo</i>		21/30	/30
<u>Geriatric Depression Scale</u>	<i>Tono dell'umore</i>		11/15	--/15
<u>Mini Nutritional Assessment</u>	<i>Stato nutrizionale</i>	11+9/30		
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<u>BARTHEL INDEX</u>	<i>Stato funzionale</i>	88/100	85/100	93/100
<u>TINETTI:</u>	<i>Stato funzionale</i>		15/28	20/28
<u>FIM:</u>	<i>Stato funzionale</i>		87/126	96/126

ARA Criteria for the Classification of Rheumatoid Arthritis (RA)

For classification purposes, a patient is said to have RA if he or she has satisfied at least 4 of the following 7 criteria. Criteria 1 through 4 must have been present for at least 6 weeks. Patients with 2 clinical diagnoses are not excluded. Designation as classic, definite, or probable RA is not to be made.

1. Morning stiffness: Morning stiffness in and around the joints, lasting at least 1 hour before maximal improvement.
2. Arthritis of 3 or more joint areas: At least 3 joint areas simultaneously have had soft tissue swelling or fluid (not bony overgrowth alone) observed by a physician; the 14 possible joint areas are right or left proximal interphalangeal (PIP) joints, metacarpophalangeal (MCP) joints, wrist, elbow, knee, ankle, and metatarsophalangeal (MPT) joints.
3. Arthritis of hand joints: At least 1 area swollen (as defined above) in a wrist, MCP or PIP joint.
4. Symmetric arthritis: Simultaneous involvement of the same joint areas (see 2 above) on both sides of the body (bilateral involvement of PIPs, MCPs, or MTPs is acceptable without absolute symmetry).
5. Rheumatoid nodules: Subcutaneous nodules, over bony prominences, or extensor surfaces, or in juxta-articular regions, observed by a physician.
6. Serum rheumatoid factor: Demonstration of abnormal amounts of serum rheumatoid factor by any method for which the result has been positive in <5% of normal control subjects.
7. Radiographic changes: Radiographic changes typical of RA on posteroanterior hand and wrist radiographs, which must include erosions or unequivocal bony decalcification localized to or most marked adjacent to the involved joints (osteoarthritis changes alone do not qualify).

Elderly Onset Rheumatoid Arthritis

Differential Diagnosis and Choice of First-Line and Subsequent Therapy

Juan Ignacio Villa-Blanco and Jaime Calvo-Alén

- Rheumatoid arthritis (RA) is a multisystem, chronic, inflammatory disorder characterized by destructive synovitis with a prevalence of approximately 2% among people aged >60 years.
- Usually, patients who develop RA between the age of 60 and 65 years are defined as having elderly onset RA (EORA). EORA patients represent a clinical subset of individuals who differ in presentation, severity, prognosis and treatment from patients with younger onset RA (YORA).
- Annual incidence rates around the world are highly variable (from 9 to 900 per 100.000), depending on sex and ethnicity.
- Genetic influences in RA have been supported by numerous studies. YORA was strongly associated with DRB1*04, whereas EORA was associated with DRB1*01 and not associated with DRB1*04. Seronegative EORA patients exhibited increased frequency of DRB1*13/*14 similar to patients with polymyalgia rheumatica (PMR).
- EORA vs YORA: a balanced sex distribution with a female to male ratio of about 1.5–2 : 1 versus 4–4.5 : 1 in YORA patients; greater incidence of large joint involvement and constitutional symptoms (fever, weight loss and fatigue); more acute disease onset, lower presence of RF and higher erythrocyte sedimentation rate .

Elderly Onset Rheumatoid Arthritis

Differential Diagnosis and Choice of First-Line and Subsequent Therapy

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Clinical Features and Subsets

Several reports suggested that RA in older patients differed from that in other adults and described different subsets among EORA patients:

1. Patients with classic RA whose clinical onset is similar to that in patients who develop seropositive RA at an earlier age. They present with high levels of disease activity, and most require aggressive management.
2. Patients with symmetrical arthritis associated with Sjogren's syndrome. The synovitis is less severe and more readily controlled than in the first subset.
3. Patients with the clinical picture mimics that of PMR. These patients have high levels of acute phase reactants, but rheumatoid factor (RF) is negative in the vast majority of cases. The arthritis in these patients is usually well controlled with low-dose corticosteroid treatment, and joint damage or radiological changes are less severe than in the other forms.

Others authors also distinguished seropositive from seronegative EORA patients. The former were very similar to YORA seropositive patients, whereas the latter (seronegative EORA) constituted a more heterogeneous group with a clinical picture overlapping with other syndromes such as PMR and remitting seronegative symmetrical synovitis with pitting oedema (RS3PE) syndrome.

Elderly Onset Rheumatoid Arthritis

Differential Diagnosis and Choice of First-Line and Subsequent Therapy

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Outcomes

Outcomes in EORA patients have been reported to be more benign than those in YORA patients. However, a large majority of studies have been observational with no direct comparison between YORA and EORA patients. More recent studies that have included cohorts of EORA and YORA patients have reported that the outcome of EORA may be comparable with or even worse than that of YORA.

A prospective study comparing clinical, radiological and functional outcomes in patients presenting with RA above and below the age of 65 years and attempting to identify predictors of poor clinical and radiological outcome after a follow-up of at least 1 year. Statistical analysis in the EORA group showed that a high Health Assessment Questionnaire (HAQ) score (odds ratio [OR] = 7.42) and RF seropositivity (OR = 8.17) predicted poor functional outcome. The analysis also showed that, overall, EORA patients were more likely to go into clinical remission (OR = 2.99), with the remission rate being much higher in the seronegative EORA group than in other groups of patients, including seronegative YORA patients.

HEALTH ASSESSMENT QUESTIONNAIRE

Please tell us how your arthritis affects your ability to carry out your daily activities.

DRESSING & GROOMING

WITHOUT ANY
DIFFICULTY

WITH SOME
DIFFICULTY

WITH MUCH
DIFFICULTY

UNABLE
TO DO

Are you able to:

Dress yourself, including shoelaces and buttons?

Shampoo your hair?

ARISING

Are you able to:

Stand up from a straight chair?

Get in and out of bed?

EATING

Are you able to:

Cut your meat?

Lift a full cup or glass to your mouth?

Open a new milk carton?

WALKINGWITHOUT ANY
DIFFICULTYWITH SOME
DIFFICULTYWITH MUCH
DIFFICULTYUNABLE
TO DO**Are you able to:**

Walk outdoors on flat ground?

Climb up five steps?

Please check any AIDS OR DEVICES that you usually use for any of the above activities: Devices Used for Dressing
(button hook, zipper pull, etc.) Built up or special utensils Crutches Cane Wheelchair Special or built up chair Walker**Please check any categories for which you usually need HELP FROM ANOTHER PERSON:** Dressing and Grooming Arising Eating Walking

Please place an "X" in the box which best describes your usual abilities OVER THE PAST WEEK.

HYGIENE

WITHOUT ANY DIFFICULTY WITH SOME DIFFICULTY WITH MUCH DIFFICULTY UNABLE TO DO

Are you able to:

Wash and dry your body?

Take a tub bath?

Get on and off the toilet?

REACH

Are you able to:

Reach and get down a 5 pound object (such as a bag of sugar) from above your head?

Bend down to pick up clothing from the floor?

GRIP

Are you able to:

Open car doors?

Open previously opened jars?

Turn faucets on and off?

ACTIVITIESWITHOUT ANY
DIFFICULTYWITH SOME
DIFFICULTYWITH MUCH
DIFFICULTYUNABLE
TO DO**Are you able to:**

Run errands and shop?

Get in and out of a car?

Do chores such as vacuuming or yard work?

Please check any AIDS OR DEVICES that you usually use for any of these activities: Raised toilet seat Bathtub bar Bathtub seat Long-handled appliances in bathroom Long-handled appliances for reach Jar opener (for jars previously opened)**How much pain have you had because of your arthritis IN THE PAST WEEK:**PLACE A SINGLE VERTICAL MARK THROUGH THE LINE TO INDICATE THE SEVERITY OF THE PAINNO
PAIN

0

SEVERE
PAIN

100

MEDICAL HISTORY

1. In the **PAST 6 MONTHS (January through June)**, did you stay in the **hospital overnight** for any reason?

Yes No

If Yes, total number of hospitalizations.

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MEDICAL CONDITIONS

1. In the **PAST 6 MONTHS (January through June)**, have you had any of the following **cardiovascular (heart) procedures**? Yes No If Yes, mark all that apply and please record any hospitalization(s) above:

Coronary Artery Bypass Surgery (CABG)

Heart Catheterization

Angioplasty

Stent

Thrombolytic Infusion (IV) (dissolves clots)

2. In the **PAST 6 MONTHS (January through June)**, have you been diagnosed with a **heart attack, myocardial infarction (MI), stroke, or cerebrovascular accident (CVA)**? Yes No

If Yes, please complete:

Heart Attack (MI)

Date of Heart Attack:

--	--

MONTH

--	--	--	--

YEAR

Stroke (CVA)

Date of Stroke:

--	--

MONTH

--	--	--	--

YEAR

If Yes, what kind of stroke:

Thrombotic, clot in brain

Hemorrhagic, bleeding in brain

Don't know

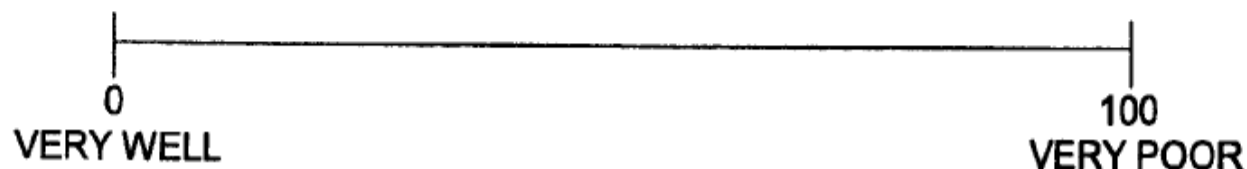
3. In the **PAST 6 MONTHS (January through June)**, have you been diagnosed or told that you have any kind of malignant tumor or cancer? Yes No If No, go to question 4.

4. In the **PAST 6 MONTHS (January through June)**, have you been diagnosed with **colon polyps (pre-cancerous growths)**?

Yes No Don't know if pre-cancerous or not

HEALTH STATUS AND HEALTH BEHAVIORS

1. Considering **all the ways that your arthritis affects you**, rate how you are doing on the following scale by placing a vertical mark through the line.



EXERCISE

During a **typical week**, do you do any of the following activities? Yes No

If Yes, please complete the following:

Approximately how much **total time (in minutes)** do you spend on each of the following types of exercise activities?

MEDICATIONS

In the **PAST 6 MONTHS (January through June)**, have you taken any of the medications listed in section A, B, or C?

Yes No

These instructions may be helpful.

First, scan down the list of medications and circle the name of any medication you have taken. If you are taking any other medications, please write them in the "Other" section.

Second, go back and complete all the information for each medication you have circled.

Third, for the last column, considering both effectiveness and side effects, please rate your satisfaction with each drug on a scale of 0 - 10. "0" means you were Totally Dissatisfied and "10" means you were Extremely Satisfied.

SIDE EFFECTS

In the **PAST 6 MONTHS (January through June)**, have you had any side effects from any of your **ARTHRITIS MEDICATIONS**? Yes No If No, go to Page 11.

Please help us understand your drug side effects.

Elderly Onset Rheumatoid Arthritis

Differential Diagnosis

Table 1. Differential diagnosis of rheumatoid arthritis

Crystalline arthropathy (gout, pseudogout or chronic pyrophosphate arthropathy)

Spondyloarthropathy

Polymyalgia rheumatica

Osteoarthritis

Remitting seronegative symmetrical synovitis with pitting oedema syndrome

Arthritis related to connective tissue disease or systemic vasculitis

Malignancy-related arthritis

Hypertrophic osteoarthropathy

Sarcoidosis

Infectious arthritis (hepatitis B and C, HIV and others)

Elderly Onset Rheumatoid Arthritis

Differential Diagnosis: Polymyalgia rheumatica

PMR may be an overlapping syndrome with seronegative EORA. A population-based study confirmed that late-onset seronegative RA may initially mimic PMR and that some patients initially considered as having PMR were finally diagnosed as having RA after an extended follow-up period because they fulfilled ACR criteria for the diagnosis of RA. Lopez-Hoyos et al. (Rheumatology , 2004) studied the prevalence of anti-CCP antibodies in EORA and PMR patients and showed that the presence of anti-CCP antibodies in a patient with clinical symptoms of PMR must be interpreted as being highly suggestive of EORA.

Differential Diagnosis: RS₃PE

Remitting Seronegative Symmetrical Synovitis with Pitting Oedema RS₃PE is a syndrome characteristic of elderly patients that develops abruptly with oedematous symmetrical arthritis involving the hands and wrist and/or feet and ankles. Extensor tenosynovitis is the lesion responsible for swelling on the dorsum of the hands and feet. Patients with RS₃PE do not develop bony erosions and lack RF. They generally respond well to low doses of corticosteroids, and the prognosis is excellent. RS₃PE like findings can be seen in PMR, other inflammatory rheumatic disorders (including RA and spondyloarthritis), and in patients with haematological and solid malignancies. Whether this syndrome is a different entity or enters into the spectrum of RA is still open to debate.

Anticorpi anti-citrullina (CCP)

G. A. Schellekens, B. A. W. de Jong, et al. :

Citrulline is an Essential Constituent of Antigenic Determinants Recognized by Rheumatoid Arthritis-specific Autoantibodies.

J. Clin. Invest. Vol. 101, Number 1, January 1998, 273-281

C. Vincent, F. de Keyser, et al. :

Anti-perinuclear factor compared with the so called « antikeratin » antibodies and antibodies to human epidermis filaggrin, in the diagnosis of arthritides.

Ann. Rheum. Dis. 1999; 58:42-48 (January)

L. Paimela, T. Palosuo, et al. :

Association of autoantibodies to filaggrin with an active disease in early rheumatoid arthritis.

Ann. Rheum. Dis. 2001; 60:32-35(January)

N. Bizzarro, G. Mozzanti, et al.:

Diagnostic Accuracy of the Anti-Citrulline Antibody Assay for Rheumatoid Arthritis.

Clinical Chemistry 47:1089-1093, 2001

S. Bas, T. V. Perneger, et al. :

Diagnostic test for rheumatoid arthritis : comparison of anti-cyclic citrullinated peptide antibodies, anti-keratin antibodies and IgM rheumatoid factors.

Rheumatology 2002; 41: 809-814

S. Genevay, G. Hayem, et al.:

An eight years prospective study of outcome prediction by antiperinuclear factor and antikeratin antibodies at onset of rheumatoid arthritis

Annals of the Rheumatic Diseases 2002; 61:734-736

D. M. Lee and P. H. Schur:

Clinical utility of the anti-CCP assay in patients with rheumatic diseases.

Annals of the Rheumatic Diseases 2003; 62:870-874

O. Meyer, C. Labarre et al.:

Anticitrullinated protein/peptide antibody assays in early rheumatoid arthritis for predicting five year radiographic damage.

Annals of the Rheumatic Diseases 2003; 62:120-126

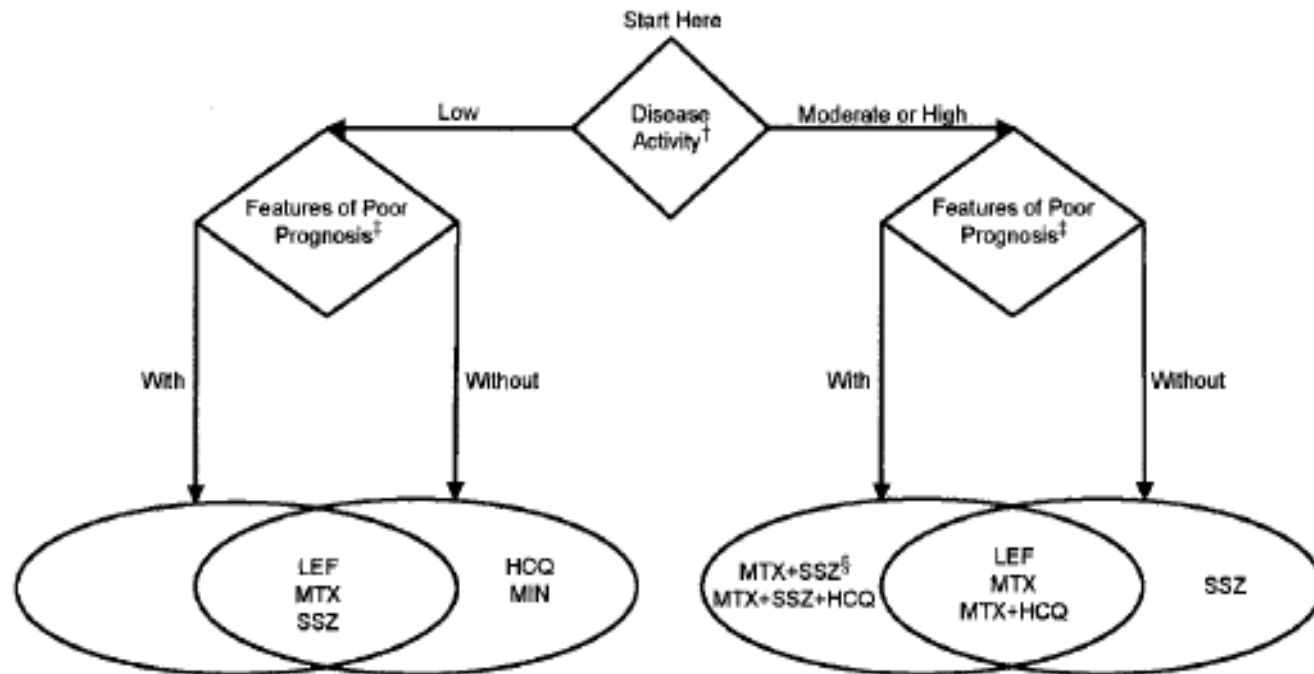
Anticorpi anti-citrullina (CCP)

Vengono ricercati anticorpi diretti verso l'antigene costituito da un peptide citrullinato ciclico. In precedenza venivano utilizzati come marcatori specifici della artrite reumatoide (AR) gli anticorpi anti filaggrina/cheratoialina o il cosiddetto fattore perinucleare. In realtà è stato dimostrato che gli anticorpi anti-CCP riconoscono una proteina epiteliale comune chiamata filaggrina, soggetta ad una modificazione enzimatica post-trascrizionale che comporta la sostituzione di alcuni residui di arginina con altri di citrullina. L'aminoacido citrullina presente nella filaggrina si è rivelato un componente importante dell'epitopo antigenico di queste molecole divenendo l'antigene di scelta come substrato in test immunoenzimatici (ELISA) di prima generazione per la determinazione degli anticorpi anti-CCP dotati di un'ottima specificità per la diagnosi di AR. L'utilizzo di peptidi citrullinati ciclici, nei test anti-CCP di seconda generazione, ha migliorato notevolmente la sensibilità del test mantenendo un'elevata specificità. I FR sono marcatori sensibili ma non molto specifici; per contro gli anti-CCP sono caratterizzati da una specificità di oltre il 90% per AR e sono rilevabili ad uno stadio molto precoce, subclinico della malattia. Circa il 70% dei pazienti con AR sono positivi per anti-CCP a fronte di solo il 2% dei soggetti di controllo Il test è stato approvato dalla *United States FDA* per l'utilizzo nella diagnosi di AR.

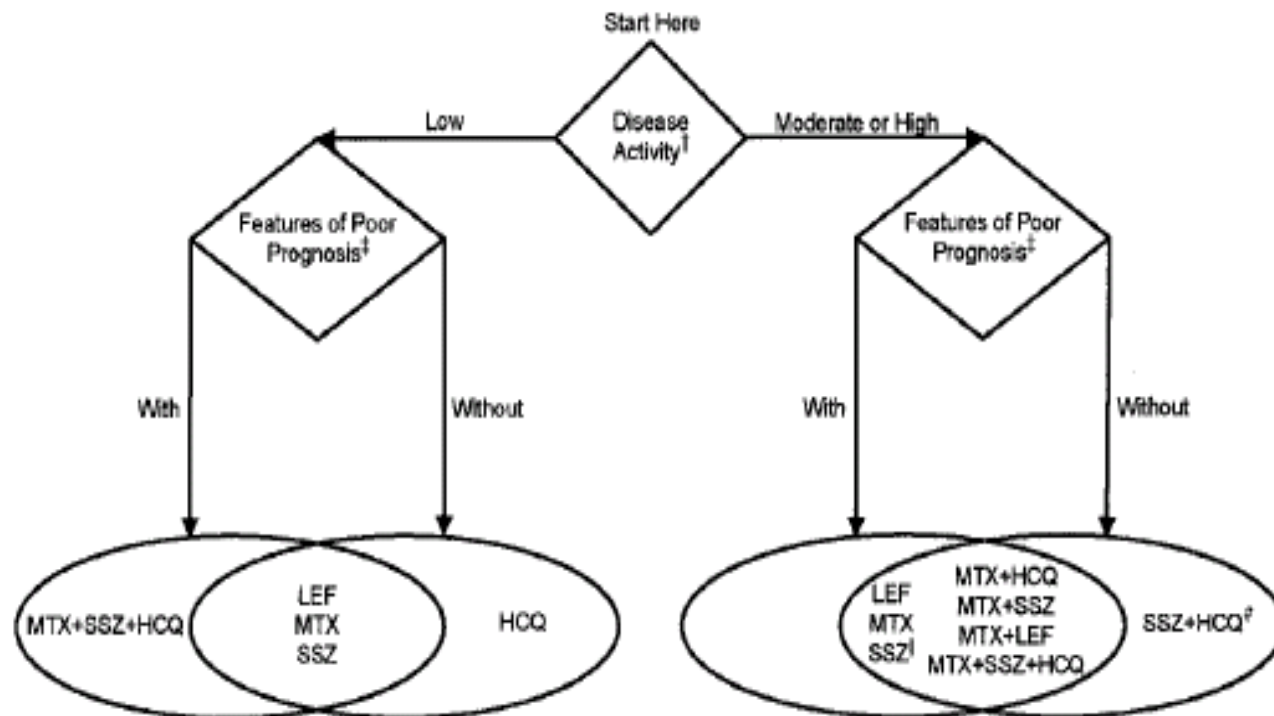
American College of Rheumatology 2008 Recommendations for the Use of Nonbiologic and Biologic Disease-Modifying Antirheumatic Drugs in Rheumatoid Arthritis

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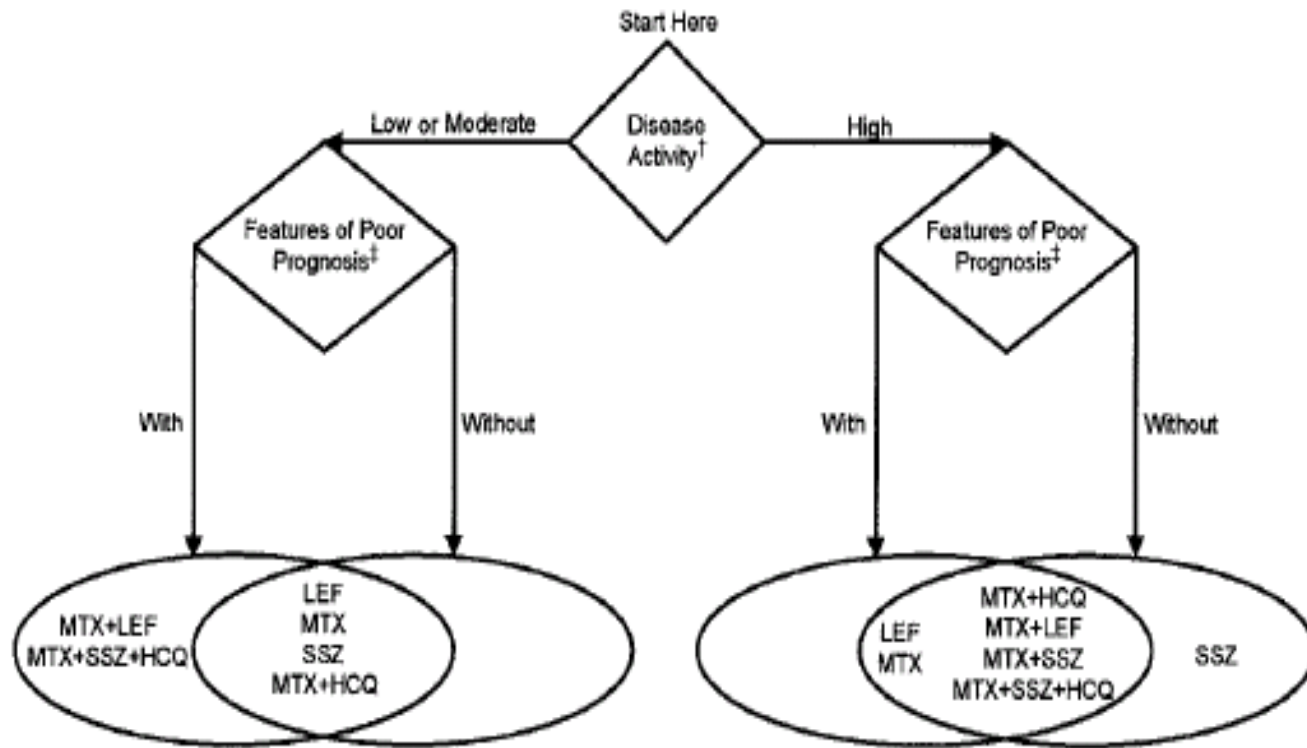
PAZIENTI CON DURATA DI MALATTIA < 6 MESI



PAZIENTI CON DURATA DI MALATTIA 6-24 MESI



PAZIENTI CON DURATA DI MALATTIA >24 MESI



Guidelines for the Use of Conventional and Newer Disease-Modifying Antirheumatic Drugs in Elderly Patients with Rheumatoid Arthritis

Alejandro Díaz-Borjón

-Whether EORA carries a better or poorer prognosis than YORA is still debatable. Co-morbidities associated with the elderly (e.g. heart disease, chronic lung disease, malignancies, etc.) may contribute to a perception of worse outcomes as well as predisposing this population to adverse drug effects and toxicities. Additionally, elderly YORA patients may have other co-morbid conditions secondary to long standing disease.

-While nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly used to treat RA and can have significant adverse effects in the elderly (e.g. cardiovascular, gastrointestinal, etc.), these agents do not have disease-modifying properties.

-In contrast, corticosteroids have been shown not only to improve the signs and symptoms of RA but also to slow radiographic damage in patients with RA.

Guidelines for the Use of Conventional and Newer Disease-Modifying Antirheumatic Drugs in Elderly Patients with Rheumatoid Arthritis

Alejandro Díaz-Borjón

- Although some trials include patients up to 70 years of age, the elderly population is under-represented in RA therapy clinical trials, and specific trials in this age group are lacking; therefore, data about the efficacy and toxicity of DMARDs and biologic agents in the elderly are scarce.
- The frequent phenomenon of polypharmacy in the old may contribute to altered DMARD metabolism and a higher incidence of toxicities or adverse effects. However, in general, there is a lack of information about DMARD pharmacokinetics in the elderly population.
- Elderly patients should not be excluded from the benefits of DMARD or biologic therapy; however, additional considerations, as well as closer monitoring for adverse medication effects, toxicities and drug drug interactions may be required.

Table 1. Toxic and adverse effects of methotrexate, and guidelines for monitoring its use in patients with rheumatoid arthritis

System/organ	Adverse/toxic effect	Baseline evaluation	Monitoring
Gastrointestinal (most common)	Oral ulcers, nausea, vomiting, abdominal pain/discomfort, diarrhoea, hepatotoxicity	Chest x-ray, liver function tests (including albumin), blood urea nitrogen, creatinine, complete blood count (including platelet count) and hepatitis B and C serology	Complete blood count (including platelet count), liver function tests (including albumin), blood urea nitrogen and creatinine every 4–8 weeks
Pulmonary	Interstitial pneumonitis, pulmonary nodulosis		
Haematological	Leukopenia, thrombocytopenia, megaloblastic anaemia, non-Hodgkin's lymphoma (Epstein-Barr virus-associated)		
Renal	Decreased creatinine clearance		
Skin	Nodulosis, alopecia		
Reproductive	Teratogenesis, oligospermia		
Metabolic	Hyperhomocysteinaemia		
Nervous system	Headache, neurotoxicity, seizures (very rare)		

Table II. Toxic and adverse effects of antimalarials, and guidelines for monitoring their use in patients with rheumatoid arthritis

System/organ	Adverse/toxic effect	Baseline evaluation	Monitoring
Eye (rare)	Retinal toxicity, corneal deposits	Ophthalmological examination if age	Ophthalmological evaluation yearly
Gastrointestinal (most common)	Nausea/vomiting, abdominal pain, diarrhoea	>40 years or pre-existing eye disease, liver function tests and creatinine	
Neuromuscular (rare)	Myopathy		
Haematological (rare)	Aplastic anaemia, agranulocytosis, thrombocytopenia		
Skin	Pigmentation of skin and mucosa (very long-term use), hair bleaching, pruritus		
Cardiovascular (rare)	Cardiomyopathy, heart block		
Nervous system	Headache and dizziness (common), ototoxicity, seizures (very rare)		

Table V. Toxic and adverse effects of other conventional (synthetic) disease-modifying antirheumatic drugs (DMARDs), and guidelines for monitoring use of these drugs in patients with rheumatoid arthritis

DMARD	Adverse/toxic effect	Baseline evaluation	Monitoring
Gold salts (intramuscular)	Stomatitis, rash, nitritoid reactions, nausea, vomiting, hepatotoxicity, myelosuppression, nephrotoxicity, pneumonitis	CBC ^a , BUN, creatinine and urinalysis; consider LFTs	CBC ^a and urinalysis every 2 weeks while on weekly injections, then with each injection; consider LFTs, BUN and creatinine every 3 months
Auranofin (oral gold)	Nausea, vomiting, abdominal pain, diarrhoea rash, stomatitis, dysgeusia, hepatotoxicity, pneumonitis, nephrotoxicity, myelosuppression	CBC ^a , BUN, creatinine, LFTs and urinalysis	CBC ^a , BUN, creatinine, LFTs and urinalysis every 4–8 weeks
Penicillamine	Myelosuppression, pneumonitis, nephrotoxicity, hepatotoxicity, SLE-like syndrome	CBC ^a , urinalysis, BUN and creatinine; consider LFTs	CBC ^a and urinalysis every 2 weeks for 6 months, then every month; consider BUN, creatinine and LFTs every 1–3 months
Minocycline	Nausea, vomiting, diarrhoea, abdominal discomfort, dizziness, vertigo, headache, skin hyperpigmentation, cytopenias, hepatotoxicity (rare)	CBC ^a , BUN, creatinine and LFTs	No specific recommendations; consider CBC ^a and LFTs periodically
Ciclosporin	Hypertension, nausea, vomiting, hirsutism, headache, nephrotoxicity, hepatotoxicity, hyperglycaemia, dyslipidaemia, hyperuricaemia (and gout), electrolyte abnormalities, cytopenias, anaemia	BP, CBC ^a , BUN, creatinine, LFTs and uric acid	BP at every visit; BUN and creatinine every 2 weeks until dose stable, then every month; CBC ^a , LFTs and electrolytes (potassium) periodically. Consider lipid panel
Azathioprine	Nausea, vomiting (treatment limiting), myelosuppression, hepatotoxicity, hypersensitivity, malignancy (including lymphoma)	CBC ^a , BUN, creatinine and LFTs; consider TPMT genotyping/phenotyping	CBC ^a every 1–2 weeks with dose changes, then every 1–3 months along with LFTs

a Including platelet count.

BP=blood pressure; **BUN**=blood urea nitrogen; **CBC**=complete blood count; **LFTs**=liver function tests; **SLE**=systemic lupus erythematosus; **TPMT**=thiopurine methyltransferase.

Table IV. Toxic and adverse effects of leflunomide, and guidelines for monitoring its use in patients with rheumatoid arthritis

System/organ	Adverse/toxic effect	Baseline evaluation	Monitoring
Gastrointestinal (most common)	Diarrhoea, nausea, abdominal pain, hepatotoxicity	Complete blood count, liver function tests (including albumin) and hepatitis B and C serology	Complete blood count and liver function tests (including albumin) every 4–8 weeks, BP monitoring at every visit
Cardiovascular	Hypertension (new onset or exacerbation)		
Skin	Alopecia, rash		
Nervous system	Anorexia, headache, peripheral neuropathy		
Haematological (rare)	Agranulocytosis, thrombocytopenia, pancytopenia		
Pulmonary (very rare)	Interstitial pneumonitis		

BP = blood pressure.

Table VI. Toxic and adverse effects of tumour necrosis factor- α inhibitors, and guidelines for their use in patients with rheumatoid arthritis

System/organ	Adverse/toxic effect	Baseline evaluation	Monitoring
Skin	Injection site reactions (etanercept, adalimumab), rash	Purified protein derivative of tuberculin, complete blood count, liver function tests and creatinine; consider chest x-ray and hepatitis B and C serology if not already done	None specifically recommended. When used in combination with synthetic DMARDs (e.g. methotrexate), perform monitoring accordingly
Systemic	Infection (including serious), opportunistic infection (tuberculosis most common), anaphylaxis, malignancy (rare), lupus-like illness, infusion reactions (infliximab)		
Haemolymphatic	Myelosuppression, lymphoma		
Cardiovascular	Congestive heart failure exacerbation		
Nervous system	Headache, demyelinating disease (rare), optic neuritis (rare), seizures (rare)		
Respiratory	Upper respiratory tract infection symptoms		
Gastrointestinal	Nausea, vomiting, abdominal discomfort, dyspepsia, hepatotoxicity (rare), hepatitis B reactivation		

DMARD = disease-modifying antirheumatic drug.

CONCLUSIONI

- L'ARTRITE REUMATOIDE AD ESORDIO TARDIVO (EORA) E' UNA MALATTIA GENETICAMENTE, CLINICAMENTE E PROGNOSTICAMENTE DIVERSA DALL'ARTRITE REUMATOIDE DELL'ADULTO (YORA)
- LA FORMA CON FR NEGATIVO, E, SOPRATTUTTO, CON ANTICORPI ANTI CCP NEGATIVI, E' CONSIDERATA UNA VARIANTE DELLA PMR: RISPONDE A BASSE DOSI DI STEROIDE E VA INCONTRO PIU' SPESSO A REMISSIONE
- NEI PAZIENTI CON EORA SIEROPOSITIVA E' NECESSARIO INIZIARE LA TERAPIA DI FONDO: QUESTA HA INFATTI DIMOSTRATO DI MIGLIORARE LA PROGNOSI FUNZIONALE A BREVE E LUNGO TERMINE
- I FARMACI BIOLOGICI SONO UN VALIDO STRUMENTO TERAPEUTICO NEGLI ADULTI (YORA) CHE NON RIPONDONO AI DMARDs TRADIZIONALI; NEGLI ANZIANI NON VI SONO STUDI NE' DI EFFICACIA NE' DI TOLLERABILITA'

