(Table). Receiver operating characteristic curves showed that M-DAS28, DAS28 (CRP) and RAPID3 had higher predictive value (area under the curve) than CDAI or SDAI for radiographic progression at M12 and M24 (Table). There was no impact of treatment arm on predictors of radiographic outcomes.

Conclusions: In this *post hoc* analysis, disease activity scores at baseline according to M-DAS28, DAS28 (CRP) and RAPID3 were good predictors of radiographic progression at M12 and M24 and were more predictive than other measures of disease activity tested, with M-DAS28 demonstrating the greatest degree of prediction.

References:
[1] Yazici Y, et al. J Rheumatol 2008;35:603–9.
[2] Salaffi F, et al. BMC Musculoskelet Disord 2011;12:120.
[3] Baker JF, et al. Arthritis Rheumatol 2014;66:794–802.
[4] Schiff M, et al. Ann Rheum Dis 2014;73:86–94.

Disclosure of Interest: E. Keystone Grant/research support from: Abbott, Amgen, AstraZeneca, Bristol-Myers Squibb, F. Hoffmann-La Roche, Janssen, Lilly, Novartis, Pfizer, sanofi-aventis, UCB, Consultant for: Abbott, AstraZeneca, Biotest, Bristol-Myers Squibb, Crescendo, F. Hoffmann-La Roche, Genentech, Janssen, Lilly, Merck, Pfizer, UCB, Speakers bureau: Amgen, Abbott, AstraZeneca, Bristol-Myers Squibb, F. Hoffmann-La Roche, Janssen, Pfizer, Sanofi, Genzyme, UCB, H. Ahmad Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Y. Yazici Grant/research support from: Genentech, Celgene, Bristol-Myers Squibb, Consultant for: Genentech, Celgene, Bristol-Myers Squibb, E. Muratti Employee of: Bristol-Myers Squibb, J. Ye Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, M. Bergman Shareholder of: Pfizer, Johnson & Johnson, Consultant for: AbbVie, Bristol-Myers Squibb, Amgen, Celgene, Genentech, Pfizer, Janssen, Speakers bureau: Norvatis, Abbvie, Celegene

DOI: 10.1136/annrheumdis-2017-eular.1930

THU0090 INFLUENCE OF AGE AT DISEASE ONSET ON CLINICAL, FUNCTIONAL, AND ULTRASONOGRAPHIC OUTCOMES IN A MONOCENTRIC EARLY RHEUMATOID ARTHRITIS COHORT

E. Galuppi, I. Farina, C. De Giorgio, C.A. Scirè, M. Govoni. *Department of Medical Sciences, UOC Rheumatology, University of Ferrara and Azienda Ospedaliero-Universitaria Sant'Anna, Ferrara, Italy*

Background: Rheumatoid Arthritis (RA) onset may occur at any age and peaks in the fifth decade. Because the mean age of general population is continually increasing and since older age could impact on outcomes, late-onset RA (LORA) will probably become a relevant issue for health care system in the next future. A better characterization of LORA could help rheumatologist in the therapeutic decision-making process tailored on the individual patient.

Objectives: To investigate the relationship between age at disease onset and clinical, ultrasonographic and functional outcomes.

Methods: Early RA (ERA) patients fulfilling 2010 ACR/EULAR, with available clinical ad ultrasonographic follow-up of at least 1 year, who consecutively attended our Early Arthritis Clinic between 2009–2014, were retrospectively analyzed. Patients were pooled into 3 groups by age at RA onset: <45 years (young-onset RA [YORA] group 1), 45 to 60 years (intermediate-onset RA [IORA] group 2), and >60 years (late-onset RA [LORA] group 3). At baseline biological, functional and ultrasonographic data were recorded. The following items were compared at baseline and after 12 months from diagnosis: $DAS28_{CRP}$ remission rate, functional disability using the Health Assessment Questionnaire (HAQ), power doppler (PWD) score, Methotrexate (MTX) treatment, use of glucocorticoids (GCs).

Table 1 Baseline demographic and disease characteristics of 3 groups.

	Whole sample (n=223)	YORA (n=46)	IORA (n=81)	LORA (n=96)	P-value (overall)	P-value LORA vs YORA	P-value LORA Vs IORA
Female, n (%)	164 (73.5)	40 (86.9)	59 (72.8)	65 (67.7)	0.051	0.014	0.4
Lag time onset to diagnosis (months), median (IQR)	4 (2-7)	5 (3-8)	4 (2-6)	3 (2-6)	0.03	0.0001	0.03
RF, n (%)	112 (50.2)	26 (56.5)	42 (51.8)	44 (45.8)	0.45	0.42	0.23
ACPA, n (%)	127 (56.9)	28 (60.8)	50 (61.7)	49 (51)	0.30	0.15	0.27
TJC, median (IQR)	6 (2-12)	2 (1-8)	6 (4-11)	7 (3.5-12)	0.0005	0.0001	0.50
SJC, median (IQR)	3 (1-7)	2 (0-4)	3 (1-7)	4 (2-8)	0.0054	0.0013	0.34
CRP (mg/dl), median (IQR)	0.9 (0.4-2.1)	0.58 (0.24-1.3)	0.7 (0.4-1.59)	1.3(0.5-2.91)	0.0014	0.001	0.0091
$DAS28_{CRP}$, median (IQR)	4.44(3.61-5.33)	3.71 (3.24-4.61)	4.40 (3.74-5.32)	4.75 (3.8-5.6)	0.0013	0.0003	0.13
SDAI, median (IQR)	24.45(15.7-33.7)	18.57 (10.8-28)	23.5 (15.5-32.9)	26.1 (18-38.5)	0.0032	0.0011	0.06
PWD MSUS, median (IQR)	5 (1-9)	1 (0-7.5)	5 (2-8)	8 (3-10.5)	0.002	0.0001	0.03
HAQ-DI, median (IQR)	0.87 (0-5-1.4)	0.65 (0.25-1.25)	0.87 (0.5-1.25)	1 (0.62-1.75)	0.0091	0.0033	0.05
MTX (%)	70.85	65.22	75.31	69.79	0.46	0.58	0.41
MTX dose mg/week, median (IQR)	10 (10-10)	10 (10-10)	10 (10-15)	10 (10-10)	0.02	0.42	0.01
GCs (%)	86.55	86.96	83.95	88.54	0.66	0.78	0.37
GCs dose (mg/daily), median (IQR)	5 (5-10)	5 (5-9)	5 (5-10)	5 (5-10)	0.59	0.42	0.76

P global comparison for 3 groups by Kruskal-Wallis test. Comparison for 2 group by Mann Whitney test.

Table 2 Adjusted odds ratios (aORs) for $DAS28_{CRP}$ remission, PWD MSUS remission and HAQ score <0.5 at 1 year follow up

Outcome 1 year	IORA	YORA		LORA	
		aOR [95%CI]	P-value vs IORA	aOR [95%CI]	P-value vs IORA
$DAS28_{CRP}$ REM	reference	1.42 (0.63-3.18)	0.38	2.95 (1.48-5.86)	0.002
PWD MSUS REM	reference	1.21 (0.40-3.69)	0.72	1.18 (0.51-2.73)	0.69
HAQ score <0.5	reference	0.75 (0.33-1.73)	0.51	1.24(0.61-2.53)	0.53

aOR: odds ratio adjusted for gender, baseline $DAS28_{CRP}$, MTX use, glucorticoid use, serology.

Results: The main baseline demographic and disease characteristics of the whole sample of ERA (n=223) and the 3 age groups- YORA (46), IORA (81) and LORA (96)- are summarised in Table 1. Age at RA-onset was independently associated with $DAS28_{CRP}$ remission at 1 year (Table 2).

Conclusions: In a cohort of ERA, older age at disease onset is associated with a more active pattern disease at the beginning but with a greater probability of $DAS28_{CRP}$ remission at 1 year.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5011

THU0091 HIGH MULTI-BIOMARKER DISEASE ACTIVITY SCORE IS ASSOCIATED WITH HIGH RISK OF RADIOGRAPHIC PROGRESSION IN SIX STUDIES

J.R. Curtis[1], C.H. Brahe[2], M. Ostergaard[2], M.L. Hetland[2], K. Hambardzumyan[3], S. Saevarsdottir[3], X. Wang[4], E.H. Sasso[4], T.W. Huizinga[5]. *[1]Univ. of Alabama at Birmingham, Birmingham, United States; [2]Copenhagen Center for Arthritis Research, Copenhagen, Denmark; [3]Karolinska Univ. Hospital and Karolinska Institutet, Stockholm, Sweden; [4]Crescendo Bioscience Inc., South San Francisco, United States; [5]Leiden Univ. Medical Center, Leiden, Netherlands*

Background: The multi-biomarker disease activity (MBDA) test uses a validated algorithm with 12 serum protein biomarkers to assess disease activity in patients with RA. The MBDA score has previously been found to be a predictor of risk for radiographic progression (RP).

Objectives: To evaluate data from six cohorts to collectively establish the relationship between the MBDA score and risk for RP.

Methods: Clinical, MBDA score and radiographic data were analyzed for 6 cohorts with N>100: Leiden, SWEFOT Year 1, SWEFOT Year 2, OPERA Year 1, and AMPLE Year 1 (abatacept and adalimumab arms) (see Figure). Analyses used published results when available or patient-level data when not (i.e., for Leiden; and for OPERA CRP analyses). Frequency of RP over one year was determined by category of MBDA score (low, moderate [30–44], high on a scale of 1–100) at the start of the year for four cohorts and by category of MBDA score at the end of the year for AMPLE cohorts (as published). RP was defined using the threshold for change in total modified Sharp score (ΔmTSS) specific to each study (2 to >5 TSS units). Positive and negative predictive values (PPV and NPV) were determined for each study by comparing patients with high MBDA score (>44), DAS28-(ESR/CRP) (>5.1 or >4.09) or CRP (>3 mg/dL) vs. those in a not-high category. Relative risk (RR) for RP was determined for each study, and in a meta-analysis of the non-overlapping patient groups with MBDA scores available at the start of the year (Leiden, SWEFOT Year 1 and OPERA Year 1). Results of multivariate analyses and analyses that combined MBDA score with other risk factors for RP were summarized.

Results: The 6 study cohorts included patients receiving csDMARDs alone or with adalimumab, infliximab or abatacept. Overall rates of RP were 10–26%. In each study, RP was most frequent among patients with a high vs. not-high MBDA score (>44 vs. ≤44). For high MBDA scores, NPVs were 93–97% and PPVs were 18–32%, with RR values of 3.6–9.5 (P=0.002 to <0.0001) (Figure). In a meta-analysis of the Leiden, SWEFOT Year 1 and OPERA Year 1 cohorts, RR was 5.1 (P<0.0001) for MBDA categories, and 1.4 (P=0.23) and 1.6 (P=0.01) for categories of DAS28-CRP or CRP, respectively. Previously published multivariate analyses in the Leiden and SWEFOT Year 1 cohorts showed that MBDA score was an independent predictor of RP compared with other predictors. In the Leiden cohort, MBDA score was the strongest predictor and high MBDA score

Association between radiographic progression (RP) and high MBDA score (>44)

Cohort	N	RP cutoff	Overall % RP	PPV for MBDA >44	NPV for MBDA >44	Relative Risk[1] (95% CI)	P-value
Leiden	163	>5.0	17%	31%	93%	4.3 (1.9, 9.5)	<0.0001
OPERA Year 1	164	≥2.0	26%	31%	97%	9.5 (1.4, 66.3)	0.0009
SWEFOT Year 1	235	>5.0	18%	21%	97%	7.1 (1.0, 49.9)	0.008
Meta-analysis (LEIDEN + OPERA Year 1 + SWEFOT Year 1)						5.1[3] (2.5, 10.1)	<0.0001
SWEFOT Year 2	133	>5.0	13%	32%	95%	6.2 (2.4,16.5)	0.0001
AMPLE Year 1 (Aba)	181	>2.2[4]	10%	18%	96%	4.5 (1.6,13.1)	0.003
AMPLE Year 1 (Ada)	186	>2.2[4]	11%	24%	93%	3.6 (1.6,8.1)	0.002

PPV, positive predictive value; NPV, negative predictive value. 1. Relative risk = PPV/(1-NPV). 2. Random-effect model used for meta-analysis. 3.Aggregated relative risk. 4. ΔTSS cutoff for RP was defined in Fleischmann et al (*Arthritis Rheumatol* 2016;68:2083–9) as >smallest detectable change (SDC), however no value was specified; SDC for AMPLE was specified as 2.8 and 2.2 in prior AMPLE publications (Weinblatt 2013; Schiff 2014).

Treatments; reference; data source:
LEIDEN (csDMARDs); Li et al. *Rheumatology (Oxford)*. 2013;55:357–66; Unpublished patient-level data only.
OPERA (MTX+placebo-adalimumab+IA corticosteroids/MTX+adalimumab+IA corticosteroids); Brahe et al. *Arthritis Rheumatol*. ACR 2016 Abstract 2520; Published data and unpublished patient-level data for analysis of CRP categories.
SWEFOT Year 1 (MTX/ triple therapy/MTX+infliximab); Hambardzumyan K, et al. *Ann Rheum Dis*. 2015;74:1102–9; Published data only.
SWEFOT Year 2 (triple therapy/MTX+infliximab); Hambardzumyan K et al, *RMD Open*. 2016 Mar 1;2(1):e000197; Published data only.
AMPLE Year 1 (abatacept and adalimumab arms, analyzed separately); Fleischmann et al. *Arthritis Rheumatol* 2016;68:2083–9, Curtis et al. *Arthritis Rheumatol*. 2016 Nov 3. doi: 10.1002/art.39981 and *Fleischmann et al. *Arthritis Rheumatol*. 2016 Dec 19. DOI: 10.1002/art.40021; Published data only, from Fleischmann et al(*).

discriminated between high and low risk for RP among patients with high SJC (>5) or high DAS28-CRP, with PPV as high as 57%.
Conclusions: High MBDA scores were associated with increased risk for RP in 6 study cohorts, including patients treated with csDMARDs, TNFi and abatacept. Based on high NPVs (≥93%), the MBDA score used alone had clinical value for identifying patients with little or no risk of RP. Combining the MBDA score with clinical measures yielded PPVs approaching 60%, suggesting that biomarkers can help stratify patients by their risk for RP.
Disclosure of Interest: J. Curtis Grant/research support from: Crescendo Bioscience Inc., Consultant for: Crescendo Bioscience Inc., C. Brahe: None declared, M. Ostergaard Grant/research support from: AbbVie, BMS, Boehringer-Ingelheim, Eli Lilly, Janssen, Merck, Pfizer, Roche, UCB, Celgene, Sanofi, Regeneron, Novartis, T Jensen, M. Hetland Grant/research support from: AbbVie, BMS, MSD, Pfizer, Crescendo Bioscience Inc., UCB, Eli Lilly, Speakers bureau: Orion, K. Hambardzumyan: None declared, S. Saevarsdottir: None declared, X. Wang Shareholder of: Myriad Genetics, Inc., Employee of: Crescendo Bioscience Inc., E. Sasso Shareholder of: Myriad Genetics, Inc., Employee of: Crescendo Bioscience Inc., T. Huizinga Consultant for: Merck, UCB, Bristol Myers Squibb, Biotest AG, Pfizer, GSK, Novartis, Roche, Sanofi-Aventis, Abbott, Crescendo Bioscience Inc., Nycomed, Boeringher, Takeda, Zydus, Epirus, Eli Lilly
DOI: 10.1136/annrheumdis-2017-eular.5557

THU0092 CHORONIC PAIN INCREASES INDEPENDENT OF THE DISEASE ACTIVITY AND DEPRESSION IN FEMALES WİTH RHEUMATOİD ARTHRITIS

F.G. Yurdakul, A. Kılıçarslan, H. Bodur. *Department of Physical Medicine and Rehabilitation, Ankara Numune Training and Research Hospital, Ankara, Turkey*

Background: Chronic pain is a key component of rheumatoid arthritis (RA). Although pain is reduced with the control of inflammation at the first years of the disease, pain increases over time with different pathways just as central sensitization. Fatigue, sleep problems and depressive symptoms with chronic pain are common problems in patients with RA (1,2).
Objectives: We aimed to investigate the frequency of widespread pain, sleep disorders, fatigue, and depressive symptoms in RA patients. Furthermore discrepancy of these symptoms and disorders were analyzed between female and male RA patients.
Methods: One hundred and sixty one RA patients (female: 119, male: 42) and 68 healthy controls (female: 52, male: 16) were enrolled in the study. Widespread pain index (WPI) with nineteen body parts that was identified by 2010 fibromyalgia diagnostic criteria was interrogated. Pain visual analog scale (VAS), Health Assessment Questionnaire (HAQ), Physician global assessment (PhGA), Fatigue severity scale (FSS), Pittsburgh sleep quality index (PSQI), Beck depression inventory (BDI) were evaluated in both RA patients and healthy controls. Morning stiffness (MS), Rheumatoid arthritis quality of life (RAQOL) and disease activity score 28 (DAS28) were assessed in RA patients. Data were analyzed in female and male RA patients.
Results: The mean PhGA, HAQ, BDI, FSS, WPI values of RA patients were worse than healthy controls (p=0.012, 0.000, 0.008, 0.033, 0.044 respectively). There was no difference between RA and healthy controls in terms of sleep disorders. The mean age, disease duration, MS, swollen joint count, C-reactive protein, PhGA and BDI were similar in female and male RA patients. WPI, VAS pain, tender joint count, HAQ, RAQOL, FSS, PSQI, and DAS 28 were higher in females (Table 1).

Table 1. Clinical features in female and male RA patients

	Female RA patients (n=119)	Male RA patients (n=42)	p
Widespread pain index	4.70±4.97	2.65±3.99	0.04*
PhGA	2.87±2.16	2.09±1.63	0.08
DAS28	3.39±1.39	2.68±1.11	0.01*
CRP	10.77±13.62	12.59±14.20	0.24
Tender Joint Count	10.92±13.47	6.78±13.09	0.03*
Swollen Joint Count	0.88±2.67	0.31±0.69	0.690
HAQ	1.06±0.83	0.68±0.66	0.04*
RAQOL	14.34±10.06	7.59±8.83	0.00*
FSS	35.57±19.24	22.21±14.41	0.00*
PSQI	8.02±5.58	5.00±4.20	0.00*
BDI	15.71±13.34	11.28±12.56	0.06

PhGA: Physician global assessment, DAS: Disease activity score, CRP: C Reactive protein, HAQ: Health Assessment Questionnaire, RAQOL: Rheumatoid arthritis quality of life, FSS: Fatigue severity scale, PSQI: Pittsburgh sleep quality index, BDI: Beck depression inventory.

Conclusions: RA is a disease that increases fatigue, depressive symptoms and widespread pain.DAS 28 scores were higher due to the increased pain scores and tender joint count that are subjective parameters in female RA patients. Pain scores in females are significantly higher than in males, and pain exacerbated by central sensitization pathway in women may lead to sleep disorders and fatigue, but not increase depressive symptoms.
References:
[1] The role of central nervous system in the generation and main tance of chronic pain in rheumatoid arthritis, osteoarthritis and fibromyalgia. Lee YC, Nassikas NJ, Clauw DJ. Arthritis Research and Therapy (2011) 13:211–221.
[2] Fatigue in patients with rheumatic diseases. Dupond JL. Joint Bone Spine (2011). 78:156–160.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5846

THU0093 PERSISTENCE OF POWER DOPPLER ULTRASOUND-DETECTED RESIDUAL SYNOVITIS IN CONSECUTIVE ULTRASOUND EXAMINATIONS IN RHEUMATOID ARTHRITIS PATIENTS IN CLINICAL REMISSION PREDICTS UNFAVORABLE OUTCOME OVER ONE YEAR

G. Mouterde[1], C. Lukas[1], N. Filippi[1], G. Marin[2], N. Molinari[2], J. Morel[1], B. Combe[1]. *[1]Rheumatology department; [2]Department of Statistics, Lapeyronie hospital, Montpellier, France*

Background: Some studies revealed an association of Power Doppler (PD) ultrasound (US)-detected residual synovitis (PDUSS) and risk of relapse and radiographic progression (RP), in individual patients in rheumatoid arthritis (RA). However, the longitudinal relationship between clinical remission and repeated US residual lesions during follow-up is not so well-known.
Objectives: The aim of this study was to evaluate the ability of PDUSS in consecutive examinations to predict unfavorable outcome (i.e. clinical relapse or RP) at 1 year.
Methods: RA patients ≥18 years fulfilling 2010 ACR-EULAR criteria, treated with synthetic or biologic (b) DMARDs and in clinical remission (DAS28-ESR<2.6 and no clinically active synovitis) for less than 6 months, were included in the longitudinal prospective SONORE study (ClinicalTrials.gov identifier: NCT02618954). Clinical and biological characteristics of patients were collected at baseline, and every 3 months during 1 year. RA treatment had to be stable during follow-up. A standard US examination on 40 joints for the presence of synovial hypertrophy and PD signal was performed by an independent investigator blinded to clinical and radiographic data at each visit during 1 year. Presence of US synovitis was defined by a PD signal≥1 in at least one joint. Radiographs of hands, wrists and feet were scored at baseline and 1 year. Outcome measures: RP was defined by an increase ≥1 point of the modified total Sharp score. A relapse was defined by a DAS28>3.2 at ≥1 follow-up visits AND a change of DMARDs, excluding change due to safety issues; or an increase in the DMARD or Corticosteroid (CS) dosage (≥5mg/d). Baseline variables, including PDUSS and its persistence during the follow-up, were assessed for their association with time to progression to unfavorable outcome using univariate then stepwise multivariate Cox regression analyses to obtain adjusted HRs.
Results: The 115 included patients had a mean (SD) age of 58.9 (±12.8) years, mean disease duration of 9.3 (±9.3) years, a mean duration of remission of 2.1 (±2.3) months. 74.8% were female, 79.1% of the patients were anti-CCP positive, 51.4% had erosive disease. The mean DAS28-ESR was 2.03 (±0.63). 59.2% received methotrexate, 59.9% bDMARD and 11.7% CS. PDUSS was detected in ≥1 joint in 75 patients (72.1%) at baseline. 41/75 (54.7%) had persistence of at least one PDUSS during the follow-up. 26 (23.2%) had a relapse (after a mean duration of 9.1 (±2.6) months) or a RP at 1 year. In multivariate analysis, persistence of at least one PDUSS during the follow-up (HR=5.24 [1.74–22.5], p=0.009) and baseline number of tender joints (HR=1.32 [0.95–1.68], p=0.052) were predictors of relapse or RP at 1 year. Duration of remission, other baseline US findings including baseline PDUSS, autoantibodies, and erosive disease had no additional predictive value.
Conclusions: Persistence of a PDUSS during the follow-up, rather than baseline PDUSS, predicts unfavorable outcome at 1 year in RA patients in clinical remission. This suggests that initial US findings are not sufficient to justify therapeutic change, but that the persistence of a residual PDUSS requires careful follow-up, and might even potentially merit strategy adaptation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5479

THU0094 FACTORS ASSOCIATED WITH RADIOGRAPHIC REMISSION (RR) IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) WHILE NON-BIOLOGICALDISEASE MODIFYING ANTI-RHEUMATIC DRUGS (DMARDS) USING

O. Iaremenko, G. Mykytenko. *Internal Diseases at Stomatological Faculty, O.O. Bogomolets National Medical University, Kyiv, Ukraine*

Objectives: To assess the factors associated with RR achievement in patients (pts) with RA while non-biological DMARDs using.
Methods: A cohort of 174 pts with RA (50.6% with early RA) was prospectively assessed at baseline and 2 years by the Disease Activity Score (DAS28) and the Sharp–van der Heijde Score (SHS). Mean age at inclusion was 52.0±0.91 yrs, disease duration – 51.3±4.82 month. 82.7% of the pts were women; 62.6% were positive for rheumatoid factor (RF) and 75.9% - for antibodies against cyclic citrullinated peptides (aCCP). Pts were treated with methotrexate (MTX) (mean dose – 11.6±0.29 mg/w, n=157), leflunomide (LF) (19.2±0.28 mg/d, n=95), sulfasalazine (SS) (2 g/d, n=76) or combination of DMARDs (CD) (n=74). After 2 yrs of DMARDs therapy 41 pts (23.5%) reached RR (ΔSHS≤0.5). No one pts using low dose of MTX (7.5 mg/week) achieved remission so they were excluded from further analysis. According to RR achievement in 2 yrs pts were divided into