IS SIDE EFFECTS AND TREATMENT RESPONSE TO METHOTREXATE ASSOCIATED TO COMORBIDITY IN EARLY RHEUMATOID ARTHRITIS

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BACKGROUND

In Denmark 35.000 of the population is diagnosed with rheumatoid arthritis (RA). MTX decrease general mortality by 60% for RA patients, and therefore discontinuation of MTX is a bad outcome. It remains unclear whether side effects and treatment response to MTX is associated to comorbidity in early RA.

OBJECTIVE

To evaluate the association between comorbidity and persistence to MTX treatment and side effects for RA patients.

DATA ANALYSIS

Patient files from three centers were evaluated retrospectively. Inclusion criteria were: diagnosis obtained according to ACR/EULAR 2010 criteria for RA in the period 01/01/2010 to present, and MTX as first line of treatment.
Medical records were reviewed for side effects, dose changes of MTX, formulation changes and persistence.

Table: Cox regression of association between comorbidity, disease characteristics, comedication and discontinuation of MTX. Values showing hazard ratio (95% CI).
Crude: age and sex, Adjusted: age, sex and nephropathies

	Crude (95% CI)	Adjusted (95% CI)
Charlson index score		
Low (0)	1.00 (ref)	1.00 (ref)
Medium (1-2)	2.41 (1.06 - 5.51)	2.41 (1.06 - 5.51)
High (3-4)	4.18 (1.67 - 10.45)	4.18 (1.67 - 10.45)
Very high (5+)	0.95 (0.12 - 7.35)	1.95 (0.25 - 15.30)
Other comorbidities		
Cancer	2.26 (0.69 - 7.41)	3.41 (1.02 - 11.40)
Osteoporosis	2.72 (1.09 - 6.84)	3.66 (1.38 - 9.73)
Cardiovascular morbidity	2.80 (1.33 - 5.89)	3.17 (1.47 - 6.83)
Diabetes	1.17 (0.16 - 8.71)	1.25 (0.17 - 9.46)
Nephropathies	0.00 (0.00 - 0.00)	0.00 (0.00 - .)
Number of drugs other than MTX		
0	0.61 (0.18 - 2.01)	0.75 (0.22 - 2.53)
1-3	0.52 (0.26 - 1.05)	0.68 (0.31 - 1.47)
4+	2.36 (1.18 - 4.74)	2.39 (1.17 - 4.90)

DATA ANALYSIS cont.

Comorbidities and co-medication was evaluated by usage of the Danish National Patient Registry (DNPR), and the Odense Pharmacoepidemiological Database (OPED). Comorbidities were scored according to the Charlson Comorbidity Index (CCI), and analyzed by the cox proportional hazards model for discontinuation of MTX treatment and dose reduction.

RESULTS

501 patients were screened, 177 were eligible and analyzed at baseline for disease characteristics, medication besides MTX and comorbidities in a 5-year window before RA diagnosis baseline. The highest risk of MTX discontinuation was a CCI of 3-4, they had crude 4.18 (95% CI 1.67-10.45) increased risk compared to the reference group (RA with no comorbidities). Risk of dosage reduction was highest at CCI 1-2: 1.38 (95% CI 0.72-2.62). A CCI of 5 or higher gave a -4.83 mg (95% CI -10.24- -0.59) adjusted difference in maximum weekly tolerable MTX dosage.
Side effects occurred for 23.7%. Most likely dosage causing side effect was 20 mg (IQR 15-20 mg). Nausea occurred in 29% and hepatic events 21%.

CONCLUSION

Patients with CCI in the range of 3-4 had an increased risk for discontinuing MTX treatment.