Do patients with congestive heart failure treated with biologics for RA have a lower risk of fatal outcome of serious infections?

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Background & Objectives

Rheumatoid arthritis (RA) patients with multimorbid conditions are at high risk of developing serious infections (SI) and of premature mortality. TNF inhibitors increase the infection risk [1]. However, they are likely to decrease all-cause mortality [2].

We therefore aimed to examine (I) the infection risk and (II) the outcome of SI in a group of patients at high mortality risk: RA patients with congestive heart failure (CHF).

Patients & Methods

Data from the German biologics register RABBIT with 10,671 RA patients included at start of a synthetic or biologic DMARD (bDMARD) after at least one DMARD failure were used. In 242 patients, CHF was reported as comorbid condition at enrollment. For 238 CHF patients matched controls without CHF with the same sex, the same comorbid conditions (see Table 1) and similar age were found.

Comparisons were made within the nested case control study between cases and controls and between CHF cases and the remaining cohort. Cox-proportional hazard and multiple logistic regression were applied to investigate the risk of SI and the fatal outcome of SI in CHF patients.

		CHF patients	Matched controls	Cohort
N		238	238	10,195
Age	x	67.7	67.5	55.7
Female sex (%)	x	66.4	66.4	76.9
Hypertension (%)	x	79.0	79.0	63.7
Coronary heart disease (%)	x	42.9	42.9	5.2
Chronic lung diseases (%)	x	23.9	23.9	4.3
Chronic renal disease (%)	x	23.5	23.5	3.2
RF positive (%)		81.5	81.5	72.4
Disease duration (years)		13.8	13.6	9.9
Percent of full function (FFbH)		43.1	54.3	63.1
DAS28		5.9	5.4	5.2
CRP		35.8	18.7	23.2

Tab 1: Patient characteristics (x: matching criteria. Values are means or percentages)

Results

(I) Risk of serious infection:

- Patients with CHF were older, more frequently males, had a more active disease, and considerably more comorbidities than the remaining cohort (Tab 1)
- Serious infection rates were nearly five times higher in CHF patients than in the rest of the cohort (Tab. 2)

	CHF Patients	Matched controls	Cohort
No of serious infections (SI)	100	72	1,167
Incidence rate per 100 pyrs [CI]	13 [10.7; 15.8]	10.3 [8.2; 13.0]	3.4 [3.2; 3.6]
Pneumonia (in percent of all SI)	32 (32%)	15 (21%)	260 (22%)
Sepsis (in percent of all SI)	21 (21%)	15 (21%)	171 (15%)

Tab 2: Serious infections and incidence rates/100 patient years for 3 groups of patients

The high infection risk in RA patients with CHF can be attributed to known risk factors of serious infections:

- higher age,
- chronic renal or lung disease,
- bDMARD and GC treatment

Comparing CHF cases and matched controls the CHF disease itself did not increase the infection risk (Tab. 3)

	HR	95% HR CI
CHF	1.00	[0.68; 1.49]
bDMARD treatment	1.25	[0.81; 1.93]
Physical function (10% decrease)	1.10	[1.01; 1.19]
Log(CRP)	1.28	[1.11; 1.48]
Glucocorticoids : No	Ref.	.
<7.5mg	1.70	[0.83; 3.46]
7.5 – 15mg	2.68	[1.26; 5.70]
>15mg	4.69	[2.05; 10.76]

Tab 3: Adjusted hazard ratios of developing serious infections (Nested case control sample)

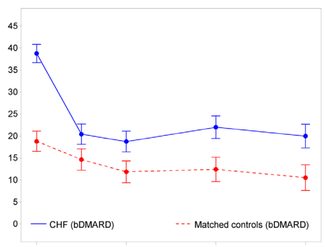

Fig. 1: CRP (mg/l) during 18 months of follow-up

Although more CHF patients than matched controls (204 vs. 172, among them TNFi: 131 vs. 121) were treated with biologic DMARDs the inflammation in CHF patients was insufficiently controlled.

(II) Risk of lethal serious infections:

Serious infections were the most frequent cause of death in patients with CHF:

- Patients with CHF: 60 patients died, 34 due to serious infections
- Matched controls: 37 patients died, 19 due to serious infections

	Odds ratio	95% CI
CHF	1.6	[0.6; 4.2]
Exposure to biologics at onset of serious infection	0.4	[0.2; 1.0]
Age (per 10 years)	2.1	[1.0; 4.2]
Male sex	1.5	[0.6; 4.1]
10% worsening of physical function	1.1	[0.9; 1.3]

Tab 4: Adjusted OR of a fatal outcome of a serious infection (30 days)

As expected, higher age, male gender, and CHF as comorbidity were associated with a higher risk of a fatal outcome of serious infections. Adjusted for these factors treatment with biologic DMARDs was associated with a lower risk (Tab. 4).

Conclusion

Patients with CHF are at increased risk of SI with a high lethality risk. Our data suggest that SI occurring in RA patients on biologic therapy tend to have a lower risk of fatal outcome.

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