Exploring Factors Associated with the Development of Opportunistic Fungal Infections in Rheumatoid Arthritis Patients

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Conclusion

Opportunistic fungal infections (OFIs) are rare, but linked to high fatality. OFIs were associated with higher disease activity, glucocorticoids > 5 mg/day, (ex-)smoking among men, and a higher number of relevant comorbidities.

Further research is necessary to better understand potential causal relationships.

Background

Data on incidence and risk of opportunistic fungal infections (OFIs), rare yet life-threatening infections in rheumatoid arthritis (RA) patients [1], remain scarce due to limited patient numbers and inconsistent case definitions.

Objectives

To investigate associations between the development of OFIs in RA patients and demographic, clinical and treatment data.

Methods

- **Data source**: German biologics register RABBIT (RA patients)
- **Study design**: nested case-control study (matched 1:5)
  - Cases: RA patients with OFI, meeting consensus definitions [2] or causing esophagitis, reported between 05/2001-12/2022
  - Controls: RA patients matched by age and enrolment year, with equal or longer observation times than cases
- **Statistics**: Multivariable logistic regression was used to assess the association of OFI occurrence with the following variables at last visit prior to OFI onset:
  - sex, disease duration, disease activity (DAS28-ESR), glucocorticoid (GC) use, b/tsDMARD therapy, number of previous DMARDs, sum of comorbidities predisposing for infection (table 1), (ex-)smoking, and type of enrolling institution.

Results

- **Source population**: 20,907 RA patients with 101,778 patient-years in RABBIT.
- **Cases**: 105 RA patients developed an OFI, with 56 of these being invasive.
- **Fatalities**: 19 cases died from or with infection, representing 18 % of all resp. 34 % of invasive OFI.
- **Fungal pathogen**: *Candida* spp. (60 %), *Pneumocystis jirovecii* (20 %), *Aspergillus* spp. (7 %), and unknown fungal genus (13 %).

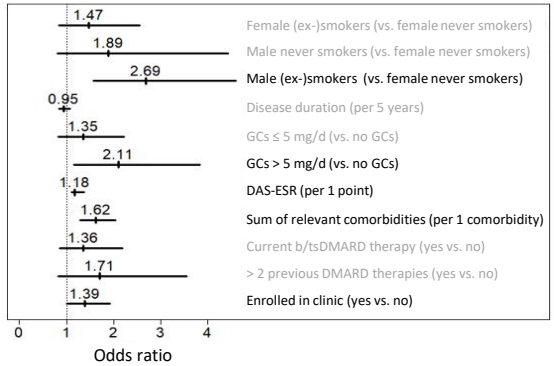
Table 1: Patient characteristics/treatment at last visit prior to OFI onset

	Cases (n=105)	Controls** (n = 523)
Women	58 %	74 %
Age [years], matching criterion	65.4 ± 11.6	65.4 ± 11.4
Disease duration [years]	13.2 ± 10.9	13.7 ± 10.1
Seropositivity	74 %	70 %
Disease activity (DAS28-ESR)	4.1 ± 1.6	3.6 ± 1.5
Oral GC‡	77 %	60 %
GC dose‡ [mg/d]	6.6 ± 4.2	5.7 ± 4.2
GC > 5 mg/d §	39 %	25 %
Current b/tsDMARDs	70 %	58 %
# previous DMARDs	5.1 ± 2.5	4.9 ± 2.7
≥ 1 of the following comorbidities	66 %	36 %
Diabetes mellitus	25 %	14 %
History of malignancy	9 %	6 %
Renal disease	15 %	8 %
Liver disease	8 %	4 %
Lung disease	31 %	13 %
Autoimmune disease (w/o RA)	8 %	6 %
Blood count disorder	8 %	2 %
Hospitalisation, last 12 months	31 %	11 %
Current/former smoking	73 %	59 %

values are given as percentages or mean ± SD; **for 2 cases only 4 controls could be matched each; ‡6 months prior to last follow-up before OFI; § of all patients who received GC

- Cases were less often women, used more often GC, had more current b/tsDMARD therapy, had more relevant comorbidities, were more often (ex-)smokers and more often previously hospitalised than controls (table 1).
- The development of OFI was associated with higher disease activity, daily prednisolone-equivalent dose of > 5 mg, (ex-)smoking among men, a higher number of relevant comorbidities, and type of enrolling institution (figure 1).

Figure 1: Odds ratios (95% confidence intervals) for OFIs



References

[1] PMID: 27032792; [2] PMID: 26395500

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