The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

Risk of Infections in Multiple Myeloma in the Era of Novel Agents, a Population-Based Study Based on 8672 Multiple Myeloma Patients Diagnosed 2008-2021 from the Swedish Myeloma Registry

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Introduction

Despite modern therapies, infections are still a major cause of morbidity and mortality in patients with myeloma (MM). We therefore performed a large population-based study to evaluate the risk of bacterial, viral and fungal infections among 8672 Swedish symptomatic MM patients diagnosed 2008-2021 compared to 34,567 matched controls.

Materials and methods

Symptomatic patients reported to the Swedish Myeloma Registry and four matched controls per patient were analysed with occurrence and date of all infections in the centralized Swedish Patient registry that captures information on individual patient-based discharge diagnosis from inpatient and outpatient care. The Swedish MM patients were followed until death or until 31 st December 2022.

Statistical analysis

Cox proportional hazard models, with the occurrence of infection as a time dependant co-variate and cumulative incidence with competing risk models were used to estimate the risk of infections in MM compared to controls. All models were adjusted for sex, age and year of diagnosis. The effect of gender, age and calendar period of were evaluated separately. Hazard ratio (HR) and confidence intervals (95% CI) were calculated for the risk of different infections. All p-values were two-sided and a value below 0.05 was considered statistically significant. All analyses were performed with R version 4.3.1 and ethics approved.

Results

In this population-based study, 8672 Swedish symptomatic MM patients diagnosed 2008-2021 and 34,567 matched controls were included. The majority of patients (73 %) were 65 years or older at diagnosis, 57% were male, and 30 % treated with up-front autologous stem cell transplantation (auto-SCT). The median time of follow-up was 5 years. Overall, MM patients had a 5-fold (HR=4.73; [95% CI=4.59-4.89]) risk of developing *any* infection compared to matched controls. Bacterial infection had a 4-fold increased risk (HR=4.40; [4.24-4.57]), viral infection 6-fold (HR=6.11; [5.76-6.49]), and fungal infection 6-fold (HR=6.14; [5.56-6.79]) compared to controls.

More specifically, MM patients had an increased risk (p<0.05) of the following bacterial infections compared to controls: meningitis (HR=19.6; [10.0-38.1]), septicaemia (HR=8.05; [7.52-8.62]), pneumonia (HR=7.72; [7.21-8.27]), endocarditis (HR=4.9; [3.70-6.48]), cellulitis (HR=3.13;[2.57-3.80]), osteomyelitis (HR=2.89; [1.95-2.92]), pyelonephritis (HR=2.3; [2.03-2.59]), and for the viral infections influenza (HR=9.40; [8.19-10.8]) and herpes zoster (HR=9.33; [8.19-10.6]) (Table 1). The risk of infections compared to controls was 4 to 5-fold the first year after diagnosis and remained elevated up to 5 years after the myeloma diagnosis. Figure 1 illustrates the cumulative incidence of infections compared to controls over time.

MM patients diagnosed 2018 to 2021 had a slightly lower risk of infection, (HR=0.87 ([0.82-0.93] p< 0.05) compared to patients diagnosed 2008-2012, whilst the risk of infections was slightly higher 2013-2017 compared to the first time period (HR=1.06 ([1.00-1.11], p< 0.05).

The cumulative risk of infection compared to controls remained 5-fold in patients diagnosed 2008-2012 (HR=5.03; [4.78-5.29], p<0.05) and 2013-2017 (HR=4.82; [4.59-5.06], p<0.05), and 4-fold (HR=3.93, [3.66-4.21], p<0.05) in patients diagnosed 2018-2021. Females had a significantly lower risk of infections compared to males (p<0.001). Older age at diagnosis increased the risk of a first infection (p<0.001).

Discussion

This study constitutes the largest population-based study to date on the risk of infections compared to the normal population in the era of modern MM therapies. Infections still represent a major threat to myeloma patients, with an equally about five-fold increased risk for bacterial, viral and fungal infections during the first year and up to 5 years after the myeloma diagnosis, even in more recent years.

Table 1. Relative risk of selected infections after diagnosis of myeloma compared to matched controls

Disease	Myeloma (N=8,672)	Controls (N=34,567)	HR (95%CI)	
All infections	11,025	17,430	4.73 (4.59-4.89)	p<0.001
Bacterial infections	6,510	10,550	4.40 (4.24-4.57)	p<0.001
Pneumonia	1,911	1,677	7.72 (7.21-8.27)	p<0.001
Osteomyelitis	136	340	2.39 (1.95-2.92)	p<0.001
Septicaemia	2,063	1,571	8.05 (7.52-8.62)	p<0.001
Pyelonephritis	1,054	382	2.29 (2.03-2.59)	p<0.001
Cellulitis	170	297	3.13 (2.57-3.80)	p<0.001
Meningitis	42	11	19.6 (10.0-38.1)	p<0.001
Endocarditis	93	116	4.90 (3.70-6.48)	p<0.001
Viral infections	2,483	2,616	6.11 (5.76-6.49)	p<0.001
CMV	88	14	31.8 (17.6-57.2)	p<0.001
EBV	10	11	5.73 (2.61-12.6)	p<0.001
Influenza	486	333	9.40 (8.19-10.8)	p<0.001
Herpes Zoster	574	376	9.33 (8.19-10.6)	p<0.001
Covid 19	271	651	2.46 (2.12-2.85)	p<0.001
Herpes Simplex	189	208	5.20 (4.28-6.31)	p<0.001
Fungal infections	870	931	5.44 (4.95-5.97)	p<0.001
All infections 1st year	4,510	3,065	3.81 (3.63-3.99)	p<0.001
All bacterial infections 1st year	2,753	1,786	3.66 (3.45-3.89)	p<0.001
All viral infections 1st year	782	412	4.14 (3.67-4.67)	p<0.001
All fungal infections 1st year	379	168	5.15 (4.29-6.19)	p<0.001

Figure 1 Cumulative incidence of infections over time with death as competing risk in myeloma patients and their matched controls.
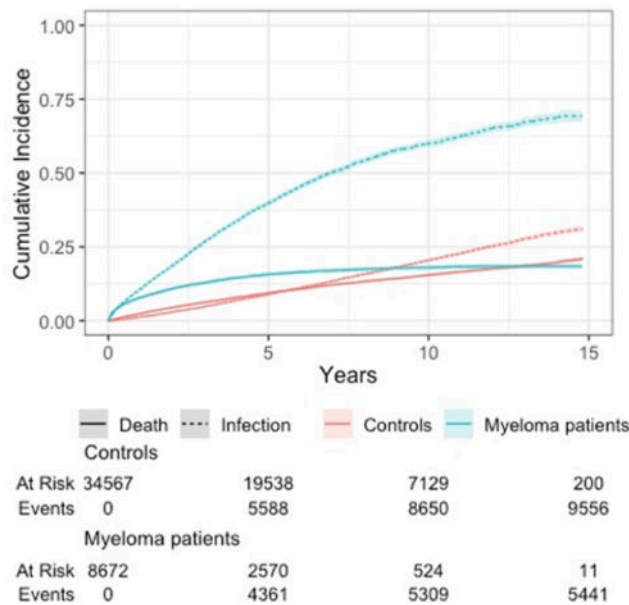

Controls				
At Risk	34567	19538	7129	200
Events	0	5588	8650	9556
Myeloma patients				
At Risk	8672	2570	524	11
Events	0	4361	5309	5441

Figure 1

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