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Multiple myeloma and infections: a population-based study on 9253 multiple myeloma patients

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ABSTRACT

Infections are a major cause of morbidity and mortality in patients with multiple myeloma. To estimate the risk of bacterial and viral infections in multiple myeloma patients, we used population-based data from Sweden to identify all multiple myeloma patients (n=9253) diagnosed from 1988 to 2004 with follow up to 2007 and 34,931 matched controls. Cox proportional hazard models were used to estimate the risk of infections. Overall, multiple myeloma patients had a 7-fold (hazard ratio =7.1; 95% confidence interval = 6.8-7.4) risk of developing any infection compared to matched controls. The increased risk of developing a bacterial infection was 7-fold (7.1; 6.8-7.4), and for viral infections 10-fold (10.0; 8.9-11.4). Multiple myeloma patients diagnosed in the more recent calendar periods had significantly higher risk of infections compared to controls (P<0.001). At one year of follow up, infection was the underlying cause in 22% of deaths in multiple myeloma patients. Mortality due to infections remained constant during the study period. Our findings confirm that infections represent a major threat to multiple myeloma patients. The effect on infectious complications due to novel drugs introduced in the treatment of multiple myeloma needs to be established and trials on prophylactic measures are needed.

Introduction

New treatments options introduced during recent decades have improved the survival of multiple myeloma (MM) patients.[1-3] Managing the complications of the disease and its treatment, such as infections, thrombosis and neuropathy, has become more important as MM patients survive longer.[4]

Infections are a significant cause of morbidity and a leading cause of death in MM patients.[5,6] In a study of over 3000 MM patients, Augustson and co-workers observed that 45% of early deaths (within 6 months) were due to infections.[7] MM-related immunodeficiency involves B-cell dysfunction, such as hypogammaglobulinemia, as well as T-cell, dendritic cell, and NK-cell abnormalities.[8] Recent studies have showed an increased risk of infections in patients with monoclonal gammopathy of undetermined significance (MGUS), highlighting the contribution of the underlying plasma cell disorder to the immunodeficiency.[9,10] It has also been shown that multiple myeloma patients display a low immune response to infections and vaccines, and that it also predicted a higher risk of infection.[11,12]

In addition to the inherent immunodeficiency, some small studies have described a changing spectrum of infections in MM, possibly related to the more intensive treatment approach of recent years, suggesting that the novel agents may increase the risk of infections in MM patients.[13-16] Several studies have indicated that elderly MM patients in particular are highly susceptible to infections.[17]

To our knowledge, no population-based study has previously been performed to evaluate the risk of infections and infection-related mortality in MM patients. Therefore, we performed a nationwide study in Sweden to establish the risk of infections overall and of specific infections in MM patients, as well as the risk of infection-related death, compared to matched controls. We also investigated whether the changes in treatment strategies in MM over three different time periods has affected the risk of infections and infection-related deaths.

Methods

Patients and control subjects

In Sweden, patients with MM are typically diagnosed and followed clinically by physicians at hospital-based hematology centers. Since 1958, all physicians and pathologists/cytologists in Sweden are obliged by law to report each case of incident cancer to the nationwide Swedish Cancer Register. In a recent validation study, the completeness and diagnostic accuracy of the Register was found to be very high (93%) for MM patients.[18] All MM patients reported to the nationwide Swedish Cancer Registry from 1988 to 2004 were included in the study. For all included patients, we obtained information on sex, date of birth, date of diagnosis, and the region/hospital where the diagnosis was made. For each MM patient, 4 population-based control subjects matched by sex, year of birth, and county of residence were chosen randomly from the Swedish Total Population Register. The control subjects had to be alive and without previous hematologic malignancy at the date of diagnosis of the corresponding MM patient.

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The Swedish Patient Registry captures information on individual patient-based discharge diagnosis from inpatient (since 1964, and with very high coverage since 1987) and outpatient (since 2000) care with high coverage and accuracy.[19] We obtained information from the Registry on occurrence and date of infections, with follow up to 2007. We used the seventh, eighth, ninth, and tenth revisions of the International Classification of Diseases (ICD) to code the specific infectious conditions.

Using the nationwide Cause of Death registry, we obtained information on date and cause of death for all subjects (MM patients and controls) who had died up to December 31, 2007. Approval was obtained from the Stockholm Ethical Review Board for this study. Informed consent was waived because we had no contact with study subjects.

Treatment strategies in multiple myeloma in Sweden

There have been major improvements in the management of multiple myeloma during the study period. In our previous studies,[3,20] we collected detailed information on the number of MM patients receiving high-dose melphalan with autologous stem cell transplantation (HDM-ASCT) and prescription of MM drugs in Sweden for different time periods were registered. Taken together, during the period of 1988-1993, most patients were treated with alkylating agents and steroids. After 1995, HDM-ASCT was recommended for all patients under 60-65 years of age. In further support of this, in studies from the Nordic Myeloma Study Group (NMSG), between 65% and 75% of all eligible patients below 60-66 years were included in studies involving HDM-ASCT in 1994-2003.[21-23] In addition, in the Swedish Myeloma registry, recording population-based and clinical data from 2008, 81% of patients 65 years of age and under and 4% of patients over 65 years of age had undergone HDM-ASCT.[24] The novel agents, primarily thalidomide, were used predominantly in Sweden after the year 2000. For elderly patients, the most common first-line treatment was MP until 2002, when NMSG introduced MP plus thalidomide in a randomized study.[25] Bortezomib was approved in Sweden in the year 2004.

Statistical analysis

Cox proportional hazard models were used to evaluate the overall and one-year risk of infections in MM patients compared to controls. In addition, the effect of sex, age and calendar period of diagnosis was evaluated. Hazard ratios (HR) and confidence intervals (CI) were calculated for the difference in occurrence of infections in patients and controls. Cumulative incidence at different time periods was calculated as a measure of absolute risk of viral and bacterial infections. We studied MM patients and their controls in the time period of 1988-2004. Follow up started at date of diagnosis of MM (date of MM diagnosis of the corresponding case for controls) and no earlier than January 1, 1988. Censoring events were death, emigration, or the end of acquisition period (December 31, 2007). An event was defined as the diagnosis of a first specific infectious disorder. Median time of follow up was calculated from the date of MM diagnosis (and selection for controls) to the date of censoring.

To evaluate the cumulative risk of infections over time and the risk of infection-related death, we also used a competing risk model. In these analyses, the censoring events were emigration or the end of acquisition period. The competing events were defined as death with diagnosis of an infectious disorder and death without diagnosis of an infectious disorder.

To assess the role of novel MM therapies in relation to the development of infections, patients were stratified to three calendar periods: 1988-1993, 1994-1999 and 2000-2004, reflecting time periods with different treatment strategies. This was also performed separately for age groups under and over 65 years of age at diagnosis. All calculations were performed using Stata v.12 (Stat corp. 2012 Stata Statistical Software; Collage Station, TX, USA).

Results

A total of 9253 MM patients, diagnosed between 1988 and 2004, identified from the Swedish Cancer registry and 34,931 population-based controls were included in the analyses (Table 1). Median age at MM diagnosis was 72 years. The median time of follow up was 2.6 years for MM patients and 7.4 years for controls. The relative 3-year survival of MM patients for the calendar periods 1988-1993, 1994-1999, and 2000-2004 was 42.3%, 45.4%, and 47.3%, respectively.

The majority of infections were bacterial: 87% in MM patients and 85% in controls.

Overall, multiple myeloma patients had a significant 7-fold (HR=7.1; 95%CI: 6.8-7.4) increased risk of developing any infection compared to matched controls. The risk of developing a bacterial infection in MM patients was 7-fold (HR=7.1; 95%CI: 6.8-7.4), and during the first year following diagnosis the risk was 11-fold (HR=11.5; 95%CI: 10.4-12.7) compared to controls. The overall risk for viral infections was 10-fold (HR=10.0; 95%CI: 8.9-11.4) higher and during the first year 18-fold (HR=17.6; 95%CI: 13.1-23.8) higher compared to controls (Table 2).

Specifically, MM patients had an increased risk (P<0.05) of the following bacterial infections compared to matched controls: meningitis (HR=16.6; 95%CI: 10.2-27.1), septicemia (HR=15.6; 95%CI: 14.3-17.1), pneumonia (HR=7.7; 95%CI: 7.2-8.1), endocarditis (HR=5.3; 95%CI: 3.4-8.1), osteomyelitis (HR=3.5; 95%CI: 2.4-5.2), cellulitis (HR=3.0; 95%CI: 2.5-3.6), and pyelonephritis (HR=2.9; 95%CI: 2.4-3.5). Multiple myeloma patients had a significantly increased risk of the viral infections [herpes zoster (HR=14.8; 95%CI: 12.1-18.2) and influenza (HR=6.1; 95%CI: 4.9-7.6)] compared to matched controls. The risk of all included infections was highest during the first year following MM diagnosis (Table 2).

The elevated risk of infections in MM patients compared to controls increased significantly with calendar period (P<0.001) and was 6-fold higher (HR=5.7; 95%CI: 5.2-6.1) in the period between 1988 and 1993, 7-fold higher (HR=7.0; 95%CI: 6.6-7.5) in the period from 1994 to 1999, and 9-fold higher (HR=8.9; 95%CI: 8.3-9.7) in 2000-2004 (Table 3 and Figure 1). Compared to patients diagnosed during the period 1988-1993, MM patients diagnosed during the time periods 1994-1999 and 2000-2004 had a significantly higher risk of infections, HR=2.1 (95%CI: 1.9-2.4) and HR=2.9 (95%CI: 2.5-3.2), respectively (P-value for trend <0.001).

Increasing age was significantly associated with a higher risk of infections [HR=1.02 (per 1 year increment); 95%CI: 1.01-1.02; P<0.001]. The increase in risk of infections in MM patients compared to controls was statistically significant during the first and five years after diagnosis. This was observed in stratified analyses based on patients diagnosed both under and over the age of 65 years (Table 4). The absolute risk of an infection expressed in cumulative incidence at five years for all MM patients was 19.4% in the years 1988-1993, 40.6% in 1994-1999, and 49.5% in 2000-2004 (Table 4). The 5-year cumulative risk of a bacterial infection in the same time periods was 14.4%, 35.8%, and 46.0%, respectively, for MM patients and

4.5%, 9.4%, and 10.4% for controls. For viral infections, the 5-year cumulative incidence in the same time periods was 4.8%, 6.3%, and 6.2% for MM patients and 0.8%, 0.9%, and 0.7% for controls (*Online Supplementary Appendix, Online Supplementary Table S1, and Figures S1 and S2*).

Females with MM had a significantly lower risk of infections compared to males (HR=0.8; 95%CI: 0.7-0.9; *P*<0.001) one year after diagnosis. For controls, the excess risk was essentially the same (HR =0.8; 95%CI: 0.6-0.9; *P*<0.001).

In a competing risk model, the 5-year cumulative risk of infections overall and specific infections was essentially the same as in the Cox regression analyses (*data not shown*).

Infection-related deaths

A total of 916 (9.9%) patients died within two months of diagnosis and 204 (22.2%) of these deaths were infection-related. The corresponding numbers at one year were 2474 (26.7%) and 555 (22.4%), respectively (Table 5).

There was no difference in infection-related deaths over time (Figure 2) computed with the competing risk model. The 3-year risk of death in infections in MM patients was 12.2% and the corresponding number for matched controls was 2.2%. There was no change in risk of infection-related deaths according to age group (>65 and ≤65 years of age) over the three calendar periods (Figure 3).

Table 1. Characteristics of patients with myeloma, and their matched controls.

	Myeloma patients	Matched controls
Total, n (%)	9253 (100)	34,931 (100)
Sex, n (%)		
Male	4984 (53.9)	18,810 (53.9)
Female	4269 (46.1)	16,121 (46.1)
Age at dx, median (range)	72 (25-101)	72 (25-101)
Age group, n (%)		
Less than 40	77 (0.8)	299 (0.9)
40-49	381 (4.1)	1460 (4.2)
50-59	1062 (11.5)	4173 (12.0)
60-69	2169 (23.4)	8382 (24.0)
70-79	3423 (37.0)	12,917 (37.0)
80 and above	2141 (23.1)	7700 (22.0)
Year of diagnosis		
1988-1993	3247 (35.1)	12,214 (35.0)
1994-1999	3259 (35.2)	12,321 (35.3)
2000-2004	2747 (29.7)	10,396 (29.7)

Table 2. Relative risk of selected infections after diagnosis of myeloma compared to matched controls.

Disease	Total			One-year follow up		
	Myeloma (n=9 253)	Controls (n=34 931)	HR* (95%CI)	Myeloma	Controls	HR (95%CI)
Any infection (combined)**	3781	6519	7.1 (6.8-7.4)	1626	672	11.6 (10.6-12.7)
Specific infections						
Bacterial***	3361	5792	7.1 (6.8-7.4)	1388	574	11.5 (10.4-12.7)
Pneumonia	2150	3504	7.7 (7.2-8.1)	770	279	12.7 (11.1-14.6)
Osteomyelitis	37	100	3.5 (2.4-5.2)	19	12	6.9 (3.4-14.3)
Septicemia	1336	960	15.6 (14.3-17.1)	464	69	29.9 (23.2-38.6)
Pyelonephritis	152	570	2.9 (2.4-3.5)	50	51	4.3 (2.9-6.4)
Cellulitis	164	564	3.0 (2.5-3.6)	47	58	3.7 (2.5-5.4)
Meningitis	51	28	16.6 (10.2-27.1)	12	3	17.3 (4.9-61.3)
Endocarditis	35	73	5.3 (3.4-8.1)	12	6	8.7 (3.3-23.1)
Viral****	607	556	10.0 (8.9-11.4)	215	54	17.6 (13.1-23.8)
Influenza	150	245	6.1 (4.9-7.6)	52	22	10.5 (6.4-17.3)
Herpes zoster	282	171	14.8 (12.1-18.2)	92	16	25.8 (15.2-43.8)

*HR: hazard ratio, CI: confidence interval. *Cox proportional hazard models were used to compare total and one-year risks of infection in myeloma patients compared to controls. Adjusted (by sex, age at diagnosis and year of diagnosis) HRs and 95%CIs were estimated. **Pneumonia, osteomyelitis, septicemia, pyelonephritis, cellulitis, meningitis, endocarditis, cystitis, CMVEBV, empyema, encephalitis, gonorrhea, hepatitis A-C, HSV, herpes zoster, HIV, intestinal infections, Lyme disease, malaria, mononucleosis, myocarditis, otitis, pharyngitis/nasopharyngitis, pericarditis, sinusitis, syphilis, tonsillitis, tuberculosis. ***Pneumonia, cellulitis, cystitis, empyema, endocarditis, gonorrhea, meningitis, osteomyelitis, otitis, pharyngitis/nasopharyngitis, pyelonephritis, septicemia, sinusitis, syphilis, tonsillitis and tuberculosis. ****HIV, HSV, herpes zoster, hepatitis (A-C), CMV, EBV, mononucleosis, encephalitis, pericarditis, myocarditis and influenza.*

Discussion

In this large population-based study based of over 9000 MM patients diagnosed in the period 1988-2004 with follow up to 2007, and almost 35,000 controls, we show that the risk of infections and infection-related death is significantly increased in MM patients compared to controls. The increase in cumulative incidence was consistently elevated in comparison to controls in all years analyzed, but highest during the first year following diagnosis. We found that the risk of infections has increased in recent years. Our results are coherent with previous smaller studies that have suggested that infections occur more often in the first six months following diagnosis.[7,8,26,27]

Our finding that the risk of infections has increased in the last decades is particularly interesting, and raises the question whether modern MM therapy increases the risk of infections. In the present study, the increase in risk of infections was observed in both young and elderly MM patients and can thus not solely be explained by HDM-ASCT. The increase in infections was, however, more pronounced in younger patients and based on data from the Swedish Myeloma Registry; younger patients are exposed to a larger extent to newer drugs and HDM-ASCT.[24] We, therefore, argue that the introduction of HDM-ASCT and novel agents both contribute to the increase in infections observed in our study. It has previously been suggested, that the novel agents, probably through their effect on the immune system, make MM patients more susceptible to infections.[13-16] Afessa *et al.* found a new pattern of bacterial and fungal infections in autologous and allogeneic stem cell recipients.[14] Offidani *et al.* reported that 42% of thalidomide-treated patients developed infections, of which 19% were severe.[13] In the APEX-study, Chanan-Khan *et al.* described an increasing incidence of herpes zoster in bortezomib-treated patients.[15] Our results are important as they suggest that the more intensive treatment given to MM patients, which has undoubtedly contributed to major improvements in survival in these patients, probably contributes to an increased susceptibility to infections that needs to be studied in more detail.

We found that the risk of both bacterial and viral infections was seven times higher in patients with MM compared to matched controls, and that the risk of specific bacterial infections such as pneumonia and septicemia, as well as viral infections like herpes zoster and influenza, is particularly high in MM patients compared to matched

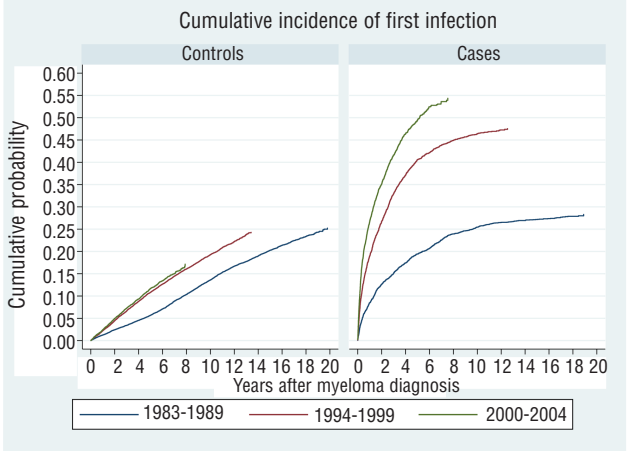


Figure 1. Cumulative incidence of first infection over time in myeloma patients and their matched controls.

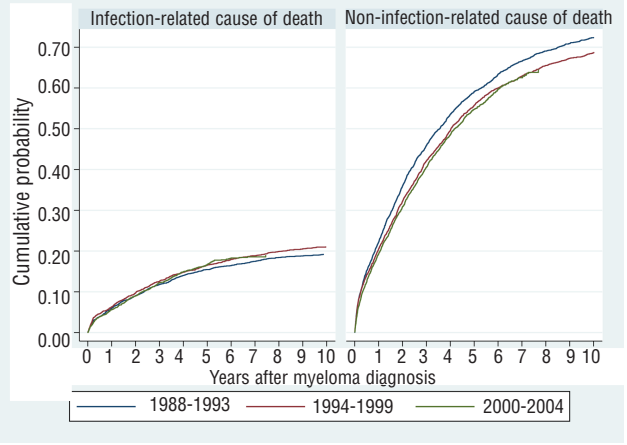
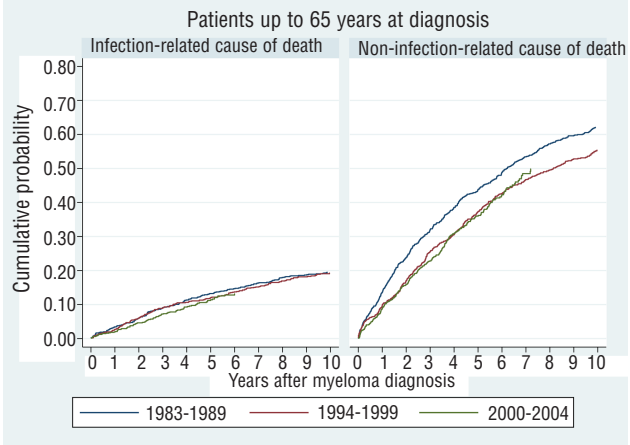


Figure 2. The cumulative probability of an infection-related death in all patients computed by competing risk analyses.



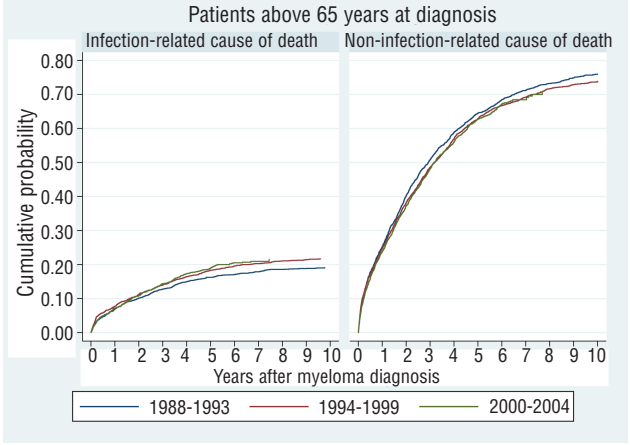


Figure 3. The cumulative probability of an infection-related death in patients up to and over 65 years of age at diagnosis, computed with competing risk analyses.

controls. This is in accordance with earlier reports, confirming the susceptibility to infections in MM.[28-30] We also analyzed viral and bacterial infections in different time cohorts, and the most significant increase in viral infections was observed between the first and the two latter time periods. No corresponding increase was seen among controls. There was a continuous increase in the risk of bacterial infections over time. In MM patients and matched controls, a 20% lower risk of infections in women compared to men the first year after diagnosis was observed. This is in good agreement with population-based data on elderly patients with community-acquired respiratory tract infections in the UK.[31]

We found that the risk of dying due to infection was 22% both at two months and one year following diagnosis. This is in contrast to the study from The Medical Research Council (MRC), which showed that nearly 50% of deaths within two months were infection-related.[7] Despite these differences, both studies stress the importance of this complication in the management of MM patients. One important observation in our study is that while the risk of infections increased with calendar period, the risk of infection-related death remained the same during the whole study period; this may be explained by the better supportive care currently available. The standard of care regarding infection prophylaxis during the study period in Sweden was mainly influenza vaccine to elderly individuals (over 65 years of age). In 2001, the authorities extended their recommendations to all cancer patients receiving chemotherapy. Prophylactic strategies specific for MM patients mainly included patients undergoing HDM-ASCT, who were recommended to receive *pneumocystis jirovecii* prophylaxis, usually with trimethoprim-sulfamethoxazole, and varicella zoster prophylaxis with acyclovir during induction and one year after treatment. In Nordic countries, in patients receiving thalidomide treatment, no specific infection prophylaxis was (or is) recommended. Most elderly MM patients were not recommended to receive any specific prophylaxis at all in the study period, and immunoglobulins were routinely only given to patients with three or more severe infections per season and a co-existing hypogammaglobulinemia. Some effort has been made in testing prophylactic antibiotic treatment during the two first months. Vesole *et al*. performed a randomized clinical trial including 212 MM patients and found no decrease in serious bacterial infections when comparing patients receiving ciprofloxacin, trimethoprim-sulfamethoxazole, or observation only.[32] Their study did not include patients treated with novel agents and analyzed only infections during the first two months, and thus only included the pre-ASCT period. Furthermore, the role of prophylactic immunoglobulin needs to be established, as the rationale for its use is mainly based on one randomized trial in MM plateau phase.[29] It is possible that MM patients would benefit from a more aggressive surveillance, prophylaxis, and treatment of infections. This might lead to a further improvement in the survival of these patients. However, these issues need to be addressed in randomized clinical trials.

Our study has several strengths, including the large sam-

Table 3. Risk of infection in myeloma patients compared to controls by calendar periods, and internal comparison by calendar period.

	1988-1993 n=3247	1994-1999 n=3259	2000-2004 n=2747
HR*	5.7	7.0	8.9
(95% CI)	(5.2-6.1)	(6.6 -7.5)	(8.3 -9.7)
HR**	1.0	2.1	2.8
(95% CI)	(Reference)	(1.9-2.4)	(2.5-3.2)
>65 years at diagnosis			
HR***	1.0	2.0	2.6
(95% CI)	(Reference)	(1.8 -2.3)	(2.3 -3.0)

**Risk of infections in all patients and controls. **Risk of infections in all patients, internal comparison by calendar periods. ***Risk of infections in patients/controls over 65 years of age, internal comparison by calendar periods.*

Table 4. The probability of a first infection during the first and five years after diagnosis/selection stratified by age at diagnosis and calendar period.

Calendar period	Myeloma % (95%CI)	Controls % (95%CI)	Ratio (pt/control)
Total first year			
1988-1993	8.5 (7.5-9.5)	1.2 (1.0-1.4)	7.1
1994-1999	19.0 (17.6-20.3)	2.1 (1.9-2.4)	9.0
2000-2004	26.7 (25.0-28.3)	2.3 (2.0-2.6)	11.6
> 65 years			
1988-1993	8.6 (7.5-9.7)	1.5 (1.3-1.8)	5.8
1994-1999	17.7 (16.2-19.3)	2.8 (2.4-3.1)	6.4
2000-2004	24.8 (22.8-26.7)	3.2 (2.9-3.7)	7.7
≤ 65 years			
1988-1993	8.2 (6.4-10.12)	0.6 (0.4-0.9)	14.2
1994-1999	22.2 (19.6-24.9)	0.8 (0.5-1.1)	24.5
2000-2004	31.2 (28.1-34.4)	0.5 (0.3-0.8)	65.4
Total five years			
1988-1993	19.4 (18.1-20.8)	5.7 (5.3-6.1)	3.4
1994-1999	40.6 (38.9-42.3)	10.8 (10.3-11.4)	3.8
2000-2004	49.5 (47.5-51.4)	11.7 (11.0-12.3)	4.2
> 65 years			
1988-1993	17.7 (16.2-19.3)	6.9 (6.4-7.4)	2.6
1994-1999	37.5 (35.5-39.4)	13.6 (12.9-14.4)	2.8
2000-2004	46.7 (44.4-49.0)	15.1 (14.3-16.0)	3.1
≤ 65 years			
1988-1993	24.3 (21.5-27.3)	2.4 (1.9-3.0)	10.1
1994-1999	48.6 (45.3-51.8)	4.0 (3.4-4.7)	12.1
2000-2004	56.1 (52.5-59.5)	3.6 (3.0-4.3)	15.6

Table 5. Infection-related and non-infection-related death at two months and one year after diagnosis.

	Myeloma (n=9253)	Controls (n=34931)
Diseased at 2 months	916	257
(% of all)	(9.9)	(0.74)
Infection-related death	204	52
(% of diseased)	(22.2)	(20.0)
Non-infection –related death	712	205
(% of diseased)	(77.7)	(80.0)
Diseased at 1 year	2474	1554
(% of all)	(26.7)	(4.4)
Infection-related death	555	275
(% of diseased)	(22.4)	(17.7)
Non-infection-related death	1919	1279
(% of diseased)	(77.6)	(82.3)

ple size and the use of population-based high-quality data from Sweden. The study included a stable population with access to standardized health care during the entire study period. By using the nationwide register-based design, we were able to rule out recall bias and ensure our findings could be generalized. As mentioned above, in a recent validation study, we have reported that ascertainment and diagnostic accuracy for lymphoproliferative disorders (including multiple myeloma) is very high (>90-95%) in Sweden.[18] The fact that 3-year relative survival has increased by approximately 2% between the last two calendar periods is unlikely to explain the increase in infections observed, and thus we believe that improved survival is not a bias in our study. We analyzed the risk of infection using both absolute and relative risk in relation to controls and the results are essentially the same. In addition, we used two different sources to estimate infection, both the Patient Registry and the Cause of Death Registry.

Our study has some limitations. For the MM cohort, we lack detailed clinical and treatment data on individuals; however, as outlined above, our interpretations are based on homogenous treatment traditions in Sweden.[3,20-25] The infections diagnosis was based on the discharge diagnosis and not on laboratory data proving the infectious agents. We chose to record only the first infection of each type and not to count infection in the same organ twice in the same individual, and as a result we do not include all infections in all patients, as some patients are diagnosed with the same infection more than once. We adopted this approach to obtain a more accurate measure of the excess risk of each infection. We considered this to be better than eventually over-estimating the risk for all MM patients due to a few subjects with repeated infections. In large hospital registries, there is a risk of registration bias. Lack of data from the outpatient registry before the year 2000 is also a limitation. For MM patients, the surveillance of infections is probably more vigilant than in the general population and might lead to more reported infections of all kinds in the MM cohort. However, most of the infections recorded, and later showing increased risks, were severe infections that would be captured in the general population as well, as they generally require hospitalization. There may also be a certain degree of under-reporting where in MM patients only the MM diagnosis is registered on the discharge list and not the infections. The same might occur when obtaining the cause of death for an MM patient in the Cause of Death registry, causing fewer infections to be reported in the registries.

In summary, in this large population-based study from Sweden we found bacterial and viral infections represent a major threat to MM patients. We found risk of specific infections, like pneumonia and septicemia, to be over 10-fold higher than for controls in the first year after MM diagnosis, and the risk of infections has been increasing in recent years. The risk of dying from an infection is significantly elevated for an MM patient compared to age-matched controls. With the introduction of the novel therapies, survival of MM patients has improved. However, the effect of these drugs on the risk of infection remains to be established and new trials on prophylactic measures are needed.

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Authorship and Disclosures

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