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SARS-CoV-2 infection in patients with multiple myeloma: survey in 23 centers across Europe and USA

Dominik Dytfeld[1*], Jakub Radocha[2], Roman Hajek[3], Guldane Cengiz-Seval[4], Meral Berkac[4], Daniel Coriu[5], Benjamin Derman[6], Andrzej Jakubowiak[6], Valdas Peceliunas[7], Gabor Mikala[8], Łukasz Bołkun[9], Dorota Hawrylecka[10], Sebastian Grosicki[11], Agata Tyczyńska[12], Jan Maciej Zaucha[12], Wanda Knopińska[13], Grażyna Semeńczuk[14], Marta Morawska[15, 16], Krzysztof Giannopoulos[15, 16], Anna Puła[17], Marcin Rymko[18], Grzegorz Charliński[19], Agnieszka Szeremet[20], Elżbieta Kalicińska[20], Lidia Usnarska[20], Tomasz Wróbel[20], Krzysztof Jamroziak[21], Agnieszka Druzd-Sitek[22], Joanna Romejko-Jarosińska[22], Waldemar Sawicki[23], Anna Waszczuk-Gajda[21], Adrian Juda[24], Marek Hus[24], Lidia Gil[1]

[1]Department of Hematology and Bone Marrow Transplantation, Poznan University of Medical Sciences, Poznań, Poland
[2]4th Department of Internal Medicine — Hematology, University Hospital Hradec Kralove, Charles University Faculty of Medicine in Hradec Kralove, Hradec Králové, Czechia
[3]University of Ostrava, Ostrava, Czechia
[4]Ankara University, Ankara, Turkey
[5]Department of Hematology and Bone Marrow Transplantation, Fundeni Clinical Institute, Bucharest, Romania
[6]University of Chicago, Chicago, USA
[7]Vilnius University Hospital, Vilnius, Lithuania
[8]Division of Hematology and Stem Cell Transplantation in Budapest, Budapest, Hungary
[9]Medical University of Bialystok, Białystok, Poland
[10]Department of Oncological Hematology in Brzozow, Brzozów, Poland
[11]Medical University of Silesia, Katowice, Poland
[12]Medical University of Gdansk, Gdańsk, Poland
[13]City Hospital in Gdynia, Gdynia, Poland
[14]10th Military Clinical Hospital, Bydgoszcz, Poland
[15]Experimental Hematooncology Department, Medical University of Lublin, Lublin, Poland
[16]Hematology Department, St. John's Cancer Center, Lublin, Poland
[17]University of Medical Sciences in Lodz, Łódź, Poland
[18]Ludwig Rydygier Provincial Integrated Hospital in Torun, Toruń, Poland
[19]Department of Hematology and Bone Marrow Transplantation, City Hospital in Torun, Toruń, Poland
[20]Wroclaw Medical University, Wrocław, Poland
[21]Warsaw University of Medical Sciences, Warsaw, Poland
[22]Department of Lymphoid Malignancies, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland
[23]Military Institute of Medicine in Warsaw, Warsaw, Poland
[24]University of Medical Sciences in Lublin, Lublin, Poland

*Address for correspondence: Dominik Dytfeld, Department of Hematology and Bone Marrow Transplantation, Poznan University of Medical Sciences, Szamarzewskiego 84, 60–569 Poznań, Poland, e-mail: dytfeld@me.com

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Abstract

Introduction: Despite several studies, the impact of coronavirus disease 2019 on patients with multiple myeloma remains uncertain.

Material and methods: We performed a survey that covered the period of the first and second waves of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic in 23 centers inseven countries. Out of 352 patients with myeloma and SARS-CoV-2, 23% died.

Results/Conclusions: Logistic regression showed a lower risk of death among patients treated with proteasome inhibitor and a higher risk of death for those who had a severe or a very severe course of disease.

Key words: myeloma, COVID-19

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Introduction

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an ongoing global health emergency. The case fatality rate (CFR), calculated by the ratio of deaths divided by the number of documented infections in the whole population, varies according to the method of calculation, the time and the country. Reported figures as of 17 September 2020 were: 12.2% in Italy, 4.9% in Spain, 3.0% in Brazil, and 3.0% in the USA. Just two months later on 12 November, 2020, these numbers had converged, with the CFR for each being 4.9%, 2.8%, 2.9%, and 2.3%, respectively [1]. Patients with cancer are purported to have poor COVID-19 outcomes, with a mortality rate approaching 50% [2]. However, the effect of infection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on patients with multiple myeloma remains uncertain. Thus, we performed a survey among 23 centers in Poland, USA, Hungary, Czechia, Turkey, Lithuania, and Romania with an estimated population of 5,780 myeloma patients to determine the epidemiology and the risk of severe COVID-19 in patients with multiple myeloma.

Material and methods

This study was a retrospective analysis performed according to the Declaration of Helsinki with the approval of the Ethics Committee at Poznan University of Medical Sciences in Poznan, Poland. Patient data was reported anonymously based on a unified questionnaire. The survey covered the period of the first and second waves of the pandemic between March 2020 and March 2021.

Results

We recorded data on 352 patients with myeloma and SARS-CoV-2 infection confirmed by polymerase chain reaction (PCR). Taking into account the population of myeloma patients in participating centers, the incidence rate was 6.1%. Among all patients (median age 67 years) 36% had newly diagnosed myeloma with the remainder having relapsed or refractory disease. The majority of patients were actively receiving chemotherapy: 20% a proteasome inhibitor (PI), 24% an immunomodulatory drug (IMID), 29% a combination of PI and IMID, 14.5% a chemotherapy containing the monoclonal antibody, and 6% other drugs (stem cell transplantation, selinexor, melflufen, melphalan). Only 6% of patients were not receiving any treatment. 24.4% of patients were in complete response (CR) or stringent complete response (sCR), 19% were in a very good partial response (VGPR), 21% were in a partial response (PR), and 20% had either stable (SD) or progressive disease (PD). The status of the disease was unknown for 14% of the analyzed subjects. A large majority of patients (69%) had at least one comorbidity, and this percentage was higher among the subpopulation of patients who eventually died. A summary of patient characteristics with a description of the subpopulation of patients who died is set out in Table I.

Mild or moderate infection was observed in 58% of cases, and in 18% the disease was considered to be severe or very severe with the necessity of hospitalization in anintensive care unit (ICU). 42 patients were intubated. Among them, only four survived. Four patients hospitalized in the ICU were not intubated but died, leading to a CFR of hospitalized patients in the ICU of 66% and 95% for patients who were ventilated. Out of all 352 analyzed patients with myeloma and SARS-CoV-2 infection, 80 died (CFR 23%).

Linear regression showed that patients with lower disease control (less than CR/sCR or VGPR) had a higher risk of death [hazard ratio (HR) 3.3, 95% CI: 1.7–6.1], while in patients treated with regimens containing a proteasome inhibitor (HR 0.3; 95% CI: 0.09–0.8) the risk of death was lower compared to other treatments. The risk of death was also higher for those who were hospitalized in an ICU (HR 9.3; 95% CI: 4.9–17.6), and those who were on a respirator

Table I. Patient characteristics

Parameter	Whole group (n = 352)	Patients who died (n = 80)
Activity of myeloma		
sCR + CR/VGPR/PR/SD + PD/unknown	25%/19%/21%/21%/14%	12%/ 14%/15%/39%/20%
Status of disease		
NDMM/RRMM	36%/74%	30%/50%
Treatment		
PI/IMMID/PI + IMMID/MoAb/other/no treatment	20%/24%/29%/14.5%/6%/6%	31%/24%/15%/21%/6%/2.5%
Comorbidities		
None/HA or CHD/DM/KF/COPD/more than one	31%/30%/3.5%/8%/5%/18%	11%/17.5%/27.5%/7.5%/24%/12.5%
Age		
<65 years of age/>65 years of age	25%/75%	25%/75%

sCR — stringent complete response; CR — complete response; VGPR — very good partial response; PR — partial response; SD — stable disease; PD — progressive disease; NDMM — newly diagnosed multiple myeloma; RRMM — relapsed and refractory multiple myeloma; PI — proteasome inhibitor; IMMID — immunomodulatory drug; MoAb — monoclonal antibody; HA — hypertension; CHD — coronary heart disease; DM — diabetes mellitus; KF — kidney failure; COPD — chronic obstructive pulmonary disease

or who had a severe course of disease (G3 and G4) (HR 3.2; 95% CI: 1.4–7.0 for G3 and 16.8; 95% CI: 6.2–45.6 for G4). Logistic regression confirmed a lower risk of death among patients treated with PI [odds ratio (OR) 0.12; 95% CI: 0.02–0.70] and a higher risk of death for those who had a severe (OR 10.14, 95% CI: 11.66–62.04) or a very severe course of disease (OR 17.37; 95% CI: 3.61–83.55).

Specific treatments for SARS-CoV-2 were reported for only 42 patients (12%). These treatments consisted of differing combinations of remdesivir, tocilizumab, dexamethasone and convalescent plasma. Only one patient was vaccinated, who was infected and developed mild symptoms of COVID-19 not requiring hospitalization. Out of those who were treated against SARS-CoV-2, there were four deaths. Due to the low number of reported treatments and variabilities, no conclusions on the impact of antiviral therapy in myeloma patients can be made.

Discussion

Although our study was conducted in conditions without the existence of a vaccine against SARS-CoV-2, and although the virulence of the virus is now lower, our observations remain relevant. Similar retrospective analyses have indicated a relatively similar range of mortality rates, varying from 22–55% [3, 4] with, notably, an analysis of 650 patients reported by Chari showing a mortality range of 34% [5].

The risk of death among hospitalized and ventilated patients is also similar, ranging from 60–100% among ventilated patients and patients who were hospitalized (10–53%). The most common reported independent predictors of adverse outcomes with COVID-19 infection are: advanced age, high-risk myeloma, renal disease, and suboptimal myeloma control.

Our survey does not exclude this observation but indicates that PI treatment is correlated with a lower risk of death that has not been previously reported. SARS-CoV-2 infection in myeloma patients is associated with a high risk of a severe course of COVID-19 and a high mortality rate. Since the effects of anti-SARS-CoV-2 treatment remain undetermined, vaccination is highly recommended especially during an outbreak of the pandemic. Any reported correlation with PI treatment must be confirmed in further studies.

Authors' contributions

DD and LG collected and analyzed data and wrote manuscript, the rest authors collected the data and supported the writing of the manuscript.

Conflict of interest

The authors declare no conflict of interest.

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None.

Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; EU Directive 2010/63/EU for animal experiments and uniform requirements for manuscripts submitted to biomedical journals.

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