

## **COVID-19 infections and clinical outcomes in patients with multiple myeloma in New York City: a cohort study from five academic centers**

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### **Running title**

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## Abstract

Patients with multiple myeloma have a compromised immune system, due to both the disease and anti-myeloma therapies, and may therefore be particularly susceptible to COVID-19. Here, we report outcomes and risk factors for serious disease in multiple myeloma patients treated at five large academic centers in New York City in the spring of 2020, during the time it was a global epicenter of the SARS-CoV-2 pandemic.

Of 100 multiple myeloma patients (male 58%; median age 68) diagnosed with COVID-19, 75 were admitted; of these 13 (17%) patients were placed on invasive mechanical ventilation, and 22 patients (29%) expired. Of the 25 non-admitted patients, four were asymptomatic. There was a higher risk of adverse outcome (ICU-admission, mechanical ventilation, or death) in Hispanic/Latinos (N=21), odds ratio (OR) 4.7 (95% confidence interval 1.3-16.7) and African American Blacks (N=33), OR 3.5 (1.1-11.5), as compared to White patients (N=36). Patients who met the adverse combined endpoint had overall higher levels of inflammatory markers and cytokine activation. None of the other studied risk factors were significantly associated ( $P>0.05$ ) with adverse outcome: hypertension (N=56), OR 2.2 (0.9-5.4); diabetes (N=18), OR 0.9 (0.3-2.9); age >65 years (N=63), OR 1.8 (0.7-4.6); high dose melphalan with autologous stem cell transplant <12 months (N=7), OR 1.2 (0.2-5.4); IgG<650 mg/dL (N=42), OR 0.9 (0.3-2.2).

In this largest cohort to date of patients with multiple myeloma and COVID-19, we found the case fatality rate to be 29% among hospitalized patients and that race/ethnicity was the strongest risk factor for adverse outcome.

## **Statement of Significance**

Multiple myeloma patients are immunocompromised, raising the question whether they are at higher risk of severe COVID-19 disease. In this large case series on COVID-19 in patients with multiple myeloma, we report 29% mortality rates among hospitalized patients, and identify race/ethnicity as the strongest risk factor for adverse outcomes.

## Introduction

The coronavirus disease 2019 (COVID-19) pandemic, caused by the SARS-CoV-2 virus, has become a global health crisis since it was first reported in Wuhan, China, in December 2019.<sup>1,2</sup> COVID-19 has so far caused over 600,000 deaths globally and has spread to the majority of countries around the world

(<https://coronavirus.jhu.edu/map.html>). New York City was one of the global epicenter for the SARS-CoV-2 outbreak in the spring of 2020 and a significant number of individuals have been infected by the virus, including both patients with underlying health conditions as well as healthy individuals.<sup>3</sup> Clinical symptoms of COVID-19 include fever, cough, fatigue, diarrhea, headaches, and shortness of breath.<sup>1</sup> They range from mild symptoms to severe disease characterized by pneumonia, hypoxia, respiratory failure, acute respiratory disease syndrome (ARDS), immune dysregulation, cytokine storm, thromboembolic events, and multiorgan failure.<sup>1</sup> Reported risk factors for severe COVID-19 disease are male gender, advanced age, smoking, and certain comorbidities such as hypertension.<sup>1,4</sup>

Several studies of varying size have suggested that patients with cancer on active therapy or recent surgery have a higher risk of a more severe COVID-19 disease course.<sup>2,5-14</sup> Patients with metastatic disease or hematological cancers have been among those with the poorest outcomes.<sup>10</sup> Additionally, recent immunotherapy treatment with checkpoint inhibitors was associated with a poorer outcome.<sup>7</sup> Patients with multiple myeloma have an inherently compromised humoral and cellular immunity from the malignant plasma cell disorder itself and its associated

hypogammaglobulinemia.<sup>15</sup> The immunosuppression seen at presentation can be exacerbated by the standard combination anti-myeloma therapies currently in use.<sup>16</sup> Among the conventional treatment options for multiple myeloma, the use of high-dose melphalan chemotherapy followed by autologous stem cell transplant is particularly associated with acute and sustained hypogammaglobulinemia and T-cell suppression.<sup>17</sup> Here, we report on the largest experience to date from a cohort of multiple myeloma patients with COVID-19 from five large academic centers in New York City during the height of the COVID-19 outbreak.

## Results

We identified a total of 100 patients with multiple myeloma and COVID-19. Median age at the time of COVID-19 infection was 68 years (range 41-91 years). Fifty-eight (58%) of the patients were male and 24 were current or former smokers (**Table 1**). Concomitant cardiovascular or pulmonary comorbidities were seen in 74 patients of which hypertension was the most common (56%). Additionally, we identified 27 patients with related plasma cell disorders; 20 with monoclonal gammopathy of undetermined significance (MGUS), 3 with smoldering multiple myeloma (SMM), 3 patients with AL amyloidosis, and 1 patient with solitary plasmacytoma (**Table 1**).

Of the 100 patients with multiple myeloma, 28 patients (28%) had newly diagnosed multiple myeloma; 26 were being treated with induction therapy, one had not yet started induction and one had opted not to start therapy. There were 35 (35%) patients with stable disease (i.e. non-active disease); 23 of these were on lenalidomide maintenance,

5 were on other forms of maintenance including ixazomib/dexamethasone and daratumumab/dexamethasone and 7 patients with stable disease were monitored off therapy. Thirty-five (35%) patients had relapse/refractory multiple myeloma of which 31 were on various anti-multiple myeloma treatments; the majority daratumumab- or carfilzomib-based. The remaining 4 relapse/refractory patients were not on active anti-myeloma therapy due to advance disease stage (hospice) or other more pressing comorbidities. Information on treatment status was missing for two patients, these had both been classified as newly diagnosed multiple myeloma. (**Table 2**) Overall, a total of 39 patients had undergone high-dose melphalan followed by autologous stem cell transplant; 7 patients within the 12 months prior to contracting COVID-19. Six patients and 1 patient had undergone high-dose melphalan followed by autologous stem cell transplant within 6 months and 3 months, respectively, prior to contracting COVID-19. Two patients had a prior allogeneic stem cell transplant several years before the COVID-19 diagnosis. (**Table 2**) Forty-two patients (42%) had hypogammaglobulinemia (IgG <650 mg/dL) and 18 patients (18%) had severe hypogammaglobulinemia (IgG <400 mg/dL).

The laboratory findings in this multiple myeloma cohort revealed lymphopenia and elevated C-reactive protein, ferritin, D-dimer, and IL-6 levels (**Table 3**). Patients who met the adverse combined endpoint (i.e. ICU-admission, invasive mechanical ventilation, or death) had overall higher levels of inflammatory markers reflecting a more severe infection and cytokine activation (**Table 3**).

Of the 100 patients with multiple myeloma and a SARS-CoV-2 positive RNA PCR test on this study, 75 (75%) were admitted due to COVID-19; 17 were admitted to the ICU and 13 of these patients were placed on invasive mechanical ventilation. Twenty-two of the multiple myeloma patients, thus 29% of those admitted, expired during the follow-up time; all reported deaths were from COVID-19.

Regarding treatments used for COVID-19, 52 patients were treated with hydroxychloroquine and 52 with azithromycin, 42 had the combination of the two and 35 received neither hydroxychloroquine nor azithromycin (**Table 4**). Twenty-seven patients were treated with steroids, mainly dexamethasone or methyl-prednisone, for COVID-19. Nine patients received treatment with IL-6 inhibitors, tocilizumab or sarilumab, and one patient was treated with the IL-1 inhibitor anakinra and the TNF-alpha inhibitor infliximab. Other treatments included broad-spectrum antibiotics and investigational anti-viral therapies such as lopinavir-ritonavir (N=4) and remdesivir (N=3). Two patients were treated with convalescent plasma.

Nine patients developed COVID19-related thromboembolic events; 7 venous thromboembolic events and 2 cerebrovascular events. Six of these patients were on active multiple myeloma therapy prior to the COVID-19 diagnosis; 4 on treatment including lenalidomide. The majority of admitted patients (N=47), were on thromboprophylaxis with heparin or low molecular weight heparin prophylaxis, unless there was a contraindication or prophylaxis was not indicated (young, mobile patient with mild disease). Nine patients were on direct anticoagulatory medication; the majority

continued while inpatient in lieu of heparin or low molecular weight heparin prophylaxis. Two patients did not receive thromboprophylaxis and information on prophylaxis was missing for one patient who developed thrombosis. Fifteen of the multiple myeloma patients continued on low dose aspirin prophylaxis, the majority of these were outpatients.

Twenty-nine patients (29%) of the 100 multiple myeloma patients met the combined adverse end-point (ICU-admission, invasive mechanical ventilation, or death). The risk of adverse outcome was highest in Hispanic/Latino patients (N=21), OR 4.7 (1.3-16.7), and African American Blacks (N=33), OR 3.5 (1.1-11.5), compared to White patients (N=36) (**Figure 1**). There was no significant difference between patients who were newly diagnosed, OR 1.2 (0.4-3.7), or patients with relapse/refractory disease, OR 1.2 (0.4-3.3), compared to multiple myeloma patients with stable disease. Based on small numbers (N=7), high-dose melphalan chemotherapy followed with autologous stem cell transplant within 12 months prior to COVID-19 diagnosis was not significantly associated with the adverse combined endpoint, OR 1.2 (0.2-7.4). None of the other studied risk factors were significantly associated ( $P>0.05$ ) with adverse outcomes, including hypertension (N=56), OR 2.2 (0.9-5.4); diabetes (N=18), OR 0.9 (0.3-2.9), age >65 years (N=63), OR 1.8 (0.7-4.6); or male gender (N=58), OR 0.9 (0.4-2.0). We did not observe any statistical association between the adverse combined endpoint and hypogammaglobulinemia (IgG <650 mg/dL) (N=42); OR 0.9 (0.3-2.2) or severe hypogammaglobulinemia (IgG <400 mg/dL) (N=18); and 1.0 (0.3-3.2), respectively (**Figure 1**).

In the entire case series of 127 patients with plasma cell disorders, the OR of severe outcome (ICU-admission, mechanical ventilation, or death) was significantly elevated for those with hypertension (N=72) (OR 2.9, 1.3-6.4) while diabetes, male gender, age >65 years, or chronic obstructive pulmonary disease/asthma were not significantly associated with the adverse combined end-point.

## **Discussion**

COVID-19 is a disease caused by the SARS-CoV-2 virus where, in the general population, the most severe outcomes are observed among elderly patients and patients with cardiovascular comorbidities.<sup>3,18</sup> There is limited data on outcomes in patients with cancers particularly patients with hematological malignancies. Here, we present a large case series of COVID-19 in patients with multiple myeloma, a plasma cell malignancy associated with a compromised immune system, due to both disease biology and anti-myeloma therapies.<sup>15</sup> Consecutive patients with multiple myeloma and related precursor diseases with confirmed presence of SARS-CoV-2 between March 1<sup>st</sup> and April 30<sup>th</sup>, 2020 from five large academic centers in New York City were included in this study. In the general population, the probability of dying from COVID-19 has been reported to be between 1-6% including all COVID-19 positive cases, and between 6-26% for patients hospitalized due to the virus.<sup>1,3,18-20</sup> Here, we show that among 75 multiple myeloma patients admitted due to COVID-19, the mortality rate was 29% which thus is to be on the high end of what has been reported in the general population.

Recent publications on COVID-19 in cancer patients have reported case fatality rates between 11-28% and for hematological malignancies up to 37%.<sup>2,7,10</sup> Robilotti et al reported on 423 cancer patients with COVID-19 diagnosed at MSK, of these 40% were admitted and 12% expired within the first 30 days after diagnosis.<sup>7</sup> Symptomatic COVID-19 in multiple myeloma patients has been indicated to have a high mortality, as high as 55% in patients undergoing systemic anti-cancer therapy for multiple myeloma.<sup>9</sup> In larger publication from hospitalized COVID-19 patients the UK (N=20,133) and one of the hospital systems in the New York area (N=5700), the case fatality rate has been between 21-26% for hospitalized patients.<sup>3,18</sup> According to the Johns Hopkins COVID resource center, on April 30<sup>th</sup> New York state had 299,000 cases and 18,100 deaths, indicating an approximate case fatality rate of 6% (<https://coronavirus.jhu.edu/map.html>, accessed on 7/14/2020). The variation between studies may be caused by study design (inpatient vs all patients), access to testing, and whether screened patients, likely capturing more asymptomatic patients, were included. Our findings on COVID-19 related mortality, 22% in the whole cohort of myeloma patients and 29% of those admitted, are in line with recent reports on a high mortality in patients with hematological malignancies in relation the general population (**Table 5**).<sup>2,10</sup>

We were motivated to better understand risk factors associated with severe outcomes from COVID-19 positive multiple myeloma patients. Specifically, we studied host characteristics as well as available variables related to the disease and treatment. We found that racial and ethnical background was significantly associated with increased with of severe outcome where the highest risks were seen in Hispanics/Latinos and in African American Blacks.<sup>21,22</sup> Underlying reasons for this may be differences in pre-

existing comorbidities and socioeconomic factors including the possibility to work from home and to practice social distancing.<sup>21,22</sup> It is possible that disparities in level of care (i.e. health insurance coverage) may have affected the outcome, however, we were unable to further address these aspects within the scope of this study. Similar to reports from the general population, there was a tendency towards a higher OR for adverse outcome (ICU-admission, invasive mechanical ventilation, or death) in patients with preexisting hypertension.<sup>3</sup> In the analysis of the entire series of COVID-19 positive patients with multiple myeloma and related plasma cell disorders (N=127), similar to the general population, cardiovascular risk factors were significantly associated with adverse outcome.<sup>3</sup>

Independent of COVID-19, typically, patients with multiple myeloma are at an increased risk of infections due to both disease and treatment associated immunosuppression.<sup>15,23</sup> Examples of these associations are the immunomodulatory and conventional chemotherapy drugs which cause myelosuppression, the targeted monoclonal antibodies such as anti-CD-38 associated with suppression of the humoral immune system.<sup>24-28</sup> In the current series, we did not identify an association between anti-myeloma treatment or hypogammaglobulinemia and adverse outcome; however, due to the lack of detailed biomarker data, we were unable to rule out associations involving other immunological mechanisms (such as T-cell suppression) that are important in the immune response towards viral and other infections. In multiple myeloma patients undergoing high-dose melphalan chemotherapy followed by autologous stem cell transplant, it is well-known that there are severe acute as well as sustained long-term

immunosuppression including broad aspects of the immune system.<sup>29,30</sup> In this study, 39 of the 100 multiple myeloma patients included had been treated with autologous stem cell transplant. Based on small numbers (N=7), the OR for the adverse combined end-point was not significantly elevated in patients who had high-dose melphalan chemotherapy with autologous stem cell transplant within 12 months prior to contracting COVID-19. Despite not seeing an increased mortality associated with high-dose melphalan chemotherapy with autologous stem cell transplant, we note the concerns of the American Society of Hematology, the European Myeloma Network, and the International Myeloma Society whose recommendations state that for transplant-eligible patients, high-dose melphalan chemotherapy followed with autologous stem cell transplant should be postponed, if possible, until the pandemic abates.<sup>31</sup> (American Society of Hematology. COVID-19 and Multiple Myeloma. 2020 at <https://www.hematology.org/covid-19/covid-19-and-multiple-myeloma> (5/8/2020), International Myeloma Society Recommendations for the Management of Myeloma Patients During the COVID-19 Pandemic. 2020. <https://cms.cws.net/content/beta.myelomasociety.org/files/IMS%20recommendations%20for%20Physicians%20Final.pdf> Accessed 5/8/2020). Given that it is unknown whether there could be additional SARS-CoV-2 outbreaks as the lockdown eases or seasonal outbreaks in following years, it is good clinical practice to have this discussion with every patient. When a safe and efficacious SARS-CoV-2 vaccine becomes available, it should be recommended to multiple myeloma patients and should be added to re-immunization programs for melphalan-induced inactivation of prior vaccines.

To minimize the risk for exposure, management of multiple myeloma including the use of infusions, injections and oral drugs has been adjusted to favor fewer visits, fewer injections/infusions and a preference for oral drugs.<sup>31-33</sup> (NCCN Coronavirus Disease 2019 (COVID-19) Resources for the Cancer Care Community 2020 at <https://www.nccn.org/covid-19/>, accessed 5/8/2020, American Society of Clinical Oncology Coronavirus Resources. 2020, <https://www.asco.org/asco-coronavirus-information>, accessed 5/8/2020, American Society of Hematology. COVID-19 and Multiple Myeloma. 2020 at <https://www.hematology.org/covid-19/covid-19-and-multiple-myeloma>, accessed 5/8/2020, International Myeloma Society Recommendations for the Management of Myeloma Patients During the COVID-19 Pandemic. 2020. <https://cms.cws.net/content/beta.myelomasociety.org/files/IMS%20recommendations%20for%20Physicians%20Final.pdf>, accessed 5/8/2020, European Society for Medical Oncology. Cancer Patient Management During the COVID-19 Pandemic. 2020 at <https://www.esmo.org/guidelines/cancer-patient-management-during-the-covid-19-pandemic>, accessed 5/8/2020). All five academic centers limited the use of high-dose melphalan and autologous stem cell transplant and only a few high risk patients have been transplanted during the outbreak. Additionally, in our experience, patients with multiple myeloma have been particularly adherent to the general recommendations for social distancing.<sup>34,35</sup> This may have contributed to the relatively low number of patients with multiple myeloma and COVID-19 in this cohort given the population of New York City (8.4 million), the overall number of confirmed cases (~300,000 at time of data cutoff), and the large catchment area covered by the five included hospital centers.

In prior reports from the general population, the immune response in patients with severe COVID-19 show a unique pattern with high IL-6, low HLA-DR expression, and dysregulation of lymphocytes characterized by CD4 lymphopenia and subsequently B-cell lymphopenia.<sup>36</sup> In the current series of multiple myeloma patients, we found high levels of IL-6, elevated ferritin, and low absolute lymphocyte levels. Furthermore, COVID-19 can lead to a hypercoagulable state and patients with severe COVID-19 have an increased risk of venous thromboembolism and stroke.<sup>4,37</sup> In this series, 9 patients had thromboembolic events and D-dimer levels were significantly elevated in patients with severe outcomes. The biological underpinnings of these observations remain to be further explained in functional studies.

Few treatments have so far shown an unequivocal beneficial effect for treatment of COVID-19. Hydroxychloroquine in combination with azithromycin was initially suggested to be an effective treatment combination; however, validation trials have been unable to confirm beneficial effects. Importantly, the World Health Organization recently expressed concern over cardiac arrhythmias and other potentially serious effects with the hydroxychloroquine-azithromycin combination and several of the initial publications have now been retracted.<sup>38-41</sup> Twenty-seven patients in this cohort were treated with steroids and dexamethasone has subsequently shown to reduce mortality in hospitalized patients with COVID-19.<sup>42</sup> A few patients in our series were treated with lopinavir-ritonavir; however, clinical trials have not shown a clinical benefit of these anti-retroviral drugs.<sup>43</sup> Recent reports on remdesivir as well as treatment with convalescent plasma therapy have showed promising results and there are case reports on

successful treatment of COVID-19 with IL-6 blockade.<sup>44-49</sup> Additionally, there are indications that the Bruton tyrosine kinase inhibitor acalabrutinib can reduce the excessive inflammatory response in patients with severe COVID-19.<sup>50</sup>

Limitations of this study includes it being a case-series from tertiary cancer centers with a selected patient population in which patients who were treated at local hospitals in the outpatient setting were less likely to be included. Nevertheless, we estimate the level of reporting to be high for multiple myeloma patients given the potential severity of COVID-19 and the high compliance among these patients. However, given the study design, asymptomatic patients may be underrepresented as in many of the published COVID-19 studies. There was missing data for certain laboratory results for some of the patients, primarily those who were treated as outpatients where not all tested for C-reactive protein, ferritin, D-dimer, or IL-6 levels.

In summary, we present data on a large case-series of COVID-19 positive patients with multiple myeloma and related precursor diseases showing case fatality of 29% among hospitalized patients. We comprehensively investigated the role of other comorbidities and found that the strongest risk factors for severe outcome were race/ethnicity background and cardiovascular comorbidities similar to those in the general population. In this cohort, multiple myeloma disease stage, type of treatment, and immunoglobulin levels were not significantly associated with adverse outcome. Ongoing larger studies with a wide range of hematological malignancies will provide additional information on important risk factors in these patients. Nevertheless, given that patients with multiple

myeloma are at an increased risk of various other infections due to both disease and treatment associated immunosuppression<sup>23</sup>, current recommendations by American Society of Hematology, the European Myeloma Network, and the International Myeloma Society state that high-dose melphalan chemotherapy followed by autologous stem cell transplant should be postponed, if possible, until the pandemic levels off.<sup>31</sup> Going forward, until there is a vaccine or effective treatment for COVID-19, clinical management and treatment of patients with multiple myeloma has to be carefully considered and adjusted to reduce the risk of exposure and minimize immunosuppression, while still aiming to achieve deep remissions in the era of COVID-19.

## **Methods**

This is a retrospective multiple center study including five large academic centers in New York; Memorial Sloan Kettering Cancer Center, New York University Langone Health, Mount Sinai, Weill Cornell Medicine, and Columbia University Medical Center. Consecutive patients with multiple myeloma and related plasma cell disorders and confirmed COVID-19 either in the inpatient or outpatient setting were included in this study. Patients were identified through automated hospital database searches using ICD10 codes (C90.0 and D47.2) among those who tested positive for SARS-CoV-2 during the peak of the outbreak between March 10<sup>th</sup> and April 30<sup>th</sup>, 2020. Additionally, all clinical faculty were requested to report if they had multiple myeloma patients diagnosed at outside clinics. Patients were followed until time of event or until July 6<sup>th</sup>, 2020, by which time all patients had either recovered or expired from COVID-19. A total

of 127 patients were included; Memorial Sloan Kettering Cancer Center (N=52), New York University Langone Health (N=30), Mount Sinai (N=23), Weill Cornell Medicine (N=13), and Columbia University Medical Center (N=9).

The presence of SARS-CoV-2 was determined using nasopharynx swabs and real time polymerase chain reactions targeting viral RNA. Patients were admitted if they had shortness of breath, decreased oxygen saturation, or other clinical symptoms such as high fever, fatigue, or failure to thrive based on the treating or admitting physicians' assessment. We obtained data on patient characteristics such as age, gender, race/ethnicity as well as comorbidities including cardiovascular comorbidities, e.g hypertension and diabetes. We manually extracted data on multiple myeloma stage, ongoing treatment and previous autologous or allogeneic stem cell transplant. Laboratory findings, e.g. blood counts and inflammatory markers from testing performed at the time of COVID-19 were included. If immunoglobulin levels were not obtained at COVID-19 diagnosis, results from up to 30 days prior were used. COVID-19 related outcomes were assessed regarding the need for admission, intensive care unit admission (ICU), invasive mechanical ventilation and whether the patient expired from COVID-19 or other causes. We also obtained information on treatments used for COVID-19; hydroxychloroquine, azithromycin, dexamethasone, anti-viral agents, IL-6 inhibitors or convalescent plasma.

Descriptive statistics was used to characterize the patient cohort and to present information on outcomes. The primary composite end-point for adverse outcome was

defined as admission to the ICU, need for invasive mechanical ventilation, or death. The assessed risk factors were categorized into clinically relevant thresholds.

Hypogammaglobulinemia was defined as immunoglobulin G (IgG) levels <650 mg/dL (lower limit of normal), and severe hypogammaglobulinemia was defined as IgG levels <400 mg/dL. Associations between continuous laboratory measurements (absolute neutrophil count, absolute lymphocyte count, platelet count, C-reactive protein, ferritin, D-dimer, interleukin-6 level) and the adverse combined endpoint were tested by the Wilcoxon rank-sum test and associations between the combined endpoint and discrete patient characteristics (age >65 years, gender, race/ethnicity, presence of comorbidities, multiple myeloma disease stage, high dose melphalan and autologous stem cell transplant within 12 months, hypogammaglobulinemia) were tested by Fisher's exact test. Univariate logistic regression was used to estimate odds ratios (ORs) with 95% confidence intervals (CI) for these risk factors associated with adverse outcomes. In general, the group absence of risk factor under study was used as the reference group. Separate analyses were performed for patients with multiple myeloma (N=100) and for all patients with plasma cell disorders (N=127). This study was approved under the MSK Myeloma Service and informed consent was waived under the retrospective research protocol (Institutional Review Board protocol 18-143).

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Drs. Jagannath, Niesvizky, Lentzsch, Morgan and Landgren equally contributed to this work.

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## **Conflicts of Interest**

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**Table 1.** Patients' characteristics.

	Number (%)
<b>All patients</b>	127 (100)
<b>Men</b>	68 (54)
<b>Women</b>	59 (46)
<b>Median age at COVID-19 (years)</b>	68 years
<b>Former/Current smoker</b>	34 (27)
<b>Never smoker</b>	92 (73)
<b>Multiple myeloma</b>	100 (79)
<b>Newly diagnosed multiple myeloma</b>	30
<b>Stable multiple myeloma without relapse</b>	35
<b>Relapse/refractory multiple myeloma</b>	35
<b>Monoclonal gammopathy of undetermined significance</b>	20 (16)
<b>Smoldering multiple myeloma</b>	3 (2.4)
<b>AL amyloidosis</b>	3 (2.4)
<b>Solitary plasmacytoma</b>	1 (0.8)

Three multiple myeloma patients had concomitant AL amyloidosis.

**Table 2.** Treatment regimens in patients with multiple myeloma at the time of COVID-19 diagnosis.

	Number
<b>All patients</b>	100
<b>Patients with ongoing treatment</b>	86
<b>Bortezomib-including regimen</b>	20
<b>Carfilzomib-including regimen</b>	15
<b>Daratumumab-including regimen</b>	24
<b>Ixazomib-including regimen</b>	6
<b>Lenalidomide maintenance</b>	22
<b>Other treatments*</b>	10
<b>Prior MEL/ASCT</b>	39
<b>Prior allogeneic transplant</b>	2
<b>Not on treatment</b>	12
<b>Missing information regarding treatment status</b>	2

MEL/ASC=high dose melphalan and autologous stem cell transplantation

\*Other treatments included DCEP (dexamethasone, cyclophosphamide, etoposide, cisplatin), low dose melphalan, panabinostat, iberomid, clarithromycin, venetoclax, selinexor, and AMG-701.

**Table 3.** Laboratory findings in patients with multiple myeloma and COVID-19

	All patients N=100			With combined adverse outcome N=29			Without combined adverse outcome N=71			Reference range	P-value
	Median	Range	N	Median	Range	N	Median	Range	N		
<b>ANC</b>	3.2	0.4-17.5	82	4.0	0.4-17.2	26	2.5	0.4-17.5	56	1.5-7.5 (x10 <sup>9</sup> /L)	0.025
<b>ALC</b>	0.7	0.1-1.8	82	0.6	0.1-1.2	26	0.7	0.1-1.8	56	0.9-3.2 (x10 <sup>9</sup> /L)	0.21
<b>Platelets</b>	152	6-507	82	119	6-350	26	164.5	19-507	56	160-400 (x10 <sup>9</sup> /L)	0.047
<b>C-reactive protein</b>	34	2.7-293	65	37	5.5-293	25	25.5	2.7-259	40	<0.50 (mg/dL)	0.25
<b>Ferritin</b>	658	2-40 000	64	2015	42- 40,000	25	476	2-7174	39	22-415 (ng/mL)	0.001
<b>D-dimer</b>	1.3	0.2-83	59	3.0	0.3-83	24	0.9	0.2-5.5	35	<0.5 (mcg/mL FEU)	0.001
<b>Interleukin-6</b>	71	6-3238	50	102	7.3-3238	21	64.5	6.0-532	29	<5.0 (pg/dL)	0.14

Adverse combined end-point=ICU-admission, mechanical ventilation, or death

ANC=Absolute neutrophil count, ALC=absolute lymphocyte count, NA=Not available, ND=Not done

Willcox-Rank test was used to compare laboratory values for patients who had the combined adverse outcome versus patients without the adverse outcome

**Table 4.** Treatment administered for COVID-19 in patients with multiple myeloma.

<b>Treatment for COVID19</b>	<b>Number</b>
<b>Total number of patients</b>	100
<b>Patient receiving therapy for COVID-19</b>	65
<b>Hydroxychloroquine</b>	52
<b>Azithromycin</b>	52
<b>Combination hydroxychloroquine and azithromycin</b>	40
<b>Corticosteroids</b>	27
<b>IL-6 blockade</b>	9
<b>Lopinavir-ritonavir</b>	4
<b>Remdisivir</b>	3
<b>Convalescent plasma</b>	2

**Table 5.** Case fatality rates in the current study in relation to published reports.

	Patient cohort	Number of patients	Setting	Case fatality rate
Current study	Multiple myeloma	100	Inpatient and outpatient	22%
Lee et al <sup>11</sup>	All cancer patients	800	Inpatient and outpatient	28%
Robilotti et al <sup>7</sup>	All cancer patients	423	Inpatient and outpatient	12%
Miyashita <sup>13</sup>	All cancer patients	334	Inpatient and outpatient	11%
Mehta et al <sup>10</sup>	All cancer patients	218	Inpatient and outpatient	28%
Mehta et al <sup>10</sup>	Hematological malignancy subcohort	54	Inpatient and outpatient	37%
Dai et al <sup>2</sup>	All cancer patients	105	Inpatient and outpatient	11%
Cook et al <sup>9</sup>	Multiple myeloma	75	Inpatient and outpatient	54.7%
Malard et al <sup>12</sup>	Hematological malignancy	25	Inpatient	36%
Docherty <sup>18</sup>	All patients	20,133	Inpatient	26%
Richardson <sup>3</sup>	All patients	5700	Inpatient	21%
Goyal et al <sup>19</sup>	All patients	393	Inpatient	10%
Deng et al <sup>20</sup>	All patients	82,719	All	1-8%
Guan et al <sup>1</sup>	All patients	1099	All	1.4%
Johns Hopkins University CCSE COVID-19 map*	All COVID-19 positive cases	~299,000	All	6%

\*Center for Systems Science and Engineering (CSSE) at Johns Hopkins University, COVID-19 map for cumulative number of cases and deaths on April 30<sup>th</sup> 2020, <https://coronavirus.jhu.edu/map.html>

## Figure Legend

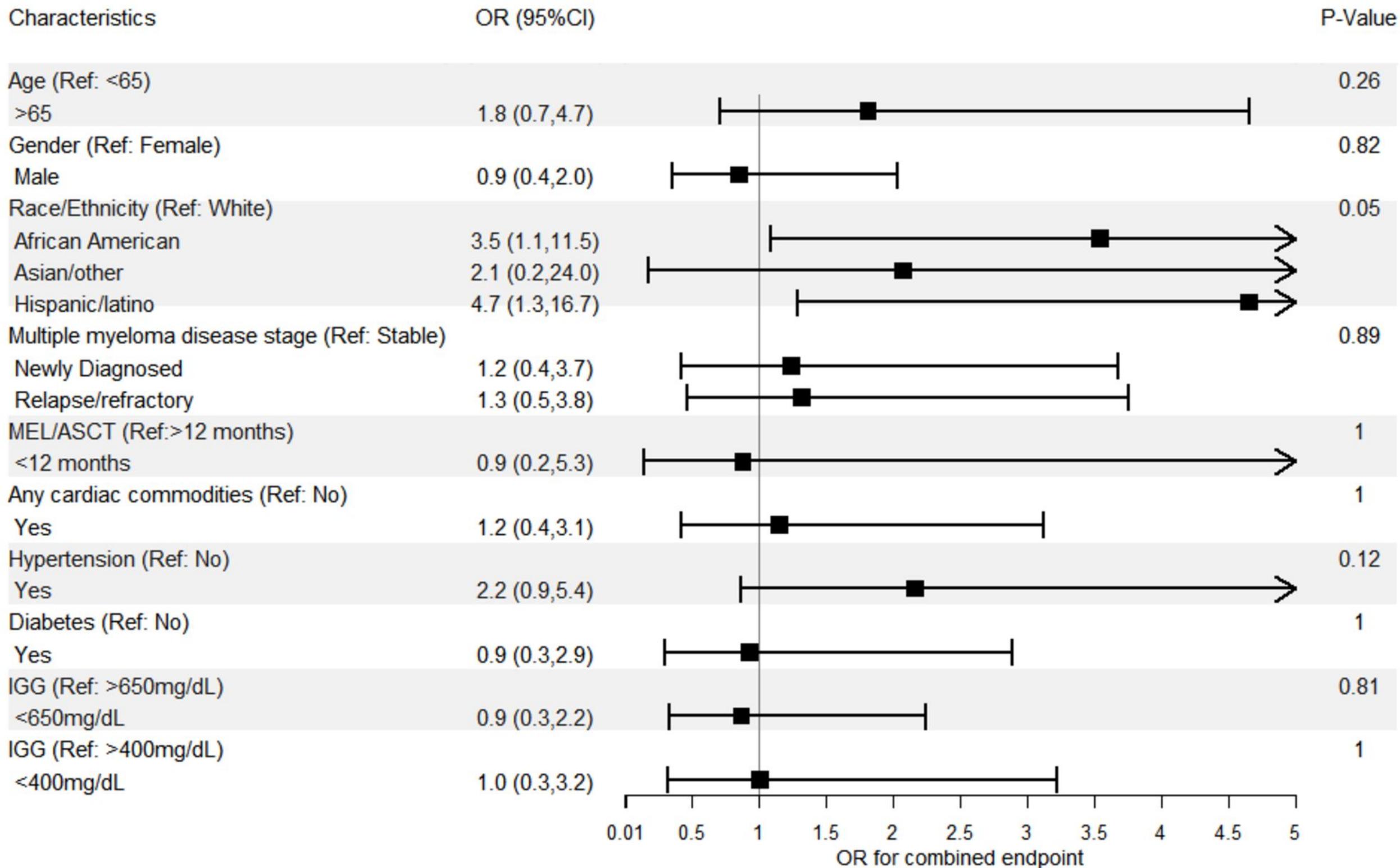
**Figure 1.** Odds Ratios (ORs) of the combined adverse end-point (intensive care unit admission, invasive mechanical ventilation, or death).

MEL/ASCT=high dose melphalan and autologous stem cell transplantation,

IGG=Immunoglobulin G level

Fisher-exact test was used to estimate odds ratios (ORs) for the combined adverse end-point in relation to clinical characteristics

### Odds Ratio (multiple myeloma subgroup)



# Correction: COVID-19 Infections and Outcomes in Patients with Multiple Myeloma in New York City: A Cohort Study from Five Academic Centers

Malin Hultcrantz, Joshua Richter, Cara A. Rosenbaum, Dhvani Patel, Eric L. Smith, Neha Korde, Sydney X. Lu, Sham Mailankody, Urvi A. Shah, Alexander M. Lesokhin, Hani Hassoun, Carlyn Tan, Francesco Maura, Andriy Derkach, Benjamin Diamond, Adriana Rossi, Roger Pearse, Deepu Madduri, Ajai Chari, David Kaminetzky, Marc J. Braunstein, Christian Gordillo, Ran Reshef, Ying Taur, Faith E. Davies, Sundar Jagannath, Ruben Niesvizky, Suzanne Lentzsch, Gareth J. Morgan, and Ola Landgren

In the original version of this article (1) as it was published online on July 30, 2020, a reference to the study (2) reporting 23 patients from Mount Sinai included in this cohort has been inadvertently omitted from the Methods. Information on patients per hospitals in this study is now specified in the Supplementary Table S1. The HTML and PDF versions of this article were corrected on the date listed below, ahead of print. The authors regret this error.

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1. Hultcrantz M, Richter J, Rosenbaum CA, Patel D, Smith ES, Korde N, et al. COVID-19 infections and outcomes in patients with multiple myeloma in New York City: a cohort study from five academic centers. *Blood Cancer Discov* 2020;1:234–43.
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# BLOOD CANCER DISCOVERY

## COVID-19 infections and outcomes in patients with multiple myeloma in New York City: a cohort study from five academic centers

Malin Hultcrantz, Joshua Richter, Cara A Rosenbaum, et al.

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