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SARS-CoV-2 infection among patients with haematological disorders: Severity and one-month outcome in 66 Danish patients in a nationwide cohort study

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Novelty Statement

- We provide outcome of SARS-CoV-2 infection among patients with haematological disorders in a population based nationwide cohort including both patients treated for the infection with or without hospital admission.
- ICU admission rate and mortality rate is high among all, but particularly high in older patients, patients with comorbidity, patients with acute leukemia/MDS, and patients with high performance status score.
- We conclude that the clinical course following SARS-CoV-2 infection is severe in this vulnerable group of patients.

Abstract

Objectives Patients with haematological disorders may be particularly vulnerable to respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, however this is unknown.

Methods We conducted a prospective, nationwide study including 66 patients in follow-up at Danish haematology departments with a malignant or non-malignant haematological disorder and with verified SARS-CoV-2 infection. Outcomes were intensive care unit (ICU) admission and one-month survival rate.

Results Mean age was 66.7 years, 60.6% were males, 90.9% had comorbidity, and 13.6% had a BMI ≥30. The most frequent diagnoses were chronic lymphocytic leukaemia/lymphoma (47.0%), multiple myeloma (16.7%), and acute leukaemia/myelodysplastic syndrome (AL/MDS) (12.1%). Treatment for the haematological disease was ongoing in 59.1% of cases. Neutropenia was present in 6.5%, lymphopenia in 46.6%, and hypogammaglobulinaemia in 26·3%. The SARS-CoV-2 infection was mild in 50·0%, severe in 36·4%, and critical in 13.6%. After one month, 21.2% had been admitted to ICU, and 24.2% died. Mortality was highest in older patients, patients with severe/critical SARS-CoV-2 infection, high comorbidity score or high performance status score, purine analogue treatment, and with AL/MDS. Although older patients and patients with comorbidities had the highest mortality rates, mortality was considerable among all haematological patients.

Conclusion

Haematological patients with SARS-CoV-2 infection has a severe clinical.

Keywords: Immunology and infectious diseases

1 INTRODUCTION

The severe, acute respiratory syndrome, corona virus 2 (SARS-CoV-2) pandemic has now led to confirmed infection in more than 25 million worldwide by the end of August 2020.[1] The case fatality rate varies considerably between countries, but particularly older patients and patients with comorbidity have been reported to suffer from complications and fatalities due to coronavirus disease 2019 (COVID-19).[1-6] Patients with cancer are vulnerable to infections, and especially patients with malignant and non-malignant haematological disorders are immunodeficient, which has been suggested as a risk factor for COVID-19 complications.[4] In addition, patients with haematological disorders have previously been found to be vulnerable to infection with other coronavirus types following stem cell transplantation.[7] Therefore, many haematological specialists have issued guidelines to suggest how treatment and follow-up may be changed, reduced, or deferred to ensure a minimum of immunosuppression and optimal shielding of patients.[8-14]

Previous studies suggest that COVID-19 outcome in patients with haematological cancer is dismal. Four small studies included between eight and 35 haematological cancer patients hospitalized with COVID-19 and reported short-term mortality rates ranging from 32% to 62%.[5,15-17] In particular, mortality was high among patients who were not in remission or patients recently diagnosed with a haematological cancer during induction treatment. Recently another study including 75 COVID-19 patients with multiple myeloma reported that mortality was 54.6% during the short follow-up period.[18] In an international collaborative study including 928 COVID-19 patients with cancer of whom 208 were haematological cancers the one-month mortality rate was 13% and particularly high among patients with active cancer disease. [19] For patients with non-malignant haematological disorders, COVID-19 outcome data are available mainly for patients with sickle cell disease. Three recent studies reported four, 10, and 83 SARS-CoV-2 - positive patients with sickle cell disease (SCD) admitted to hospital, the majority with typical signs of vaso-occlusive crisis. [20-22] Among these 97 SCD patients, 18 (19%) required intensive care unit transferal, 10 (11%) assisted mechanical ventilation, and three (3%) patients died.[20-22]

As published results of COVID-19 outcome in patients with haematological disorders are based almost exclusively on hospitalized patients, we aim to provide new insight by displaying results from a nation-wide cohort of all patients with haematological disorders verified to have SARS-CoV-2 infection. In this study, we present data regarding clinical presentation and outcome for the

first 66 adult Danish patients with malignant or non-malignant haematological disease and verified SARS-CoV-2 infection before 26 April 2020. Both patients managed with hospitalization or at home during their SARS-CoV-2 infection are included in our report.

2 METHODS

2.1 Data sources and patients

This study included all patients with haematological disorders aged ≥18 years with verified SARS-CoV-2 infection, who were in ongoing clinical follow-up at any department of haematology in Denmark. Patients with any subtype of lymphoid malignancy, myeloid malignancy, multiple myeloma, and non-malignant blood or bone marrow disorder, such as immune cytopenias, other red blood cell disorders, and bone marrow failure syndromes were included. All ten Danish haematology departments are located at public hospitals, which provide universal, free access to health care for all Danish residents and facilitate all SARS-CoV-2 testing. The very few private hospitals in Denmark are not engaged in diagnosis, treatment, or follow-up of patients with haematological disorders or infectious diseases. Danish patients with chronic haematological disorders usually remain in clinical follow-up at haematology departments in public hospitals Patients considered to be cured and without significant late effects may be discharged for subsequent follow-up with their general practitioner five years after terminating treatment. Patients currently followed for their haematological disorder are, as a national standard, instructed to contact their haematology department directly if they experience any symptoms of infections. During the study period, SARS-CoV-2 testing was performed using nasal or oropharyngeal swabs and subsequent reverse transcriptase polymerase chain reaction (PCR) techniques, according to local standards. Patients who presented with symptoms of infection, such as fever or upper/lower respiratory tract symptoms, as well as patients scheduled for stem cell transplantation were routinely SARS-CoV-2 tested throughout the study period. Patients were identified during routine clinical practice through contacts with their haematological departments, and the registered data were abstracted from medical files by local investigators. The first positive SARS-CoV-2 test in Denmark was identified on February 27, 2020. The first patient with a haematological disorder and SARS-CoV-2 infection was identified and registered in this study on March 3, 2020. From April 27, 2020, the SARS-CoV-2 testing strategy in Denmark was expanded

to routinely include all patients who were scheduled for in-hospital admission, regardless of symptoms. During the study period approximately 9,500 Danish citizens (0.2% of the Danish population) were verified by PCR to have SARS-CoV-2 infection. The median age was 48 years (inter quartile range, 33-62 years) and the 30-day mortality rate was 5.2%.[23] Based on published data of the major haematological malignancies, the prevalence of patients living with any haematological disease is estimated to be 20,000 out of 5.8 million citizens of Denmark.[24] The current study includes 66 patients with haematological disease and with verified SARS-CoV-2 infection before April 26, 2020, allowing a minimum of one month follow-up. Patients were included irrespective of severity of the infection and regardless of whether in-hospital admission was required or whether patients could be managed at home. Mortality, performance status (PS), and functional ability were re-evaluated for all patients one month after found positive for SARS-CoV-2 infection.

2.2 Baseline data

Baseline data including age, sex, height, weight, PS (before and after SARS-CoV-2 infection), living conditions, home care, haematological diagnosis, previous and current haematological treatment, remission status, comorbidity, current medication, and biochemical results at the time of SARS-CoV-2 infection were registered at the time of the verified SARS-CoV-2 infection. Comorbidities were summarized using the Charlson Comorbidity Index (CCI) [25] excluding haematological diseases as comorbid disorders as well as the Cumulative Illness Rating Scale (CIRS) [26], but individual comorbid conditions of particular interest in relation to SARS-CoV-2 infection, such as diabetes and obesity, were additionally registered.[3,27] Haematological diagnoses were categorized into four groups; multiple myeloma, chronic lymphocytic leukaemia/lymphoma, acute leukaemia/myelodysplastic syndrome, and other haematological disorders.

2.3 SARS-CoV-2 infection and COVID-19

In line with previous classifications, the severity of the SARS-CoV-2 infection was graded as either asymptomatic/mild, severe, or critical based on the symptoms and observations during the first 48 hours.[3] The infection was classified as asymptomatic or mild if patients had no symptoms

or only mild non-pneumonia/pneumonia symptoms. Patients with severe infection had fever, respiratory symptoms, dyspnea, respiratory frequency ≥30/min, blood oxygen saturation ≤ 93%, partial pressure of arterial oxygen to fraction of inspired oxygen ratio <300, and/or infiltrates in >50% of the lungs within 24 to 48 hours from presentation.[3] Patients classified as critically ill met one of three criteria: respiratory failure, septic shock, or multiple organ failure.[3] Anti-viral treatment and supportive care treatment such as steroids, tocilizumab were generally only administered within clinical trials and details regarding these treatments are provided in the designated reports and therefore not in this study.

2.4 Statistical analysis

Baseline characteristics, SARS-CoV-2 findings, and outcomes were described by means/proportions across the pre-defined diagnosis groups and classification of SARS-CoV-2 severity. Overall survival (OS) was measured from the date of verified SARS-CoV-2 infection until death or censoring (one month after SARS-CoV-2 infection), whichever came first. One-month OS was estimated as the proportion alive one month after verified infection. The risk of admission to intensive care unit (ICU) was estimated by the proportion of patients admitted to ICU within one month of verified SARS-CoV-2 infection. Confidence intervals (CIs) for one-month OS and risk of ICU admission were computed by using the exact approach by Clopper and Pearson.[28] Associations between SARS-CoV-2 severity or ICU admission and clinical risk factors were tested using Fishers' exact test for grouped exposures or univariable logistic regression for continuous exposures. One-month OS and risk of ICU admission were computed within selected clinical subgroups and depicted using forest plots. We considered only subgroups already suggested in previous publications to be associated with increased risk of complications (e.g. age, comorbidity, and specific treatments). Outcomes were shown within specific haematological treatment groups chosen based on previous reports of potential deleterious or protective effects. The treatment groups were CD20 antibodies, daratumumab, purine analogues, non-cancer immunosuppressive drugs, ibrutinib, and others.[11,14,29] Analyses were conducted in R (version 3.6.1).

2.5 Ethics

This study was approved by the Danish Data Protection Agency (record no. 20/13067). Since the study is purely observational and only utilizes information from routine clinical practice, the Danish council for patient safety (record no. 31-1521-230) and ethics committee (record no. 20202000, 53) waived informed consent.

3 RESULTS

3.1 Baseline characteristics

Among the 66 included patients with haematological disorders verified with SARS-CoV-2 infection, the mean age was 66.7 years (range 25-91 years) and 40 (60.6%) were male. The 66 patients constituted approximately 0.3% of all prevalent Danish patients with haematological disease. Chronic lymphocytic leukaemia/lymphoma was diagnosed in 31 (47.0%), 11 (16.7 %) patients had multiple myeloma, 8 (12.1%) had acute leukaemia/myelodysplastic syndrome, and 16 (24.2%) were diagnosed with other haematological malignant (myeloproliferative neoplasms, hairy cell leukaemia, T-cell large granular leukaemia, chronic myeloid leukaemia) or non-malignant disorders (immune thrombocytopenia or paroxysmal nocturnal haemoglobinuria). At the time of SARS-CoV-2 infection, the majority (59.1%) of the patients were in ongoing therapy for their haematological disorder, 17 (25.8%) were treated previously, and 10 (15.2%) were untreated (Table 1). Prior to the SARS-CoV-2 infection, 7 (10.6%) patients received stem cell transplantation (3 allogenic and 4 autologous). Almost all patients suffered from comorbidity with CCI $\geq$ 1 in 90.9% and mean CIRS score of 5.6 (SD, 4.5, Table 1). Lung diseases and diabetes were the most frequent comorbid conditions, each observed in 13.6% of the patients. Body mass index $\geq$30 was seen in 13.6%. Neutropenia (neutrophil count $< 1.0 \times 10^9$/l) was present in 6.5%, lymphopenia (lymphocyte count $< 1.0 \times 10^9$/l) in 46.6%, and hypogammaglobulinemia (IgG < 5.0 g/l) in 26.3%. Previous or current treatment for the haematological disorder included anti-CD20 antibodies in 14 (21.0%), daratumumab in 4 (6.1%), purine analogues in 7 (10.6%), ibrutinib in 3 (4.5%), non-cancer immunosuppressive treatment in 5 (9.1%) and other drugs and combinations in 7 (10.6%).

3.2 SARS-CoV-2-infection

The most common symptoms and findings were fever (80.3%), coughing (75.8%), and dyspnoea (33.3%) and only one patient had no symptoms (Table 2). Most of the SARS-CoV-2 infections were classified as asymptomatic/mild (50.0%), but a substantial proportion was severe (36.4%) or critical (13.6%). Hospitalization was required in 49 (74.2%) patients (76.9% among patients not in ongoing treatment). The proportion of mild SARS-CoV-2 infections was comparable across the haematological diagnoses (p=0.47). Overall, more than half of the patients (54.5%) were judged to have COVID-19 pneumonia based on chest x-ray or CT scan. Supplementary oxygen was administered to 63.6%, and 21.2% required ICU treatment - 9.1% using non-invasive ventilation, and 15.2% using ventilator treatment (Table 2). The proportion with severe or critical infection was elevated in patients with higher age (p=0.06), reduced physical performance prior to infection (p=0.26), current smoking (p=0.24), and lack of remission of the haematological disorder (p=0.004) (Table 3), although often not statistically significant. The proportion of patients with cellular or humoral immune deficiencies was not clearly associated with the SARS-CoV-2 severity (Table 3). Point estimates for the proportion who required ICU admission were highest among older patients, males, smokers, patients with PS > 1, and patients with comorbidity, although associated confidence intervals were wide (Figure 1). Of note, haematological treatment status was not associated with ICU admission or mortality; however, none of the three patients with concurrent ibrutinib treatment required ICU admission or died.

3.3 Survival following SARS-CoV-2 infection

The one-month OS following verified infection was 75.8% (95% CI, 63.6-85.5, Figure 2). The one-month OS was particularly high among patients with limited comorbidities (CCI ≤2, 93.1% [95% CI 77.2-99.2%]), ECOG PS <1 (87.5%, [95% CI, 71.0-96.5%]), age <65 years (85.7, [95% CI, 67.3-96.0%]). One-month OS in patients with mild SARS-CoV-2 infection was (97.0% [95% CI, 84.2-99.9%]) and significantly better than among patients with severe or critical infection (p<0.001). One-month OS was 81.8% (95% CI, 48.2-97.7%) among patients with multiple myeloma, 80.6% (95% CI, 62.5-92.5%) among patients with chronic lymphocytic leukaemia/lymphoma, 37.5% (95% CI, 8.5-75.5%) among patients with acute leukaemia/myelodysplastic syndrome, and 81.3% (95% CI, 54.3-96.0%) among patients with other haematological disorders (Figure 2).

Among survivors, 57.1% reported to be more fatigued than usual, 45.9% reported reduced functional abilities, and 33.3% felt dyspnoea one month after verified infection (Table 2). The proportion who reported ongoing symptoms or reduced functioning was higher in patients that had experienced severe/critical infection (p = 0.06, Table 3), albeit not statistically significant. Among patients previously treated with purine analogues, dismal one-month OS (57.1% [95% CI, 18.4-90.1%]) was observed (Figure 2).

4 DISCUSSION

In our study including nationwide data of patients with malignant and non-malignant haematological disorders and verified SARS-CoV-2 infection, we found that during the first month, 21.2% were admitted to an ICU, 15.2% required ventilator treatment, and mortality was 24.2%. One-month OS was associated with age and comorbidity. While mortality was elevated among current/former smokers, patients with PS>1, and patients previously treated with purine analogues statistical testing of many associations lacked power presumable due to the limited sample size. For patients alive at one month, a considerable proportion reported symptoms or reduced usual functioning.

In line with previous studies, mortality in our study was particularly high among older patients and patients with comorbidity.[2,3,18,19,23,30,31] Studies including patients with haematological diseases and SARS-CoV-2 are relatively few. A study from a single institution in Spain included 34 patients who were admitted to hospital with haematological malignancies and COVID-19. Patients were included if they were SARS-CoV-2 PCR positive (n=27) or suspected with COVID-19 (n=7).[17] The median age was 72.5 years, the case fatality rate 32%, and similarly to our results, advanced age, increased PS, and lack of remission of the haematological disease were associated with COVID-19 mortality.[17] Additionally, the status of haematological treatment was not associated with mortality.[17] In a recent study of COVID-19 related in-hospital mortality found that hazard ratios for death in patients with haematological cancer vs. no haematological cancer ranged from 1.9 to 3.5.[31] The highest hazard ratio was seen when comparing non-cancer patients to patients with a recent haematological cancer diagnosis possibly reflecting active malignancy, or induction treatment and therefore in line with our results.[31] From other studies, it is also not evident that concurrent or previous treatment for the haematological disease or the degree of

cellular or humoral immune deficiency is associated with COVID-19 outcome.[15] Intriguingly, a recent report suggested that continuing ibrutinib treatment during ongoing COVID-19 may mitigate the clinical course.[29] In our study, only three patients received ibrutinib during their SARS-CoV-2 infection, none of whom required ICU admission or died.

In line with previous studies, approximately 20% of our patients did not present with fever.[18,32] This emphasizes that a liberal testing strategy is still warranted particularly in vulnerable patients, such as patients with haematological disorders.

Despite the inclusion of nationwide routine data from a health care system with universal coverage and free access, our study may have limitations. It is conceivable that some patients with milder symptoms may have been reluctant to contact a hospital or other health care professionals and therefore would not have been tested for SARS-CoV-2 . Also, during the early weeks of the epidemic, testing was not as widely applied as later, and patients with milder and self-limiting symptoms may therefore have been advised to stay at home without being offered a diagnostic test. Both scenarios would lead to a disproportionate reduction of patients with mild infection and therefore tend to lead to overestimation of mortality rate at one-month. Compared to some other European countries with comparable health care services, Denmark has had relatively few SARS-CoV-2 infected citizens and an overall 30-day mortality rate of 5.2% during 27 February to 19 May 2020.[23] The low number of adverse outcomes in our study may, in part, reflect these overall risks for Danish patients, and the statistical power for detailed studies of predictors for complications and mortality is consequently reduced. Also, our defined groups of patients with lymphoid disorder, myeloid disorders and other rarer disorders are somewhat heterogenic for extrapolating results. Our one-month SARS-CoV-2 mortality rate in patients with haematological disease is high and approximately five times higher than the overall Danish mortality rate.[23] Even when comparing with all patients and patients aged 70-79 years in Denmark with verified SARS-CoV-2 infection and one or two comorbid conditions, the mortality rate reported in the present study is dismal[23]. In these groups the 30-day mortality is 16-19% for all patients and 14% for 70-79 year olds, which is considerably lower than the 24% we observe in the present study.[23] This suggests that the clinical course following SARS-CoV-2 infection is severe in patients with haematological disorders. From our study it cannot be concluded whether it is the haematological disease per se, immune deficiency, comorbidity, and/or other late effects that mediate the elevated

mortality. International collaboration for studies of specific types of haematological diseases and/or treatments is required to inform management guidelines.

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DECLARATION OF INTERESTS

We declare no competing interest.

AUTHOR CONTRIBUTIONS

H Frederiksen conceptualized the idea for the study. H Frederiksen, A Glenthøj, L Jakobsen, J Ryg, A Kodahl, M Severinsen, and M Clausen participated in the design of the study. H Frederiksen performed the literature search. All authors contributed to collection of data. A Glenthøj and L Jakobsen performed the data management, data analyses, and computed the figures. All authors participated in interpretation of data. H Frederiksen and L Jakobsen wrote the first draft of the paper, and all authors participated in writing subsequent drafts. All authors approved the final version.

DATA SHARING STATEMENT

Data in the present publication are personal to all patients and are available only to the physicians involved in their treatment as well as to designated researchers in the current study. They can therefore not be made publicly available. Analytical scripts and similar can be made available upon reasonable request to the correponding author.

REFERENCES

TABLE 1 Basic descriptives at time of verfied SARS-CoV-2 infection in patients with haematological disease

	All patients (n=66)	**Multiple myeloma (n=11)**	**Chronic lymphocytic leukaemia / lymphoma (n=31)**	**Acute leukaemia / Myelodysplastic syndrome (n=8)**	**Other * (n=16)**
Age, mean(SD)	66.7(15.4)	66.4(11.3)	67.0(16.7)	70.2(15.5)	64.8(16.3)
Age ≥65 years, n(%)	38(57.6)	5(45.5)	18(58.1)	5(62.5)	10(62.5)
Age > 80 years, n(%)	13(19.7)	2(18.2)	6(19.4)	3(37.5)	2(12.5)
Males, n(%)	40(60.6)	6(54.5)	19(61.3)	5(62.5)	10(62.5)
Performance status prior to infection ≥2, n(%)	16(24.6)	3(30.0)	5(16.1)	3(37.5)	5(31.2)
BMI ≥30, n(%)	8(13.6)	2(18.2)	3(10.7)	1(14.3)	2(15.4)
Current smokers, n(%)	3(5.2)	0(0.0)	2(7.1)	0(0.0)	1(6.7)
Living alone, n(%)	24(36.4)	2(18.2)	14(45.2)	3(37.5)	5(31.2)
Home care, n(%)	17(28.8)	4(44.4)	8(25.8)	1(16.7)	4(30.8)
Charlson comorbidity index score >2, n(%)	37(56.1)	6(54.5)	18(58.1)	6(75.0)	7(43.8)
Cumulative illness rating scale, mean(SD)	5.6(4.5)	7.3(5.5)	5.0(3.7)	6.0(4.0)	5.5(5.4)
Heart disease, n(%)	3(4.5)	0(0.0)	2(6.5)	0(0.0)	1(6.2)
Lung disease, n(%)	9(13.6)	1(9.1)	5(16.1)	0(0.0)	3(18.8)
Diabetes, n(%)	9(13.6)	4(36.4)	3(9.7)	1(12.5)	1(6.2)
Renal disease, n(%)	7(10.6)	3(27.3)	0(0.0)	2(25.0)	2(12.5)
Liver disease, n(%)	1(1.5)	0(0.0)	0(0.0)	1(12.5)	0(0.0)
Solid cancer, n(%)	4(6.1)	1(9.1)	1(3.2)	2(25.0)	0(0.0)
Treatment for hematological disorder, n(%)					
- Ongoing	39(59.1)	10(90.9)	12(38.7)	7(87.5)	10(62.5)
- Recent (0-6 months)	9(13.6)	0(0.0)	7(22.6)	1(12.5)	1(6.2)

- Previous (>6 months)	8(12.1)	0(0.0)	5(16.1)	0(0.0)	3(18.8)
- Untreated	10(15.2)	1(9.1)	7(22.6)	0(0.0)	2(12.5)
Remission status, n(%)					
- CR	17(37.8)	3(42.9)	8(38.1)	2(28.6)	4(40.0)
- PR	8(17.8)	2(28.6)	5(23.8)	0(0.0)	1(10.0)
- SD/PD	20(44.4)	2(28.6)	8(38.1)	5(71.4)	5(50.0)
Neutrophils x 10^9/l, mean(SD)	6.3(10.4)	5.1(3.2)	4.5(2.8)	16.0(27.1)	5.3(3.9)
Neutrophils < 1.0 x 10^9/l, n(%)	4(6.5)	0(0.0)	1(3.6)	3(37.5)	0(0.0)
Lymphocytes x 10^9/l, mean(SD)	3.3(7.2)	0.8(0.5)	5.7(10.1)	2.8(4.0)	0.9(0.6)
Lymphocytes < 1.0 x 10^9/l, n(%)	27(46.6)	5(50.0)	10(38.5)	3(42.9)	9(60.0)
IgG, mean(SD)	8.8(6.9)	8.6(6.3)	7.1(4.4)	24.9(20.0)	10.8(1.7)
IgG < 5.0 g/l, n(%)	10(26.3)	3(27.3)	7(33.3)	0(0.0)	0(0.0)

* Myeloproliferative neoplasms, immune thrombocytopenia, paroxysmal nocturnal hemoglobinuria, aplastic anaemia, etc.

TABLE 2 Clinical features and one-month follow-up of verfied SARS-CoV-2 infection in patients with haematological disease

	All patients (n=66)	**Multiple myeloma (n=11)**	**Chronic lymphocytic leukaemia / lymphoma (n=31)**	**Acute leukaemia / Myelodysplastic syndrome (n=8)**	**Other (n=16)**
Fever (%)	53(80.3)	9(81.8)	24(77.4)	6(75.0)	14(87.5)
Cough (%)	50(75.8)	8(72.7)	24(77.4)	6(75.0)	12(75.0)
Dyspnoea (%)	22(33.3)	2(18.2)	11(35.5)	1(12.5)	8(50.0)
Headache (%)	11(16.7)	1(9.1)	6(19.4)	0(0.0)	4(25.0)
Myalgia (%)	6(9.1)	0(0.0)	3(9.7)	2(25.0)	1(6.2)
Diarrhoea (%)	3(4.5)	0(0.0)	3(9.7)	0(0.0)	0(0.0)
COVID severity					
- Mild	33(50.0)	7(63.6)	16(51.6)	2(25.0)	8(50.0)
- Severe	24(36.4)	2(18.2)	14(45.2)	3(37.5)	5(31.2)
- Critical	9(13.6)	2(18.2)	1(3.2)	3(37.5)	3(18.8)

Hospitalized (%)	49(74.2)	9(81.8)	25(80.6)	7(87.5)	8(50.0)
Asymptomatic (%)	1(1.5)	0(0.0)	0(0.0)	0(0.0)	1(6.2)
Respiratory frequency / min, mean(SD)	21.1(6.9)	19.8(7.6)	20.7(6.2)	19.8(3.3)	23.4(8.9)
Blood oxygen saturation < 90% (%)	5(8.5)	3(30.0)	0(0.0)	0(0.0)	2(16.7)
X-ray/CT of thorax performed (%)	48(72.7)	9(81.8)	23(74.2)	5(62.5)	11(68.8)
COVID-19-related pneumonia	36(54.5)	8(72.7)	17(54.8)	5(62.5)	6(37.5)
Performance status ≥2 (%)	31(47.7)	5(50.0)	10(32.3)	5(62.5)	11(68.8)
Site of transmission (%)					
- Household	8(12.1)	1(9.1)	7(22.6)	0(0.0)	0(0.0)
- Imported	6(9.1)	2(18.2)	2(6.5)	0(0.0)	2(12.5)
- Hospital	3(4.5)	0(0.0)	3(9.7)	0(0.0)	0(0.0)
- Other close contact	5(7.6)	0(0.0)	3(9.7)	0(0.0)	2(12.5)
- Unknown	44(66.7)	8(72.7)	16(51.6)	8(100.0)	12(75.0)
Supplementary oxygen (%)	42(63.6)	7(63.6)	19(61.3)	6(75.0)	10(62.5)
ICU (%)	14(21.2)	3(27.3)	6(19.4)	2(25.0)	3(18.8)
CPAP / NIV (%)	6(9.1)	1(9.1)	3(9.7)	1(12.5)	1(6.2)
Ventilator (%)	10(15.2)	2(18.2)	3(9.7)	2(25.0)	3(18.8)
Outcome 1 month					
- Alive	50(75.8)	9(81.8)	25(80.6)	3(37.5)	13(81.2)
- Deceased	16(24.2)	2(18.2)	6(19.4)	5(62.5)	3(18.8)
Reductions in functional level					
- More fatigued than usual (%)	20(57.1)	4(66.7)	10(62.5)	1(50.0)	5(45.5)
- More dyspnoea than usual (%)	13(33.3)	2(28.6)	8(47.1)	0(0.0)	3(23.1)
- Functional abilities reduced (%)	17(45.9)	3(50.0)	9(52.9)	0(0.0)	5(41.7)

TABLE 3 Severity and outcome of SARS-CoV-2 infection infection in patients with haematological disease

	Mild (n=33)	**Severe (n=24)**	**Critical (n=9)**
Age, mean(SD)	64.4(13.0)	69.8(19.6)	67.2(10.0)
Age ≥65 years, n(%)	16(48.5)	17(70.8)	5(55.6)
Age > 80 years (%)	3(9.1)	9(37.5)	1(11.1)
Males (%)	21(63.6)	12(50.0)	7(77.8)
Performance status prior to infection ≥2 (%)	6(18.2)	7(30.4)	3(33.3)
BMI ≥30 (%)	3(9.7)	2(10.0)	3(37.5)
Current smokers (%)	0(0.0)	2(9.1)	1(14.3)
Living alone (%)	8(24.2)	11(45.8)	5(55.6)
Home care (%)	7(24.1)	7(30.4)	3(42.9)
Charlson comorbidity index score ≥1 (%)	14(42.4)	17(70.8)	6(66.7)
Cumulative illness rating scale, mean(SD)	4.5(3.7)	7.0(5.2)	6.2(4.3)
Heart disease (%)	0(0.0)	3(12.5)	0(0.0)
Lung disease (%)	4(12.1)	4(16.7)	1(11.1)
Diabetes (%)	3(9.1)	4(16.7)	2(22.2)
Renal disease (%)	2(6.1)	4(16.7)	1(11.1)
Liver disease (%)	0(0.0)	0(0.0)	1(11.1)
Solid cancer (%)	1(3.0)	1(4.2)	2(22.2)
Treatment for haematological disorder (%)			
- Ongoing	16(48.5)	18(75.0)	5(55.6)
- Recent (0-6 months)	7(21.2)	0(0.0)	2(22.2)
- Previous (>6 months)	6(18.2)	1(4.2)	1(11.1)
- Untreated	4(12.1)	5(20.8)	1(11.1)
Remission status (%)			
- CR	15(55.6)	1(8.3)	1(16.7)
- PR	6(22.2)	2(16.7)	0(0.0)
- SD/PD	6(22.2)	9(75.0)	5(83.3)
Neutrophils x 109/l, mean(SD)	3.9(2.2)	8.1(15.9)	8.9(6.1)
Neutrophils < 1.0 x 109/l (%)	1(3.4)	2(8.3)	1(11.1)
Lymphocytes x 109/l, mean(SD)	3.6(9.0)	3.1(5.9)	2.8(3.7)
Lymphocytes < 1.0 x 109/l (%)	13(50.0)	11(45.8)	3(37.5)
IgG, mean(SD)	7.0(3.5)	11.3(6.2)	11.6(15.5)
IgG < 5.0 g/l (%)	6(27.3)	1(9.1)	3(60.0)
Haematological disease subtype (%)			

- Multiple myeloma	7(21.2)	2(8.3)	2(22.2)
- Chronic lymphocytic leukaemia / lymphoma	16(48.5)	14(58.3)	1(11.1)
- Acute leukaemia / Myelodysplastic syndrome	2(6.1)	3(12.5)	3(33.3)
- Other	8(24.2)	5(20.8)	3(33.3)
Supplementary oxygen (%)	14(42.4)	19(79.2)	9(100.0)
ICU (%)	2(6.1)	4(16.7)	8(88.9)
CPAP / NIV (%)	2(6.1)	4(16.7)	0(0.0)
Ventilator (%)	0(0.0)	3(12.5)	7(77.8)
Outcome 1 month			
- Alive	32(97.0)	14(58.3)	4(44.4)
- Deceased	1(3.0)	10(41.7)	5(55.6)
Reductions in functional level			
- More fatigued than usual (%)	11(45.8)	5(71.4)	4(100.0)
- More dyspnoea than usual (%)	5(17.9)	4(57.1)	4(100.0)
- Functional abilities reduced (%)	7(26.9)	6(85.7)	4(100.0)

FIGURE LEGENDS

FIGURE 1 Proportion of Danish patients with haematological disorders verified with SARS-CoV-2 infection during the COVID-19 pandemic admitted to intensive care unit.

FIGURE 2 One month overall survival among Danish patients with haematological disorders verified with SARS-CoV-2 infection during the COVID-19 pandemic, overall and stratified according to clinical subgroups.

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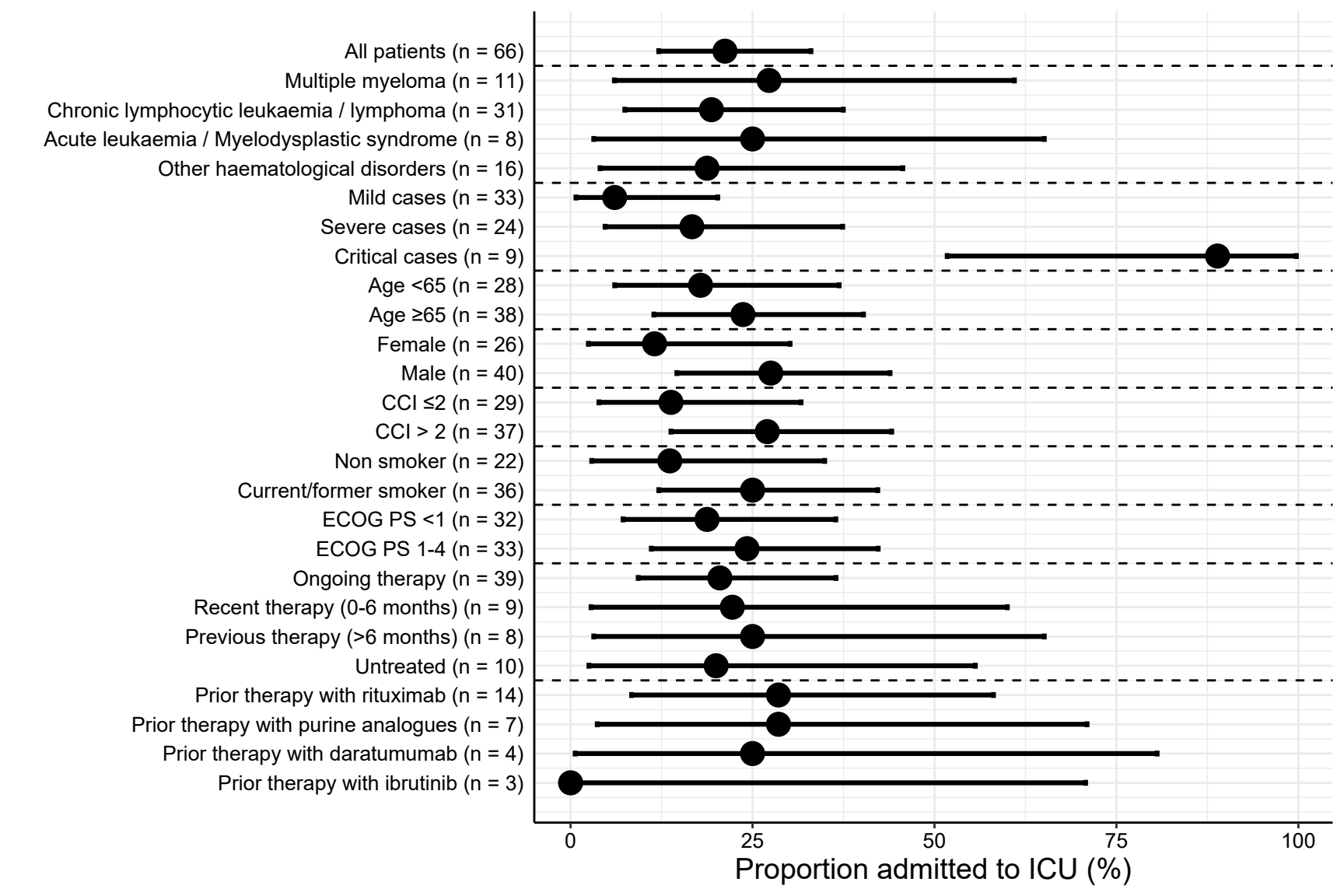
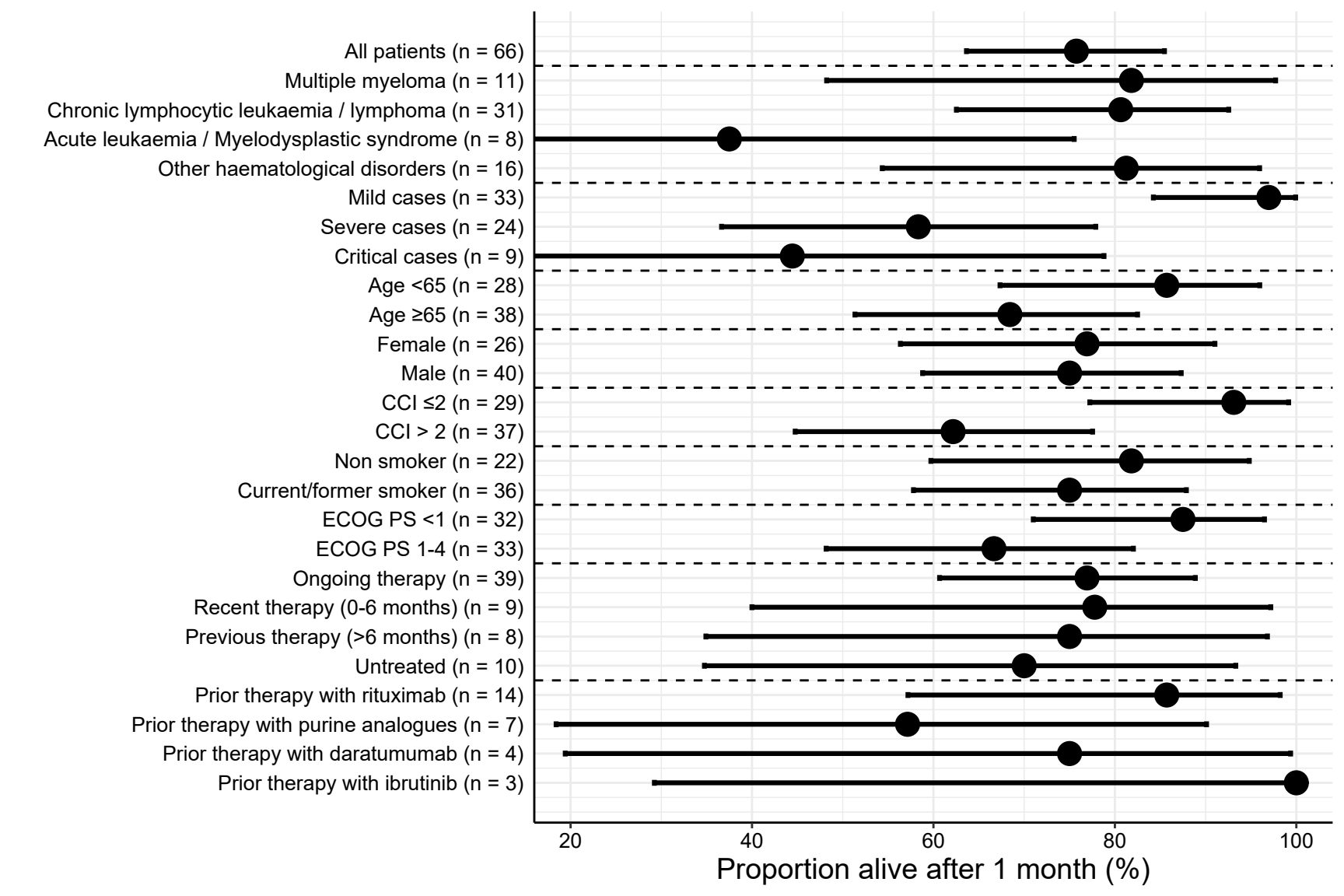

All patients (n = 66)
Multiple myeloma (n = 11)
Chronic lymphocytic leukaemia / lymphoma (n = 31)
Acute leukaemia / Myelodysplastic syndrome (n = 8)
Other haematological disorders (n = 16)
Mild cases (n = 33)
Severe cases (n = 24)
Critical cases (n = 9)
Age <65 (n = 28)
Age ≥65 (n = 38)
Female (n = 26)
Male (n = 40)
CCI ≤2 (n = 29)
CCI > 2 (n = 37)
Non smoker (n = 22)
Current/former smoker (n = 36)
ECOG PS <1 (n = 32)
ECOG PS 1-4 (n = 33)
Ongoing therapy (n = 39)
Recent therapy (0-6 months) (n = 9)
Previous therapy (>6 months) (n = 8)
Untreated (n = 10)
Prior therapy with rituximab (n = 14)
Prior therapy with purine analogues (n = 7)
Prior therapy with daratumumab (n = 4)
Prior therapy with ibrutinib (n = 3)
0
25
50
75
100
Proportion admitted to ICU (%)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Untreated (n = 10)
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Prior therapy with purine analogues (n = 7)
Prior therapy with daratumumab (n = 4)
Prior therapy with ibrutinib (n = 3)
20
40
60
80
100
Proportion alive after 1 month (%)