Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Journal of Clinical Virology 130 (2020) 104574

Contents lists available at ScienceDirect

Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv

Nosocomial outbreak of SARS-CoV-2 infection in a haematological unit – High mortality rate in infected patients with haematologic malignancies

Monika M Biernat[a,*], Aleksander Zińczuk[b], Paweł Biernat[c], Aleksandra Bogucka-Fedorczuk[d], Jacek Kwiatkowski[e], Elżbieta Kalicińska[f], Dominik Marciniak[g], Krzysztof Simon[h], Tomasz Wróbel[i]

[a] Department and Clinic of Haematology, Blood Neoplasms, and Bone Marrow Transplantation, Wroclaw Medical University, Pasteura Street 4, 50-367, Wroclaw, Poland
[b] Department of Forensic Medicine, Wroclaw Medical University, Infectious Diseases Unit, Gromkowski Regional Hospital in Wrocław, Mikulicz-Radecki Street 4, Koszarowa Street 5, 51-149 50-345, Wroclaw, Poland
[c] Department of Drugs Form Technology, Wroclaw Medical University, Borowska Street 211A, 50-556, Wroclaw, Poland
[d] Department and Clinic of Haematology, Blood Neoplasms, and Bone Marrow Transplantation, Wroclaw Medical University, Pasteura Street 4, 50-367, Wroclaw, Poland
[e] Department and Clinic of Haematology, Blood Neoplasms, and Bone Marrow Transplantation, Wroclaw Medical University, Pasteura Street 4, 50-367, Wroclaw, Poland
[f] Department and Clinic of Haematology, Blood Neoplasms, and Bone Marrow Transplantation, Wroclaw Medical University, Pasteura Street 4, 50-367, Wroclaw, Poland
[g] Department of Drugs Form Technology, Wroclaw Medical University, Borowska Street 211A, 50-556, Wroclaw, Poland
[h] Department of Infectious Diseases and Hepatology, Wroclaw Medical University, Koszarowa Street 5, 51-149, Wroclaw, Poland
[i] Department and Clinic of Haematology, Blood Neoplasms, and Bone Marrow Transplantation, Wroclaw Medical University, Pasteura Street 4, 50-367, Poland

ARTICLE INFO

Keywords:
Hospital-acquired infection
Haematological malignancies
COVID-19

ABSTRACT

Background: Here we report nosocomial outbreak of COVID-19 among patients in a haematological unit. To our knowledge this is the first report from Central Europe comparing morbidity and mortality in infected and non-infected patients after exposure to SARS-CoV-2.

Methods: The outbreak involved 39 individuals: 19 patients and 20 health care workers. The SARS-CoV-2 test by nasopharyngeal swabs was performed by real-time RT-PCR. Exposed patients were divided into two groups: quarantine patients with and without COVID-19. All patients were prospectively examined at the following time points: 0, 7 days, 14 days, 21 days and 28 days after confirmation or exclusion of SARS-CoV-2.

Results: Infection was confirmed in a total of 5/20 health care workers and 10/19 patients. Among the patients positive for SARS-CoV-2 infection, the mortality rate was 36.8 %. The probability of death in patients infected with SARS-CoV-2 increased 8-fold ($p = 0.03$). Bacterial, fungal, and viral co-infection significantly decreased survival in these patients ($p < 0.05$). Additionally, the probability of death was much higher in patients older than 40 years of age ($p = 0.032$).

Conclusion: This study showed significantly higher mortality rate in COVID-19 patients with haematologic diseases compared to the non-infected patient group. Haematologic patients with COVID-19 have 50 % less chance of survival.

1. Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic was announced on March 10, 2020 by the World Health Organization (WHO). The virus has caused severe illness in over 9 million people in 216 countries around the world and has resulted in the death of over 470,000 people [1,2]. In Poland, the first case of the novel coronavirus disease 2019 (COVID-19) was confirmed on March 4, according to the Ministry of Health. The number of active infections on June 20th was relatively low compared to other European countries with about 14,000. By June 25th, the number of infected people was 30,000+, over 1396 people have died, and the mortality rate was 2.6. Furthermore, the number of infected people in Lower Silesia has increased to 2851 and 150 people have died [3]. SARS-CoV-2 is a new coronavirus similar to SARS-CoV-1 and MERS-CoV – probably originating from bats and has the ability to activate the immune system

* Corresponding author.
E-mail addresses: monika.biernat@umed.wroc.pl (M.M. Biernat), alek.zinczuk@gmail.com (A. Zińczuk), pawel.biernat@umed.wroc.pl (P. Biernat), aleksandra.bogucka-fedorczuk@umed.wroc.pl (A. Bogucka-Fedorczuk), j.k.kwiatkowski@wp.pl (J. Kwiatkowski), elzbieta.kalicinska@umed.wroc.pl (E. Kalicińska), dominik.marciniak@umed.wroc.pl (D. Marciniak), krzysztof.simon@umed.wroc.pl (K. Simon), tomasz.wrobel@umed.wroc.pl (T. Wróbel).

https://doi.org/10.1016/j.jcv.2020.104574
Received 27 July 2020; Accepted 30 July 2020
Available online 01 August 2020

Table 1
Characteristics of patients involved in the nosocomial outbreak.

		SARS-CoV-2 positive n (%)	SARS-CoV-2 negative n (%)	Total n (%)
Number of patients		10/19 (53)	9/19 (47)	19 (100)
Male		2/5 (40)	3/5 (60)	5/19 (26.3)
Female		8/14 (57)	6/14 (43)	14/19 (73.7)
Age (median, range)		58 (30 − 69)	62 (23 − 72)	62 (23 − 72)
Diagnosis	Acute leukaemia	4/6 (67)	2/6 (33)	6/19 (31.6)
	Myelodysplastic syndrome	2/2 (100)	0/2 (0)	2/19 (10.6)
	Hodgkin lymphoma	0	1(100)	1/19 (5.2)
	Non-Hodgkin lymphoma	3/7 (43)	4/7 (57)	7/19 (36.8)
	Multiple myeloma	1/2(50)	1/2(50)	2/19 (10.6)
	Chronic lymphocytic leukaemia	0	0	0
	Aplastic anaemia	0	1/1 (100)	1/19 (5.2)
Haematologic malignancy status	First line treatment	3/7 (43)	4/7 (57)	7/19 (36.8)
	Relapsed or progression	5/7 (71)	2/7 (29)	7/19 (36.8)
	Remission	2/5 (40)	3/5 (60)	5/19 (26.3)
Comorbidities	Hypertension (HT)	5/10 (50)	2/9 (22.2)	7/19 (36.8)
	Diabetes type 2	2/10 (20)	0/9 (0)	2/19 (10.5)
	VTE	2/10 (20)	1/9 (11.1)	3/19 (15.8)
	Others	3/10 (30)	7/9 (77.7)	10/19 (52.6)
COVID-19 pneumonia	Yes	10/10 (100)	0/10 (0)	10/19 (52.6)
	No	0/9 (0)	9/9 (100)	9/19 (47.4)
ECOG status	< 2	7/15 (47)	8/15 (53)	15/19 (78.9)
	≥ 2	3/4 (75)	1/4 (25)	4/19 (21)
Outcome	Survival	3/10 (30)	7/9 (78)	10/19 (52.6)
	Non-survival	7/10 (70)	2/9 (22)	9/19 (47.4)

ECOG- Eastern Cooperative Oncology Group Performance Status, COVID-19 - novel coronavirus disease 2019, VTE -venous thromboembolic events.

uncontrollably, causing massive inflammation [4]. SARS-CoV-2 multiplies rapidly in the upper respiratory tract epithelium, and can infiltrate further into the lungs leading to inflammation, oxidative stress, thrombosis, and death [5,6]. The infection spreads rapidly from person to person through virus-laden droplets that are aerosolised during speech or by coughing [7]. The main symptoms of infection are fever, shortness of breath cough, sore throat, and loss of taste or smell. However, in many cases the infection is asymptomatic. Severe infections are also possible, especially in older people with comorbidities such as: cancer, hypertension, diabetes, obesity, cardiopathies, or chronic respiratory diseases [8,9].

In haematologic patients, the disease status with chemotherapy can lead to severe immunosuppression. This critical state may lead to the increase risk of serious SARS-CoV-2-related complications. However, clinical observations show conflicting results [10,11]. Additionally, data on the spread of the virus in the hospital environment, the course of the infection, and the outcome in this group of patients are non-existent. Due to the fact that Poland's number of cases is consistently high, it is important to implement effective infection control strategies to protect haematologic patients. Here we report a nosocomial COVID-19 outbreak among patients and medical staff in our haematological unit. We report the details for demographics, laboratory tests, clinical course, and outcome of infection in patients with haematologic malignancies, positive and negative for SARS-CoV-2. To our knowledge this is the first report on COVID-19 infections in haematologic patients from Central Europe, and the first report comparing morbidity and mortality in infected and non-infected patients after exposure to SARS-CoV-2.

2. Material and methods

Since the first COVID-19 case in Poland, visitors have been limited in both the hospital and clinic. The first ward infection was confirmed in a medical staff member on April 7th, and was considered the index case. COVID-19 diagnosis was determined by the WHO's interim guidance, where a patient must test positive for SARS-CoV-2 by two independent laboratory tests [12]. Positive cases were classified as hospital acquired if the infection was confirmed by RT-PCR and appeared 48 h after hospital admission and were in contact with the index case. Screening tests were performed on the all patients and medical staff in the ward after the infection in the index case was confirmed. SARS-CoV-2 testing was carried out by swabbing the nasopharynx region and immediately processing the sample in house at our hospital laboratory. The test was carried out twice with the Vitassay dual-generation real-time RT-PCR test using the Quant Studio 6 Flex from Applied Biosystems. The test detects the ORF1ab and N gene. Results were obtained within 8 h. SARS-CoV-2 tests were performed every seven days until a negative result was obtained. Patients were divided into two groups: patients with and without COVID-19. These patients were prospectively examined at the following time points: day of infection confirmation as 0, 7 days, 14 days, 21 days and 28 days after confirmation or exclusion of SARS-CoV-2. Demographics, laboratory data, clinical characteristics and outcome in both groups were then analysed. All patients had given their written consent to participate in and to publish the study. The study was approved by the local Bioethics Committee No 315/2020.

2.1. Statistical analyses

The analysed variables were nominal, including dichotomous. The statistical analysis was based on the assigned multi-divisional quantity tables. First, general correlations between the analysed variables were assessed using correspondence analysis and generalised analysis of main PCA components. Built PCA model was estimated using NIPALS iterative algorithm. The Convergence Criterion was set at 0.00001– setting the maximum number of iterations equal to 50. The number of components was found by determining the maximum predictive capacity Q^2 using the V-fold cross-check method, and setting the maximum number of them at Vmax = 7. The obtained optimal PCA model was

Table 2
Clinical characteristics, symptoms, laboratory results and treatment of haematological patients with and without COVID-19 at time point 0, 7, 14, 21, 28 day after confirmation or exclusion of SARS-CoV-2.

		Total (n = 19)		Infected (n = 10)						Not infected (n = 9)				p
				Not recovered Non-survival (n = 5)		Recovered (n = 5)								
						Survival (n = 3)		Non-survival (n = 2)		Survival (n = 7)		Non-survival (n = 2)		
		(n/n)	%	(n/n)	%	(n/n)	%	(n/n)	%	(n/n)	%	(n/n)	%	
Age	Under 40	4/19	21	0/10	0	1/10	10	0/2	0	3/9	33.3	0/9	0	p = 0.032
	Over 40	15/19	79	5/10	50	2/10	20	2/10	20	4/9	44.4	2/9	22.2	
Symptoms	Dyspnoea	11/19	57.9	5/10	50	3/10	30	0/10	0	1/9	11.1	2/9	22.2	p = 0.002
	Cough	7/19	36.8	1/10	10	3/10	30	1/10	10	1/9	11.1	1/9	11.1	p = 0.007
	Fever	7/19	36.8	1/10	10	1/10	10	2/10	20	1/9	11.1	2/9	22.2	p = 0.04
	Sore throat	4/19	21	0/10	0	0/10	0	0/10	0	3/9	33.3	1/9	11.1	p > 0.05
	Other symptoms	13/19	68.4	4/10	40	1/10	10	1/10	10	7/9	77.7	2/9	22.3	p > 0.05
The presence of lung infiltrates	Chest X-Ray	8/19	42.1	4/10	40	3/10	30	0/10	0	0/9	0	1/9	11.1	p = 0.02
	CT scan	4/19	21	1/10	10	1/10	10	1/10	10	1/9	11.1	0/9	0	p > 0.05
Other infections	Bacterial infection	7/19	36.8	1/10	10	1/10	10	1/10	10	2/9	22.2	2/9	22.2	p = 0.003
	Fungal infection	3/19	15.8	0/10	0	0/10	0	0/10	0	1/9	11.1	2/9	22.2	p = 0.004
	Infection caused by other viruses	3/19	15.8	1/10	10	0/10	0	0/10	0	1/9	11.1	1/9	11.1	p = 0.007
	Sepsis	3/19	15.8	0/10	0	1/10	10	0/10	0	1/9	11.1	1/9	11.1	p = 0.04
Laboratory tests results	Saturation [%;m]	97		94		96.5		97		98		93.5		p > 0.05
	WBC [G/L;m]	3.225		0.78		6.57		3.25		3.2		179.05		p > 0.05
	Neutrophil [G/L;m]	1.9		0.15		3.2		2.7		1.5		12.33		p > 0.05
	Lymphocytes [G/L;m]	0.6		0.2		0.3		0.65		0.83		21.75		p > 0.05
	Platelets [G/L;m]	107		25		64		115		109		111		p > 0.05
	Hgb [g/dl;m]	10		9.1		10.4		9.5		10		8.75		
	CRP [mg/dl;m]	14.75		140		16		27.4		3.4		165.5		p > 0.05
	PCT [ng/mL;m]	0.1		0.17		0.107		0.506		0.02		1.715		p > 0.05
	D-dimer [ug/mL;m]	3.65		4721.5		924.5		1275		1.1		10.7		p > 0.05
	Prothrombin [%;m]	78.5		62		93		69		82		68.5		p > 0.05
	Na [mmol/l;m]	140		139.5		142		137		140		142.5		p > 0.05
	K [mmol/l;m]	3.92		4.01		3.9		4.285		3.9		3.35		p > 0.05
	Creatinine [mg/dl;m]	0.7		0.56		0.43		0.96		0.7		1.95		p > 0.05
	Urea [mg/dl;m]	39		41.5		32.5		51.5		35.5		65.5		p > 0.05
	ALT [U/L;m]	20		27		32		20		18.5		31.5		p > 0.05
	ASP [U/L;m]	19.6		19.25		23.85		27.7		17		46.5		p > 0.05
	Bilirubin [mg/dl;m]	0.5		0.5		0.65		0.35		0.6		2.15		p > 0.05

(*continued on next page*)

Table 2 (*continued*)

			Total (n = 19)		Infected (n = 10)						Not infected (n = 9)				p
					Not recovered Non-survival (n = 5)		Recovered (n = 5)								
							Survival (n = 3)		Non-survival (n = 2)		Survival (n = 7)		Non-survival (n = 2)		
			(n/n)	%	(n/n)	%	(n/n)	%	(n/n)	%	(n/n)	%	(n/n)	%	
COVID-19 treatment		Hydroxychloroquine	4/19	21	3/10	30	1/10	10	0/10	0	–	–	–	–	n/a
		Tocilizumab	1/19	5.2	1/10	10	0/10	0	0/10	0	–	–	–	–	n/a
		Convalescent plasma	1/19	5.2	0/10	0	0/10	0	1/10	10	–	–	–	–	n/a
		Remdesivir + Lopinavir + Ritonavir + Tocilizumab + convalescent plasma	1/19	5.2	0/10	0	1/10	10	0/10	0	–	–	–	–	n/a
		Hydroxychloroquine + Lopinavir + Ritonavir + Tocilizumab + convalescent plasma	1/19	5.2	0/10	0	1/10	10	0/10	0	–	–	–	–	n/a
Other treatment	Antibiotic treatment	Beta-lactams	10/19	52.6	5/10	50	1/10	10	1/10	10	1/9	11.1	2/9	22.2	n/a
		Quinolones	9/19	47.4	1/10	10	3/10	30	0/10	0	5/9	55.5	0/9	0	n/a
		Macrolides	3/19	15.8	2/10	20	1/10	10	0/10	0	0/9	0	0/9	0	n/a
		Glycopeptides	6/19	31.6	1/10	10	1/10	10	1/10	10	1/9	11.1	2/9	22.2	n/a
		Tigecycline	1/19	5.3	0/10	0	1/10	10	0/10	0	0/9	0	0/9	0	n/a
		Trimethoprim-sulfamethoxazole	6/19	31.6	3/10	30	1/10	10	0/10	0	2/9	22.2	0/9	0	n/a
	Raltegravir + Emtricitabine + Tenofovir		1/19	5.3	0/10	0	0/10	0	1/10	10	0/9	0	0/9	0	n/a
	Fungal prophylaxis		16/19	84.2	5/10	50	1/10	10	1/10	10	8/9	88.9	1/9	11.1	n/a
	Glucocorticosteroids treatment		3/19	15.8	1/10	10	2/10	20	0/10	0	0/9	0	0/9	0	n/a
	Other viral treatment		13/19	68.4	3/10	30	3/10	30	0/10	0	6/9	66.6	1/9	11.1	n/a
	LMWH		9/19	47.4	1/10	10	2/10	20	2/10	20	3/9	33.3	1/9	11.1	n/a
	Oxygen therapy		10/19	52.6	5/10	50	2/10	20	0/10	0	1/9	11.1	2/9	22.2	p = 0.007
	Mechanical ventilation/ICU admission		2/19	10.5	1/10	10	1/10	10	0/10	0	0/9	0	0/9	0	p > 0.05
	Blood products supplementation		13/19	68.4	4/10	40	2/10	20	2/10	20	5/9	55.5	2/9	22.2	p > 0.05
	Moderate or severe ARDS		4/19	21	3/10	30	1/10	10	0/10	0	0/9	0	0/9	0	p > 0.05

COVID-19 - novel coronavirus disease 2019, SARS-Cov-2 - severe acute respiratory syndrome coronavirus 2, ARDS – acute respiratory distress syndrome, LMWH – low molecular weight heparin, ICU – intensive care unit, m-median.

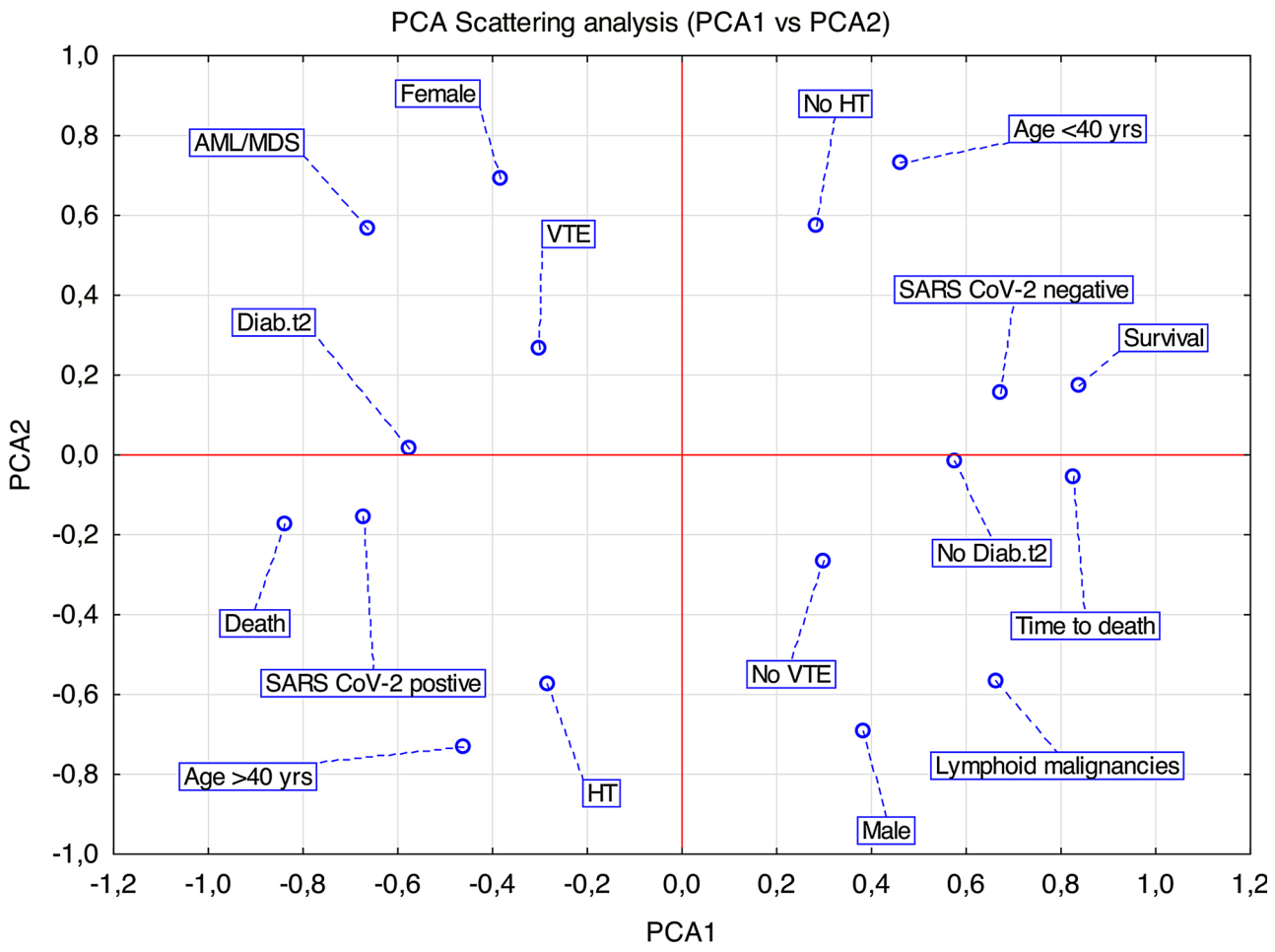

Fig. 1. Overall survival according to haematologic malignancies diagnosis in patients with COVID-19.
AML – acute myeloid leukaemia, MDS – myelodysplastic syndrome, lymphoid malignancies: T-cell lymphoma, B-cell lymphoma, multiple myeloma, acute lymphoblastic leukaemia

reduced to 2 components. The PCA analysis, the results of which are presented in the pca1 vs. pca2 load diagram, allowed to preselect the variables with the most significant impact on the built model and to select the most significant correlations between them. The variables selected were then subjected to further statistical evaluation. The statistical significance between nominal variables was evaluated by the chi-quadrant test with a Yates correction, and the accurate Fisher test. A non-parametric analysis of survival was performed based on a non-parametric model of proportional Cox gambling. In all tests a significance level of $p = 0.05$ was assumed, the assumption of proportionality of the Cox model was evaluated graphically.

3. Results

COVID-19 was confirmed in a total of 5/20 health care workers and 10/19 patients. A positive result was obtained initially in one medical staff member, a nurse who was considered as the index case and in six patients within seven days after exposure, followed by four more patients and four medical staff members after 14 days of exposure. The nurse who was the index case and one doctor with confirmed COVID-19 had symptoms of upper respiratory tract infection, two another nurses were asymptomatic. The clinical characteristics of patients involved in the COVID-19 outbreak presents Table 1. All patients exposed to SARS-CoV-2 had recently received chemotherapy or immunosuppressive treatment. COVID-19 positive patients were transferred immediately to the Infectious Diseases Unit for further treatment. A strict sanitary regime was introduced in the ward, the remaining patients were isolated and staff who had contact with the patients were quarantined for two weeks. The outbreak was reported to the local public health department. The staff who took care of the exposed and infected patients followed strict personal protective equipment guidelines, using filtering face peace (FFP)-3 masks, gowns, aprons, and gloves. After 14 days from the first contact with the index case, another 4 quarantined patients were confirmed as SARS-CoV-2 positive. These patients were immediately transferred to the infectious disease ward. The local infection control team performed contact tracing and testing until no further cases among health care workers or patients in quarantine were identified. The results among the staff after 7 days and 14 days were negative. The unit was disinfected.

Positive SARS-CoV-2 patients presented a variety of symptoms and the course of infection was different (Supplementary materials). Out of the ten COVID-19-positive patients, three displayed a fever, one had dyspnoea, and one patient had a sore throat. None of the patients complained about loss of taste or smell, so these symptoms were

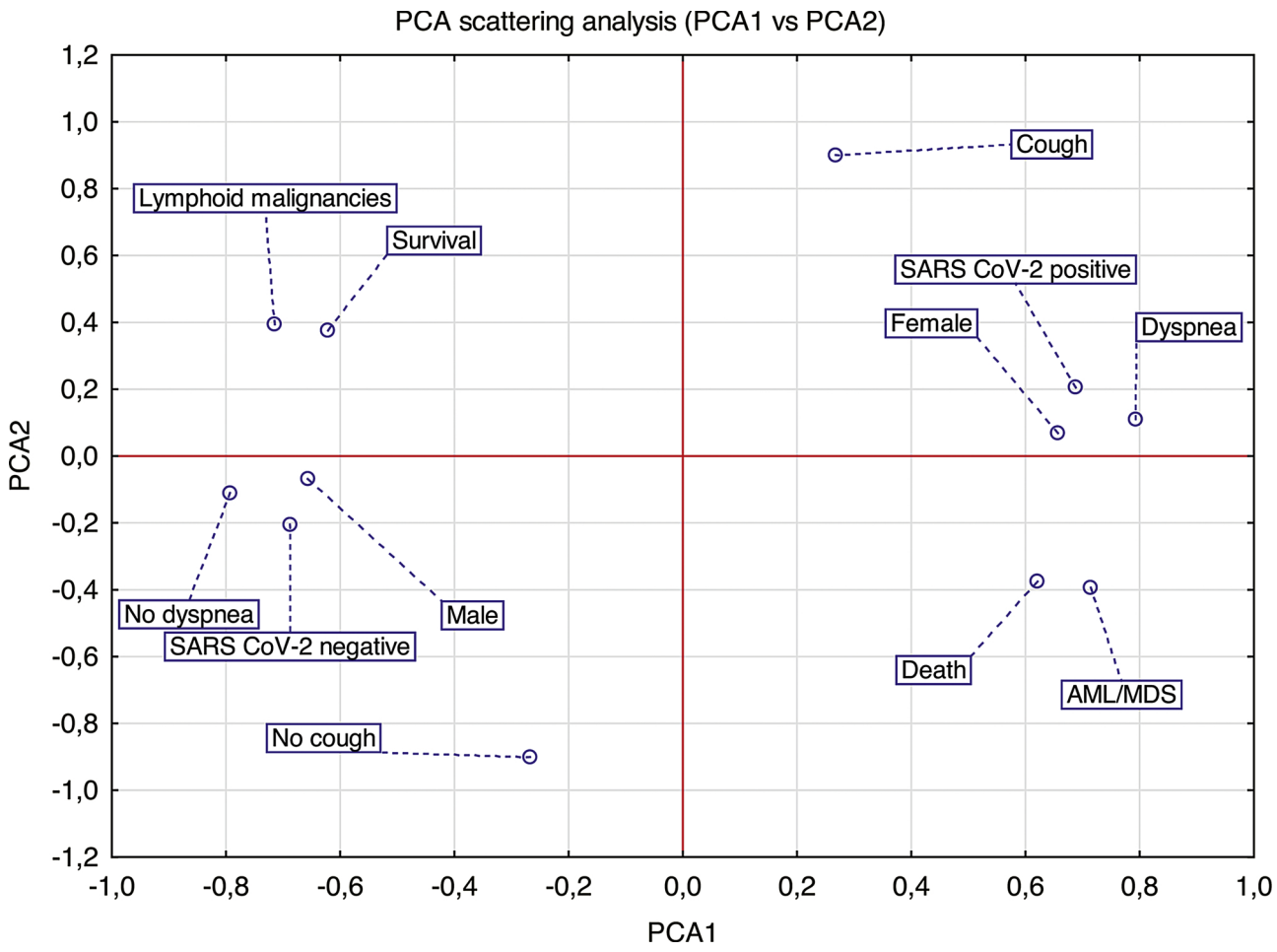

Fig. 2. Overall survival according to COVID-19 diagnosis in patients with haematological malignancies involved in outbreak.

excluded from the analysis. Tracking the symptoms that COVID-19 positive patients on day 0, 7, 14 21, 28 showed a present fever at the beginning of the infection ($p = 0.04$), dyspnoea on day 7 from infection ($p = 0.007$), and a cough on day 14 from infection ($p = 0.007$). These factors significantly increased the probability of death in haematologic patients (Table 2).

About three days before the infection was confirmed, 7/10 patients with leukopenia with lymphopenia had increased levels in C-reactive protein (CRP) and D-dimers. The infiltration was examined by chest X-ray on day 7 after confirmation of infection, indicating a significantly likelihood of increased death ($p = 0.02$). Co-morbidities were observed in 8/19 patients– with hypertension in 5/19, diabetes in 2/19, and coagulation disorders in 2/19. Two patients had concomitant viral infections including one patient with HIV, and the another patient had cytomegalovirus (CMV) reactivate during COVID-19 treatment. Four people developed acute respiratory distress syndrome (ARDS), one had liver failure, and 3 had multiple organ failure. Bacterial co-infection by 28 day, fungal and viral co-infection by 14 day ($p = 0.003$), fungal and viral co-infection by 14 day ($p = 0.004$ and $p = 0.007$) after confirmation of SARS-CoV-2 significantly increased the probability of death. Oxygen therapy, chloroquine, anti-retroviral drugs, tocilizumab, plasma from cured healthy volunteers, antibiotics, oxygen therapy were used. Of the ten patients, five died during treatment, another five achieved a negative result more than a month after the diagnosis of the infection and recovered from COVID-19. Since then, two of the five patients have died after recovering from COVID-19 due to the progression of the underlying disease. One another patient who recovered is still receiving chemotherapy for multiple myeloma, while the other two patients have not yet started their cytostatic treatment due to persistent pancytopenia and poor clinical condition. Among the patients exposed to SARS-CoV-2 infection, the mortality rate was 7/19 (36.8 %); of the infected patients, 7/10 (70 %) died. These data suggest that after contact with a person infected with SARS-CoV-2, the probability of death increased 8 times ($p = 0.03$, OR = 8.166). Taking into account the age of the examined patients, the probability of death was much higher in patients older than 40 years of age ($p = 0.032$). The difference for patients over 65 and older was not statistically significant. We examined the overall survival and showed that COVID-19 patients with acute leukaemia and MDS and compared to COVID-19 patients with lymphoid malignancies is decreased by half (Fig. 1 and Fig. 2). This data suggests patients with COVID-19 are 50 % less likely to survive by day 30 vs. without COVID-19. Furthermore, PCA multidimensional analysis showed that the highest risk of death in COVID-19-positive haematologic patients is correlated with elevated CRP and D-dimer values at the time of diagnosis, symptoms such as dyspnoea and cough, female sex, myeloid malignancies, and comorbidities as shown in Figs. Fig. 33, Fig. 44 and Fig. 55.

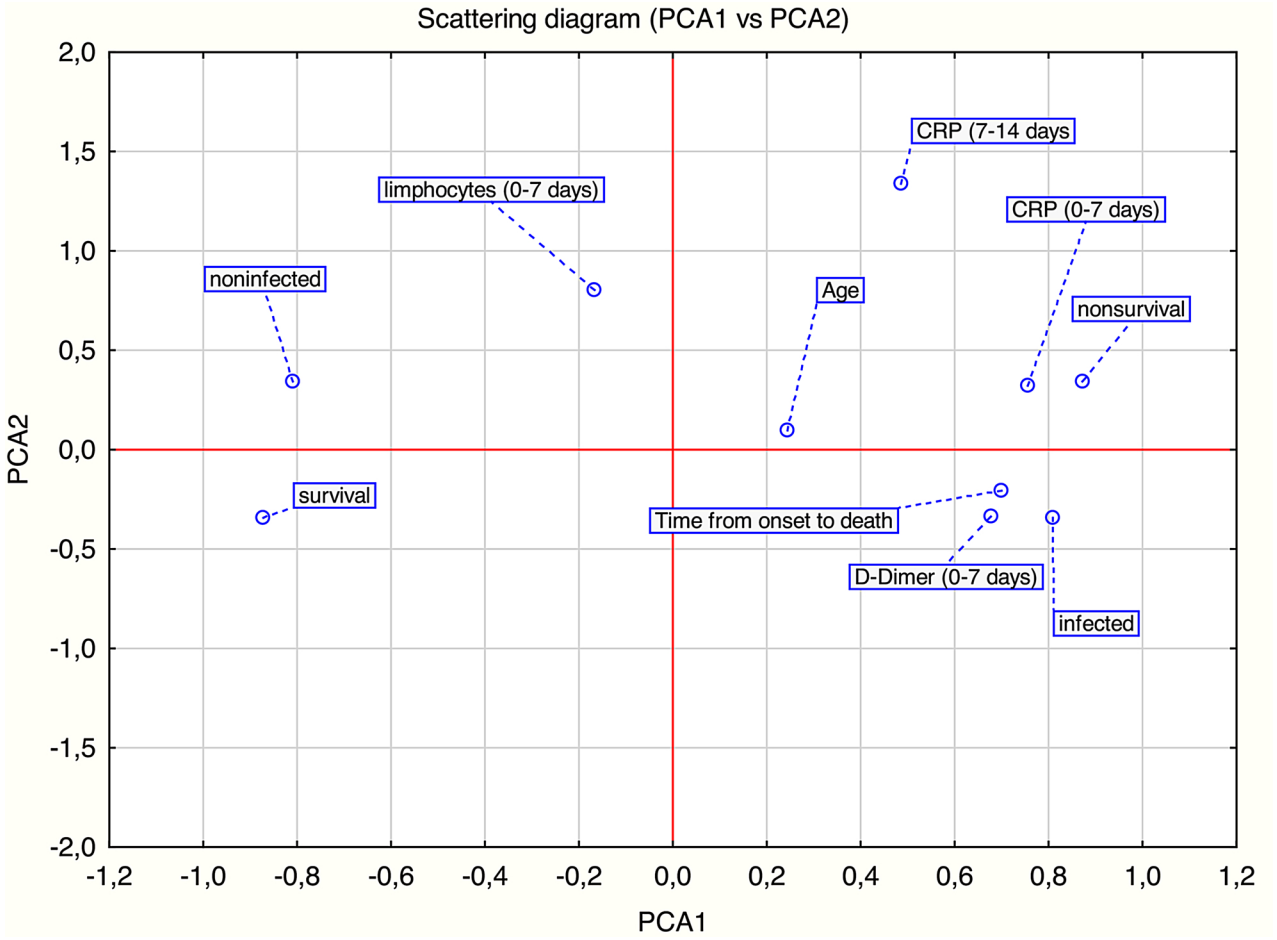

Fig. 3. The PCA analysis presented in the pca1 vs. pca2 load diagram. The variables such as CRP, number of lymphocytes, age, time from infection from death, number of survivors and deceased patients and number of infected were analysed. After analysis, the highest probability of death is noted in the group of patients over 40 years of age with COVID-19, who had high CRP and D-dimers in the first 7 days of infection.

4. Discussion

After an early epidemic introduction in Poland, the freezing of the economy, closing of schools, locking down people temporarily in their homes, and restrictions to maintain social distance and cover mouths and noses in public has resulted in a dampened spread of COVID-19. The current rate of R virus reproduction for Poland in June is 1.11, at the beginning of the epidemic it was 3.4 [3]. Authors from Wuhan, China– the initial centre of the epidemic– and from other countries show that the frequency of infection in patients with cancer is higher than in COViD-19 patients without comorbidities [13,14]. The study presents a ward outbreak of SARS-CoV-2 infection in the haematology department. To our knowledge it is the first report concerning COVID-19 positive in patients with haematologic malignancies from Poland and the first report analysing the survival of infected and not infected after exposure to SARS-CoV-2. Our observations show that COVID-19-positive patients with haematologic malignancies have 8-times higher mortality rates than non-infected patients. Moreover, the overall survival in COVID-19-positive haematologic patients was about 40 %, which is much lower than in the non-infected patients. Our study has shown that the symptoms of SARS-CoV-2 infection may be indistinguishable from other bacterial or viral infections. These observations are consistent with the clinical data from other studies [15–17]. Interestingly, the shedding of the virus may be prolonged, similarly to the influenza virus. We still detected SARS-CoV-2 after 14–21 days in the majority of the COVID-19-positive patients, which is consistent with other viral infections in patients with haematologic malignancies [16]. It is unclear whether the prolonged incubation period is related to the immunosuppression status or rather to the fact that the source virus inoculum was small that the infection was largely asymptomatic. Moreover, 4 patients were positive 14 days after contact with the index case. Others, like Wu Y et al., reported on delayed COVID-19 cases after exposure [15]. In our experience, the infectivity potential of the virus is high and it is very easy to spread in the hospital environment. The highest mortality was reported among patients with AML and MDS. Yang et al. demonstrated that patients with haematologic malignancies have poorer prognoses than patients with solid tumours [13]. The authors showed that 41 % of patients died, while mortality among our patients was slightly lower (36 %). The high mortality of patients is significantly higher due to symptoms such as ECOG > 2, dyspnoea and fever, or with elevated CRP and D-dimer at the beginning of infection. Similar observations were made by Martin-Moro et al. [18]. Co-infection with other pathogens in the course of COVID-19 infection significantly affects mortality in this group of patients. Infected patients

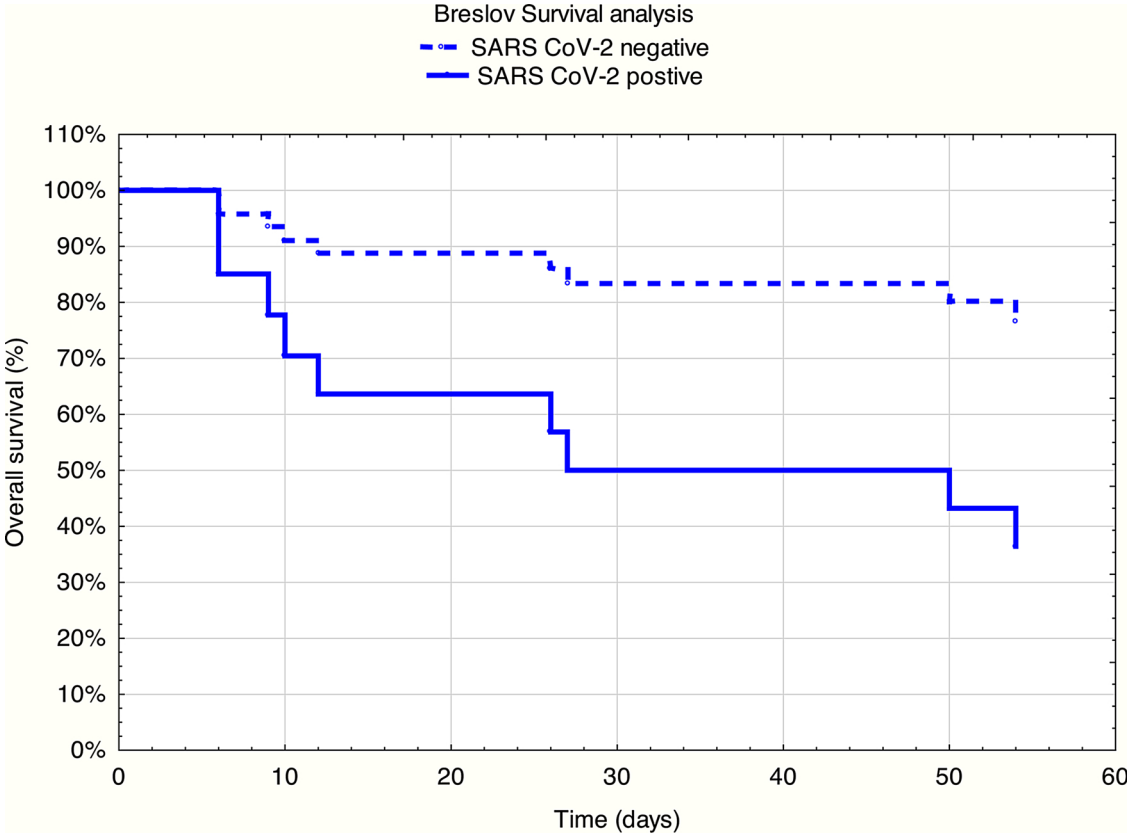

Fig. 4. The PCA analysis presented in the pca1 vs. pca2 load diagram. The variables such as dyspnoea, cough, gender, type of haematological malignancies and number of infected patients were analysed. After the analysis, the highest probability of death is noted in the group of women with AML/MDS with COVID-19 who had symptoms of dyspnoea and cough in the first 7 days of infection.

were treated with different therapy strategies. More research is needed on what treatment is most effective for this group of patients. A separate problem is the continuation of chemotherapy after curing COVID-19. Not much is known yet about the prognosis of patients with haematologic malignancies infected with SARS-CoV-2. Multi-centre studies are needed. Of our patients who have been cured, only one has continued chemotherapy. But two other patients are unfortunately unable to start cytostatic treatment due to persisting pancytopenia and poor clinical condition. This has enormous consequences for the future survival of these patients.

Despite strict control measures, the hospital environment poses a great risk of infection. Immediately after the epidemic was introduced preventive measures were installed at the hospital including mandatory screening tests were performed on patients before admission to the haematology department, screening tests among medical staff were performed every 7 days, and we are insistent on wearing barrier clothes, masks and visors. Because the medical staff can be asymptomatic, it is necessary to implement these procedures to protect immunosuppressed patients against infection. Recent studies confirm the transmission of infection by asymptomatic individuals, including health care workers [19,20]. The use of personal protective equipment and reduction of social interaction as well as isolation of patients is an effective way to reduce infection in the hospital environment [21]. Our actions were consistent with the global recommendations by our panel of experts that manage patients with acute leukaemia and myeloid neoplasms [22].

In summary, the study showed significantly higher mortality rate in haematologic patients with and without COVID-19. Patients with COVID-19 had a 50 % less chance of survival. Additionally, the risk of death in haematologic patients with COVID-19 in his population increases significantly already after 40 years of age. The use of personal protective equipment and screening tests among patients and medical staff, as well as isolating the infected was an effective way to reduce the spread of infection in the hospital environment. The main limitations of the study are the small cohort size and heterogeneous group of patients. We believe that multi-centre observational studies on a larger group of patients will better stratify of risk groups improved patient care, and improve our understanding of an effective treatment.

Authors' contributions

MMB and PB designed the study, was responsible for data analysis and interpretation, writing, AZ, MMB, EK, and KS contributed to data collection, PB and DM was responsible for statistical analyses, MMB wrote the manuscript and all authors participated in editing the manuscript, MMB, TW and KS contributed valuable ideas and participated on data analysis and interpretation.

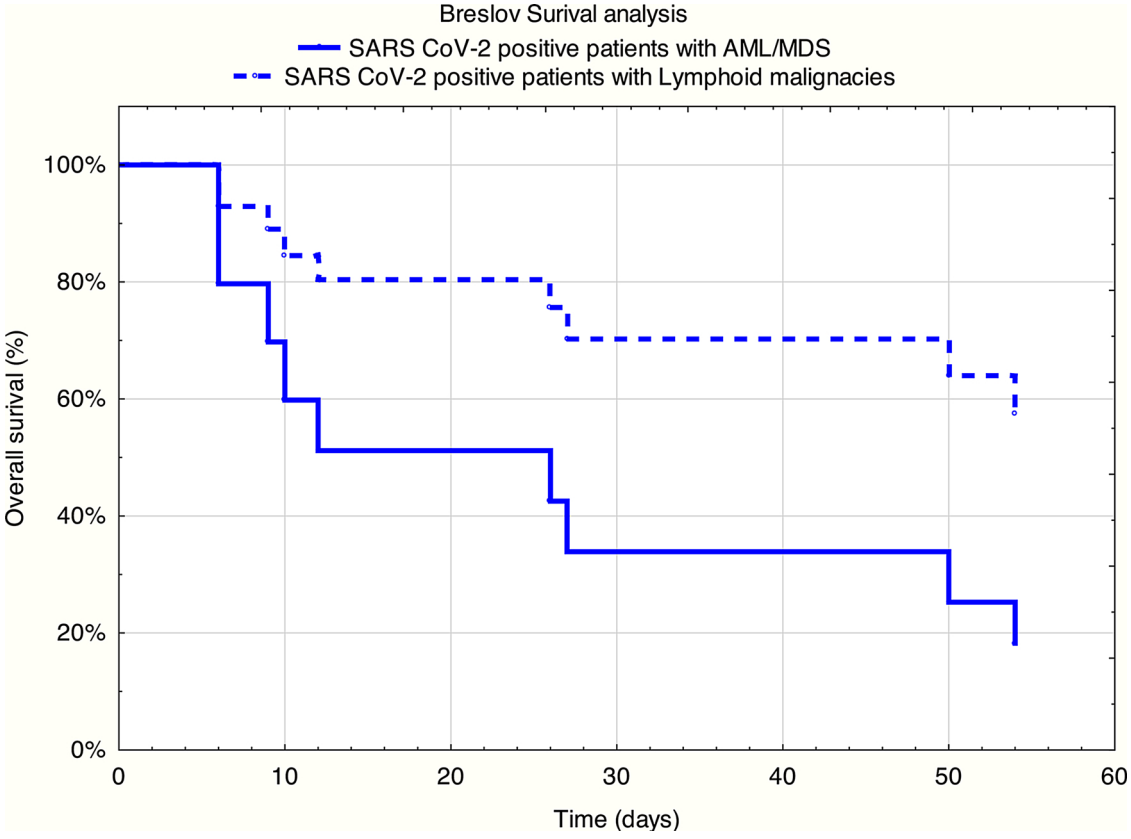

Fig. 5. The PCA analysis presented in the pca1 vs. pca2 load diagram. The variables such as age, hypertension, diabetes t.2, VTE, gender, type of haematological malignancies and number of infected patients were analysed. After the analysis, the highest probability of death is noted in the group of women older than 40 years of age with COVID-19 and hypertension. The presence of VTE and/or diabetes also increases the risk of death.
VTE – venous thromboembolism, Diab.t2 – diabetes type 2, HT – hypertension, AML – acute myeloid leukaemia, MDS – myelodysplastic syndrome, lymphoid malignancies: T-cell lymphoma, B-cell lymphoma, multiple myeloma, acute lymphoblastic leukaemia

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest

There are no conflicts of interest by all authors.

Acknowledgments

We thank Mark Jeremy Hunt and native speakers of English from Ecorrector for the correction of the manuscript.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.jcv.2020.104574.

References

[1] covid-19.who.int, data last updated 2020/6/24.
[2] Coronavirus disease, (COVID-19) In the EU/EEA and the UK – Tenth Update, 11 June 2020 ECDC, Stockholm, 2019, p. 2020.
[3] www.gov.pl/web/coronavirus/ list of coronavirus-associated infections-SARS-Cov-2, update, 25 June 2020.
[4] P. Zhou, X.L. Yang, X.G. Wang, B. Hu, L. Zhang, W. Zhang, et al., A pneumonia outbreak associated with a new coronavirus of probable bat origin, Nature 579 (March (7798)) (2020) 270–273, https://doi.org/10.1038/s41586-020-2012-7.
[5] G. Li, Y. Fan, Y. Lai, T. Han, Z. Li, P. Zhou, et al., Coronavirus infections and immune responses, J. Med. Virol. 92 (4) (2020) 424–432.
[6] X. Li, S. Xu, M. Yu, K. Wang, Y. Tao, Y. Zhou, et al., Risk factors for severity and mortality in adult COVID-19 in patients in Wuhan, J. Allergy Clin. Immunol. (2020), https://doi.org/10.1016/j.jaci.2020.04.006 Apr.
[7] F. Wu, S. Zhao, B. Yu, Y.M. Chen, W. Wang, Z.G. Song, et al., A new coronavirus associated with human respiratory disease in China, Nature 7798 (2020) 265–269, https://doi.org/10.1038/s41586-020-2008-3.
[8] Z. Wu, J.M. McGoogan, Characteristics of and important lessons from the coronavirus disease 2019 (Covid-19) outbreak in China: summary of a report of 72314 cases from the Chineses center for disease control and prevention, Jama 323 (2020) 1239–1242.
[9] W. Liang, W. Guan, R. Chen, W. Wang, J. Li, K. Xu, et al., Cancer patients in SARS–CoV-2 infection: a nationwide analysis in China, Lancet Oncol. 21 (3) (2020) 335–337.
[10] Minotti, F. Tirelli, E. Barbieri, C. Giaquinto, D. Dona, How is immunosuppressive status affecting children and adults in SARS-CoV-2 infection? A systematic review, J. Infect. 81 (2020) 62–66 Ch..
[11] R. Antonio, M. Silvia, Immunosuppression drug-related and clinical manifestation of Coronavirus disease 2019: a therapeutical hypothesis, Am. J. Transplant. (April 15) (2020), https://doi.org/10.1111/ajt.15905.
[12] World Health Organization, Clinical Management of Covid-19: Interim Guidance, WHO/2019-nCoV/clinical/2020.5. (May 27) (2020).
[13] K. Yang, Y. Sheng, Ch. Huang, Y. Jin, N. Xiong, K. Jiang, H. Lu, et al., Clinical characteristics, outcomes, and risk factors for mortality in patients with cancer and COVID-19 in Hubei, China: a multicentre, retrospective, cohort study, Lancet Oncol. S1470-2045 (20) (2020) 30310–30317, https://doi.org/10.1016/S1470-2045(20)30310-7 May 29, Online ahead of print..
[14] N.M. Kuderer, T.K. Choueiri, D.P. Shah, Y. Shyr, S.M. Rubinstein, D.R. Rivera, et al., Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study, Lancet 395 (10241) (2020) 1907–1918.
[15] Y. Wu, F. Liu, Y. Fang, X. Lu, Y. Wu, L. Xia, M. Hong, A report of clustered Covid-19 in a hematology ward, Blood Adv. 4 (12) (2020) 2736–2738.
[16] N. Lehners, J. Tabatabai, C. Prifert, M. Wedde, J. Puthenparambil, B. Weissbrich, et al., Long-term shedding of influenza virus, parainfluenza virus, respiratory syncytial virus and nosocomial epidemiology in patients with hematological disorders, PLoS One 11 (2016) e0148258.
[17] J. Yu, W. Ouyang, M.L.K. Chua, MBBS, C. Xie, SARS-CoV-2 transmission in patients with cancer at a tertiary care hospital in Wuhan, China, JAMA Oncol. (2020) e200980 March 25.
[18] F. Martín-Moro, J. Marquet, M. Piris, B.M. Michael, A.J. Sáez, M. Corona, et al.,

Survival study of hospitalised patients with concurrent COVID-19 and haematological malignancies, Br. J. Haematol. (2020) 7, https://doi.org/10.1111/bjh.16801 May.
[19] Y. Wang, H. Kang, X. Liu, Z. Tong, Asymptomatic cases with SARS-CoV-2 infection, J. Med. Virol. (2020) 1–3 PMID: 32383171.
[20] L. Rivett, S. Sridhar, D. Sparkes, M. Routledge, J.K. Jones, S. Forres, et al., Screening of healthcare workers for SARS-CoV-2 highlights the role of asymptomatic carriage in COVID-19 transmission, Elife 9 (2020) e58728, https://doi.org/10.7554/eLife.58728 May 11.
[21] A.J. Kucharski, P. Klepac, A.J.K. Conlan, S.M. Kissler, M.L. Tang, H. Fry, J.R. Gog, W.J. Edmunds, CMMID COVID-19 working group. Effectiveness of isolation, testing, contact tracing, and physical distancing on reducing transmission of SARS-CoV-2 in different settings: a mathematical modelling study, Lancet Infect. Dis. (20) (2020) S1473–3099 30457-6 June 15.
[22] A.M. Zeidan, P.C. Boddu, M.M. Patnaik, J.P. Bewersdorf, M. Stahl, R.K. Rampal, et al., Special considerations in the management of adult patients with acute leukaemias and myeloid neoplasms in the COVID-19 Era: recommendations from a panel of international experts, Lancet Haematol. 18 (2020) S2352-3026 (20) 30205-2.