

Research Article

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The Multisystem Disease COVID 19: proBNP at ICU-Admission Might Help in The Prognostication of a Patient's Hospital-Survival



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Abstract

Background: COVID-19 presents a wide spectrum of clinical manifestations from asymptomatic infection to severe pneumonia accompanied by ARDS and multisystemic failure. N-terminal-pro-B-type natriuretic peptide (NT-proBNP) has been proven to be a good predictor of outcomes in patients with ARDS and might be an indicator of severity for SARS-CoV-2 infection, too.

Methods: We conducted a single-centre, retrospective cohort study of critically ill adult patients at the intensive care unit (ICU) with confirmed COVID-19 infection at the clinical centre of Hanau, Germany. Patients were admitted from March 19th to May 25th and were followed-up until June 25th, 2020.

Results: Of 34 patients admitted for COVID-19 to the ICU, 18 (52.9%) survived and 16 (47.1%) died. The majority was male 27 (79.4%). Many patients had cardiovascular diseases 23 (67.6%), chronic kidney diseases 12 (35.3%) and thrombo-embolic events 11 (32.4%). Non-survivors were older than survivors (76.0±7.3 vs. 58.5±14.9 years; p=0.003). In non-survivors we found significant higher levels of d-dimers, creatinine, urea and lactate at ICU-admission compared to survivors. In our population, NT-pro-BNP-Level at ICU-admission could partially help in the prognostication of patients' hospital survival

Conclusion NT-proBNP may help to categorize the severity of the multisystem COVID-19 disease at admission to the ICU.

Keywords: COVID-19, pro-BNP, ARDS, multi-organ failure, cardiac insufficiency

Abbreviations: COVID-19: Coronavirus disease 2019; pro-BNP: Pro-B-Type Natriuretic Peptide, Acute Respiratory Distress Syndrome: ARDS

Introduction

Coronavirus disease 2019 (COVID-19) has spread rapidly throughout China (Wuhan, Hubei) and almost all countries around the world. Its etiological agent is the coronavirus SARS-CoV-2 [1]. On March 11th, 2020 the World Health Organization (WHO) declared a pandemic. The number of fatalities owing to COVID-19 is escalating and estimated more than 3.1 million patients died world-wide [2].

Patients with COVID-19 present with clinical symptoms of variable severity which might range from detection of virus RNA without symptoms to multiorgan failure and acute respiratory distress syndrome (ARDS) in up to 15% of patients [3,4]. It is difficult to estimate the clinical course in advance and some patients may deteriorate rapidly [3].

The immune response to SARS-CoV-2 is known to involve all the components of the immune system that together appear responsible for viral elimination and recovery from the infection [5]. In the late stage of the disease, severe cases suffer from ARDS, metabolic disorders, multiple organ dysfunction (MODS) and coagulation disorders.

Up to now the exact pathophysiological mechanisms responsible for the different clinical courses of COVID-19 patients are not clear. In some patients a severe inflammatory response might lead to a decrease and functional impairment of CD4+ T cells and CD8+ T cells, extraordinarily increased neutrophils, disseminated intravascular coagulation and finally even death [6].

In patients with ARDS of other origin Lai et al. concluded 2017 that N-terminal proB-type natriuretic peptide (NT-proBNP) is a good predictor of outcomes. B-type natriuretic peptide (BNP) was first described in the porcine brain, but BNP in humans originate primarily from the heart's ventricular myocardium. The secretion of BNP is mediated by the ventricles of the heart in response to excessive stretching of heart muscle cells. Several studies have reported that BNP or NT-proBNP was elevated in patients with ARDS. But only Determann et al. and Park et al. focused on NT-proBNP. Accordingly, this peptide may theoretically be used as an indicator of clinical severity for SARS-CoV-2 infection. In a meta-analysis including 13 observational studies and a total of 2248 patients, Sorrentino et al. [4] demonstrated that an elevated NT-proBNP level on admission is associated with a worse prognosis in COVID-19 patients [4].

Therefore, we investigated during the first wave of the pandemic in Germany whether the level of NT-proBNP is a possible predictor of mortality in patients with COVID-19.

Materials and Methods

Trial design

We conducted a single-center, retrospective cohort study of consecutive adult patients hospitalized and admitted to ICU with confirmed COVID-19 infection by positive reverse transcription polymerase chain reaction at the clinical center of Hanau, Germany. The hospital is a designated hospital to treat patients with COVID-19 and teaching hospital of the University of Frankfurt, Germany. Patients were admitted from March 19th, 2020 to May 25th, 2020, and they were followed-up until June 25th, 2020. One patient was included despite a negative SARS-CoV-2 PCR due to the typical clinical course and radiological findings in the thorax CT typical for a COVID-19 pneumonia. Clinical information was collected on admission and during ICU stay by attending physicians. This project was performed in accordance with the Declaration of Helsinki and after approval of the local Ethics Committee of the Landesärztekammer Hessen, Frankfurt, Germany (2020-1795-evBO; 28.08.2020).

Data collection

The medical records of the patients were reviewed by a trained team of physicians working in the Hospital of Hanau, Germany, during the epidemic period. Patient data including demographics, medical history, laboratory examinations, comorbidities, complications, procedures, and outcomes (death, need for intensive care unit {ICU}, intubation, mechanical ventilation, renal replacement therapy, ICU- and hospital length of stay {LOS}, and hospital discharge) were collected and analyzed.

Statistical analysis

Continuous variables are presented as mean±SD and median

(25%, 75% quartil). Categorical variables are expressed as absolute number of patients and percentage. The mean values for continuous variables were compared using independent group t tests when the data were normally distributed, otherwise, the Mann-Whitney test was used. For pro-BNP we calculated the area under the receiver operating characteristic {ROC} in respect of survival and explored the optimal cutoff value. By means of Kaplan-Meier curves, the survival of patients with pro-BNP below / above the cutoff is illustrated. A p-value less than 0.05 was considered statistically significant. Because of the explorative nature of the study, we did not perform an α -correction for multiple testing, therefore the p-values must be interpreted carefully. All statistical analyses were performed with IBM® SPSS®, version 27 for Windows.

Results

A total of 34 patients were admitted to ICU for COVID-19 during this study period. We had 18 (52.9%) survivors and 16 (47.1%) non-survivors. 27 of them were male patients (79,4%). The age of the total cohort was 67.8±13.9 years. Basic clinical characteristics and respiratory parameters before intubation and extreme values during the first 24 hours of ventilation on the ICU are shown in Table 1. The comorbidities of our patients are demonstrated in Table 2. Most of the patients had cardiovascular diseases 23 (67.6%), chronic kidney diseases 12 (35.3%) and thromboembolic events 11 (32,4%). In the absence of contraindications our patients were anticoagulated slightly elevated to reach a level between prophylactic and therapeutic anticoagulation. Laboratory data are shown at hospital admittance and the first value measured on intensive care unit (ICU) (Table 3).

All 34 patients were admitted to the ICU due to progressive respiratory failure. We treated 28 (82.4%) patients with high-flow oxygen therapy, 24 (70.6%) patients were intubated and invasively ventilated, 22 (64.7%) were prone and only 3 patients (8.8%) were non-invasively ventilated. Many patients (28, 82.4%) showed laboratory or clinical signs of kidney injury, 15 (44.1%) patients developed a new AKI, 9 (26.5%) an acute on chronic kidney injury and only 4 (11.8%) patients chronic kidney injury. 19 patients (55.9%) needed renal replacement therapy at any time during their ICU stay whereof only 4 (11.8%) had pre-existing end-stage renal disease.

From our 34 ICU patients, almost half (16, 47.1%) died during their hospital stay. Non-survivors were older than the survivors (75.5±7.3 vs. 60.9±14.9; p=0.003); the youngest non-survivor was 64 years old; the oldest survivor was 88 years old. The laboratory data demonstrated for the non-survivor group at admission on ICU increased levels of IL-6, abnormal levels for d-dimers, pro-BNP, creatinine, urea and lactate compared to survivors. The survivors had a higher paO₂ level and Horovitz index before intubation. The total duration of high-flow nasal cannula oxygenation therapy (NFHC) was longer for the survivors.

Table 1: Clinical characteristics (values are mean / median (1.; 3. Quartil); F_{iO_2} fraction of inspired oxygen, *NHFC* high-flow nasal cannula oxygen therapy, *LOS* length of stay, *NIV* non-invasive ventilation, PaO_2 partial pressure of oxygen in arterial blood, $PaCO_2$ partial pressure of carbon dioxide in arterial blood, *PEEP* positive end-expiratory pressure, P_{insp} inspiratory pressure, *RRT* renal replacement therapy).

Characteristics	Total (n= 34)		Survivor (n= 18; 52.9%)		Non-Survivor (n= 16; 47.1%)		p-value
	Mean±SD	Median (1.; 3. quartil)	Mean±SD	Median (1.; 3. quartil)	Mean±SD	Median (1.; 3. quartil)	
Basics							
Age (years)	67.9±13.9	70.0 (58.3; 78.0)	60.9±14.9	58.0 (49.0; 76.0)	75.5±7.3	76.0 (70.0; 82.0)	0.003
Hospital LOS (days)	33.9±21.9	26.0 (17.0; 78.2)	37.9±24.6	38.0 (17.0; 51.9)	29.4±18.1	23.1 (17.3; 37.6)	0.384
ICU LOS (days)	20.1±16.0	14.0 (8.9; 32.4)	20.6±17.9	13.1 (9.2; 35.8)	19.7±14.2	17.7 (6.8; 28.9)	0.901
Duration of ventilation (hours)	180.4±215.6	128.0 (2.5; 271.8)	143.2±227.8	96.0 (0; 149.8)	222.3 ±199.9	161.5 (105.5; 286.8)	0.042
Duration of RRT (days)	25.8±21.6	24.0 (6.5; 32.5)	25.8±22.3	42.5 (25.3; 58.3)	19.2±18.7	15.0 (4.0; 30.0)	0.360
Highest body temperature (°C)	40.1±0.9	39.5 (38.7; 39.7)	39.2±0.8	39.3 (38.7; 39.6)	39.4±1.1	39.6 (38.9; 40.1)	0.244
Duration of NHFC (hours)	68.2±74.7	53.0 (4.0; 92.4)	103.6±84.3	69.0 (47.6; 176.8)	30.2±37.3	4.0 (1.5; 62.5)	0.007
Before intubation							
Respiratory rate (1/min)	24.6±6.0	24.0 (21.3; 29.3)	26.2±7.3	27.5 (22.3; 31.5)	23.0±4.1	22.5 (21.3; 24.8)	0.269
F_{iO_2}	0.6±0.1	0.6 (0.6; 0.7)	0.6±0.1	0.6 (0.6; 0.6)	0.7±0.1	0.6 (0.6; 0.8)	0.094
PaO_2 (mmHg)	77.2±24.1	75 (56.7; 91.4)	88.6±23.5	84.6 (67.4; 110.1)	68.5±21.4	67.0 (50.1; 81.0)	0.067
Horovitz (PaO_2/F_{iO_2})	131.5±54.1	128.0 (95.0; 145.7)	160.2±61.0	140.9 (119.8; 199.5)	109.5±37.0	125.0 (78.0; 139.4)	0.077
Duration of NHFC (hours)	35.6±54.3	8.0 (2.8; 46.8)	43.7±70.0	7.5 (4.0; 46.8)	26.8±30.7	10.0 (2.4; 45.0)	0.744
Duration of NIV (hours)	39.5±17.0	40.0 (33.5; 45.5)	27.5±n.a.	27.5 (27.5; 27.5)	51.5±n.a.	51.5 (51.5; 51.5)	1.000
Values during first 24 hours ventilation on ICU							
Maximum P_{insp} (mmHg)	27.5±3.2	27.0 (26.0; 29.3)	27.8±2.6	27.0 (26.3; 28.5)	27.4±3.7	26.0 (26.0; 29.8)	0.613
Maximum PEEP (mmHg)	13.0±2.0	12.0 (12.0; 14.0)	13.7±2.1	13.0 (12.0; 14.8)	12.4±1.7	12.0 (12.0; 14.0)	0.183
Maximum F_{iO_2}	0.8±0.1	0.8 (0.6; 0.8)	0.7±0.2	0.7 (0.6; 0.8)	0.8±0.1	0.7 (0.7; 0.8)	0.093
P_{insp} - PEEP (mmHg)	14.4±2.3	15.0 (14.0; 15.3)	14.1±1.6	15.0 (13.3; 15.0)	14.6±2.7	14.5 (14.0; 16.0)	0.549
Minimum paO_2 (mmHg)	81.4±17.7	80.0 (67.1; 91.5)	85.2±16.9	81.0 (75.5; 93.5)	77.1±18.2	73.2 (64.3; 87.5)	0.224
Minimal Horovitz (PaO_2/F_{iO_2})	141.5±45.4	143.0 (107.8; 169.6)	159.5±50.8	151.4 (129.0; 187.2)	127.4±36.4	120.7 (107.2; 155.8)	0.125
Maximum $PaCO_2$ (mmHg)	53.6±13.3	51.0 (44.3; 59.6)	53.0±15.6	47.7 (43.4; 56.7)	54.1±10.7	54.3 (46.6; 60.0)	0.442

Table 2: Comorbidities (COPD chronic obstructive pulmonary disease, ICB intracranial bleeding, NIDDM non-insulin dependent diabetes, OSAS Obstructive sleep apnea syndrome, TIA transient ischaemic attack).

Comorbidities	(n, %)
Hypertension	22 (64.7%)
Cardiac insufficiency	8 (23.5%)
Cardiac arrhythmia	11 (32.4%)
Coronary heart disease	6 (17.6%)
Arterial vascular disease	8 (23.5%)
Carotid arteria stenosis	4 (11,8%)
Amnestic TIA/ Apoplex/ ICB	5 (14,7%)
Thrombo-embolic event	11 (32,4%)
Chronic kidney disease	12 (35.3%)
Chronic liver disease	4 (11.8%)
Malignancy	6 (17.6%)
NIDDM	6 (17.6%)
IDDM	7 (20.6%)
Autoimmune disease	2 (5.9%)
COPD	7 (20.6%)
Pulmonary fibrosis	0 (0.0%)
Asthma bronchiale	1 (2.9%)
OSAS	3 (8.8%)
Psychiatric disease	1 (2.9%)
Alcohol abusius	1 (2.9%)

Table 3: Laboratory data (values are median±SD; BNP B-type natriuretic peptide, CRP C-reactive protein, CK creatine kinase, CK-MB creatine kinase myocardial band, IL-6 interleukine-6, LDH lactate dehydrogenase, PCT procalcitonin, WBC white blood cells).

Laboratory data	Total (n= 34)		Survivor (n= 18; 52.9%)		Non-Survivor (n= 16; 47.1%)		p-value
	Mean±SD	Median (1.; 3. quartil)	Mean±SD	Median (1.; 3. quartil)	Mean±SD	Median (1.; 3. quartil)	
IL-6 at admittance (pg/ml)	257.1±660.0	84.7 (52.9; 126.2)	113.4±123.0	72.4 (40.5; 130.3)	568.4±1167	100.3 (86.5; 118.8)	0.244
First IL-6 on ICU (pg/ml)	282.3±392.4	166.7 (73.2; 277.4)	177.0±210.0	112.7 (43.8; 207.0)	402.7±513.1	186.7 (135.9; 447.1)	0.038
PCT at admittance (ng/ml)	3.5±11.9	0.5 (0.5; 1.0)	0.7±0.3	0.5 (0.5; 0.7)	9.2±20.6	0.8 (0.5; 1.5)	0.150
First PCT on ICU (ng/ml)	2.3±5.1	0.7 (0.5; 1.4)	1.9±3.9	0.5 (0.5; 1.0)	2.9±6.3	1.1 (0.5; 1.5)	0.148
CRP at admittance (mg/dl)	10.5±11.1	7.5 (2.1; 14.5)	9.6±10.5	6.8 (1.7; 12.4)	11.6±12.0	7.5 (2.2; 16.5)	0.756
First CRP on ICU (mg/dl)	17.0±11.4	15.9 (8.4; 24.7)	17.1±12.8	17.1 / 16.1 (7.1; 25.4)	16.9±10.0	15.2 (10.6; 22.5)	0.932
WBC at admittance (1000/µl)	9.3±5.9	8.2 (5.4; 9.7)	8.4±5.3	8.4 / 6.9 (5.1; 9.1)	10.2±6.5	8.8 (6.1; 11.2)	0.388
First WBC on ICU (1000/µl)	8.4±4.6	7.3 (5.2; 11.4)	7.6±3.6	7.6 / 6.1 (5.2; 10.4)	9.3±5.6	7.9 (6.0; 12.8)	0.360
First lymphocytes on ICU (1000/µl)	1.0±0.4	1.0 (0.7; 1.2)	0.9±0.4	0.93 / 1.0 (0.6; 1.2)	1.0±0.4	1.2 (0.8; 1.3)	0.343

D-Dimers at admittance (µg/l)	1512±1587	1155 (676; 1367)	1655±1924	814 (566; 16070)	1202±148	1194 (1164; 1212)	0.416
First D-Dimers on ICU (µg/l)	1506±1245	1015 (802; 1526)	1287±1087	900 (692; 1211)	1896±1472	1157 (1078; 1526)	0.037
Pro-BNP at admittance (pg/ml)	2694±1739	3109 (2066; 3737)	3109±634	3109 (2885; 3333)	2279±2823	2279 (1280; 3277)	1.000
First pro-BNP on ICU (pg/ml)	1502±1966	548 (163; 2342)	974±1609	236 (52; 840)	2294±2263	1665 (365; 3568)	0.031
Troponin T at admittance (ng/ml)	0.0±0.0	0.01 (0.01; 0.02)	0.01±0.03	0.01 (0.01; 0.02)	0.02±0.00	0.02 (0.02; 0.02)	0.212
First troponin T on ICU (ng/ml)	0.1±0.2	0.02 (0.01; 0.05)	0.01±2499.99	0.01 (0.01; 0.04)	0.03±0.25	0.03 (0.01; 0.06)	0.063
LDH at admittance (U/l)	366±153	346 (275.8; 454.3)	353±128	353 (275; 426)	272±192	272 (220.5; 458.5)	0.541
First LDH on ICU (U/l)	467±198	449 (344; 534)	452±228	367 (343; 506)	465±164	465 (364; 546)	0.234
CK-MB-fraction at admittance (%)	14.1±19.2	6.7 (3.6; 10.7)	3.3±3.3	2.0 (1.8; 3.6)	12.6±9.7	8.2 (7.3; 13.5)	0.240
First CK-MB-fraction on ICU (%)	16.8±16.1	12.4 (7.1; 22.3)	18.30±19.9	11.9 (3.5; 25.1)	14.3±6.2	12.8 (9.2; 18.5)	0.907
Creatinine at admittance (mg/dl)	2.0±2.5	1.1 (0.9; 1.6)	1.9±2.9	1.0 (0.8; 1.2)	2.2±2.12	1.4 (1.0; 2.2)	0.030
First creatinine on ICU (mg/dl)	1.9±2.3	1.0 (0.8; 1.7)	1.7±2.6	0.9 (0.8; 1.0)	2.2±2.0	1.2 (1.1; 1.9)	0.006
Urea at admittance (mg/dl)	55.9±42.3	42.0 (29.0; 67.3)	40.9±26.7	30.5 (26.3; 47.0)	72.8±50.6	58.0 (43.0; 79.3)	0.004
First urea on ICU (mg/dl)	52.9±36.3	38.5 (26.0; 63.5)	39.2±29.0	26.0 (25.0; 41.3)	68.3±38.3	61.0 (40.8; 78.0)	0.002
CK at admittance (U/l)	608.4±1527.0	203.5 (86.5; 543.0)	789±1908	195 (72; 628)	292±238	204 (137; 438)	0.973
First CK on ICU (U/l)	1013±3509	128 (67; 245)	672±1386	113 (61; 329)	1396±4962	142 (79; 244)	0.704
First hemoglobin on ICU (g/dl)	11.8±2.1	11.8 (10.0; 13.5)	12.3±1.9	12.3 (11.4; 13.8)	11.2±2.3	10.4 (9.8; 12.4)	0.088
First lactate on ICU (mmol/l)	2.3±2.8	1.4 (1.1; 2.1)	1.7±1.4	1.3 (1.0; 1.5)	3.0±3.7	1.7 (1.3; 2.7)	0.084
Maximum lactate in first 24 hrs on ICU (mmol/l)	5.8±4.9	3.5 (2.4; 7.4)	1.9±1.3	1.5 (1.4; 1.7)	3.5±3.6	2.2 (1.7; 3.8)	0.044
Fluid balance (ml) after first complete day in ICU	1071.3±1029.2	1095 (335; 1870)	999±933	655 (360; 1583)	1205±1171	1205 (275; 2070)	0.608

Because of the described elevation of pro-BNP in ARDS and its potential use as a prognostic marker in ARDS we looked in more detail at the pro-BNP level at admittance on ICU and survival. We calculated the receiver operating characteristic (ROC) curve for pro-BNP in respect of survival, which resulted in an AUC of 0.760 ($p = 0.007$). This is a hint, that pro-BNP is a significant predictor of the survival. We received a pro-BNP value of >244 pg/ml as the optimal cut-off value for our sample. With this cutoff value the sensitivity is 1 and the specificity 0.533. As the adjacent cutoff-value

is 252, we determined 250 as optimal cutoff.

The Kaplan-Meier analysis (Figure 1) shows the survival of patients with proBNP ≤ 250 pg/ml vs. patients with proBNP > 250 pg/ml. All patients with proBNP ≤ 250 pg/ml survived until their hospital discharge, which is their censoring time. Only 32% of the patients with proBNP > 250 pg/ml could be discharged alive. The curve illustrates the times of the successive deaths and censorings (discharge alive).

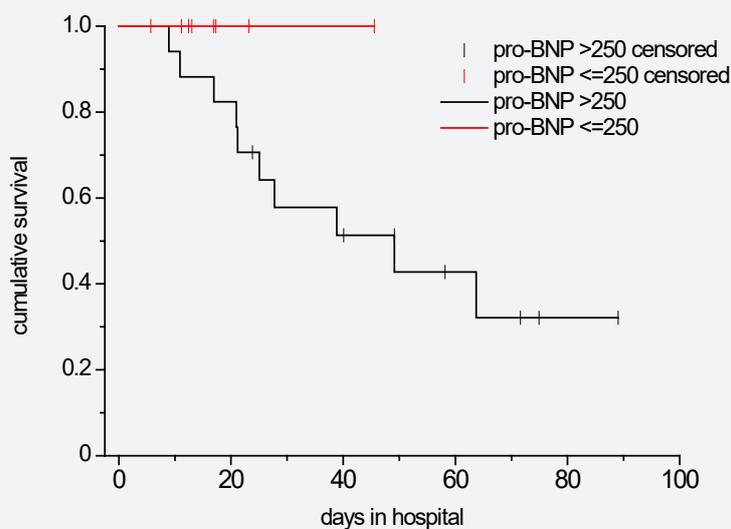


Figure 1: Kaplan-Meier analysis.

Kaplan-Meier analysis showing the survival of patients with proBNP \leq 250 pg/ml vs. patients with proBNP $>$ 250 pg/ml when measured at admittance on ICU. All patients with proBNP \leq 250 pg/ml survived until their hospital discharge, which is their censoring time. Only 32% of the patients with proBNP $>$ 250 pg/ml could be discharged alive. The curve illustrates the times of the successive deaths and censorings (discharge alive).

Discussion

In this retrospective analysis of 34 ICU patients with respiratory insufficiency due to a COVID-19 infection during the first part of the pandemic in a municipal hospital in Germany we found clinical courses similar to those in other studies [7,8]. Severe respiratory failure in patients with SARS-CoV-2 infection is only one sign of the multisystem inflammatory syndrome [9-11], which is consistent with the high rate of patients with renal failure and the need for renal replacement therapy in more than half of the patients [12,13]. The high rate of multiorgan failure together with the increased age of our patients may at least partially explain the high mortality of our patients which is comparable to data from other studies with COVID-19 ICU patients [14].

More than two third of our patients were invasively ventilated and only a minority was non-invasively ventilated because at that time - during the "first wave" in Germany - we worried about an increased risk of transmission for the ICU staff with the use of non-invasive ventilation. Accordingly, we suggested a reduced risk of transmission of SARS-CoV-2 when patients were intubated timely. In the meantime, it has been demonstrated that is reasonable, safe and recommended in the guideline to try nasal-high flow oxygen and non-invasive ventilation in patients with respiratory insufficiency due to COVID-19 when patients are closely monitored [2,15-18].

Very soon after the first patients with COVID-19 had been treated it was recognized that there is an increased risk for thrombo-embolic events in these patients due to an inflammatory

alteration of the endothelium and an inflammatory pro-coagulatory state [19,20]. It was difficult and potentially misleading to count the number of thrombo-embolic events in our patients because we did not screen systematically for these events as other groups did [20].

The major finding in this - small group - of patients with COVID-19 is that an elevated pro-BNP level on admission to the ICU shows the tendency of a worse prognosis.

Many clinical data described a cardiovascular manifestation induced by this viral infection especially in critical ill patients. Acute myocardial injury manifested mainly by elevated levels of high-sensitive troponin I, and arrhythmias have been detected [9,21]. Guo et al. [3] reported in their study among 187 patients with COVID-19, 52 (27.8%) exhibited myocardial injury as demonstrated by elevation of troponin T (TnT) levels, and the mortality was markedly higher in patients with elevated TnT levels than in patients with normal TnT levels (59.6% vs 8.9%). The authors suggest that myocardial injury due to the inflammation might play a major role in the clinical deterioration of COVID-19 patients and that those patients with elevated troponin T levels (27.8% of patients) had more malignant arrhythmias and a higher mortality [3]. Consistent with our results of increased levels of pro-BNP in non-survivors they found a correlation between elevated pro-BNP and troponin T levels [3].

In our group of non-survivors TnT levels were a bit higher at admission to the ICU (0.03 ± 0.25) and proBNP was significantly higher in the non-survivor group (2294 ± 2263 ; $p = 0.031$)

compared to the survivors. The comorbidities of our patients represented mostly cardiovascular diseases, hypertension on top of all (64.7%). Alvarez-Garcia et al. [5] pointed out that patients with a history of heart failure (HF) hospitalized for COVID-19 face nearly 3 times the risk of mechanical ventilation and twice the risk of mortality compared with patients without HF [5]. Similar to our results Sorrentino et al. demonstrated a correlation between increased pro-BNP levels and severity of COVID-19 disease but in contrast in their study the pro-BNP levels in non-survivors were already increased at admittance to hospital compared to survivors [4]. In our investigation patients with COVID-19 had also elevated levels of proBNP at admission to the hospital. Thus, we learned from several investigations during the pandemic that predictors of a fatal outcome in COVID-19 cases included age, the presence of underlying diseases, the presence of secondary infection and elevated inflammatory indicators in the blood [5,14,22,23]. Although the high accuracy of NT-proBNP is already established in the diagnosis of acute heart failure, the prognostic value of this marker for patients with COVID-19 remains uncertain [4].

Our study has several limitations. Only 34 patients with COVID-19 were included during the first wave in Germany, and a larger randomized cohort study is needed to verify our conclusions. Unfortunately, we could not provide more information regarding cardiovascular complications as e.g., cardiovascular ultrasound or detailed hemodynamic monitoring. Due to the restricted options and the increased efforts in the isolation ward data was not complete in all patients.

Last but not least, the data of this retrospective study permit a preliminary assessment of the clinical course and outcomes of patients with COVID-19.

The causes of death may involve multiple organ dysfunction in most cases, and it is difficult to differentiate the myocardial injury as the main and direct cause in an individual case. Long-term observation and prospective study design on the effectiveness of treatments are needed. We still have to wait for long-term results after surviving Covid-19 disease [24].

Conclusion

Many critically ill patients with COVID-19 pneumonia suffer from multi-organ dysfunction including cardiac insufficiency. We concluded the measurement of specific laboratory data as NT-proBNP may help to categorize the severity of the COVID-19 disease at admission to the ICU.

Declarations

○ Ethical approval was given before analysing data by the „Ethik-Kommission bei der Landesärztekammer Hessen“, Germany (2020-1795-evBO; 28.08.2020), Hanauer Landstraße 152, 60314 Frankfurt, Fon: 0049 69 97672-314, Fax: 0049 69 97672-377, E-Mail: ethikkommission@laekh.de, <https://www.laekh.de/fuer-aerztinnen-und-aerzte/rund-ums-recht/ethik-kommission>

○ Due to the retrospective design it was not possible to get „informed consent“ for study participation and in the approval by the „Ethik-Kommission bei der Landesärztekammer Hessen“, Germany (2020-1795-evBO; 28.08.2020) our study design and procedure was accepted due to the anonymous retrospective analysis of the data.

○ This project was performed in accordance with the Declaration of Helsinki.

- Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request

Competing Interests

The authors declare that they have no competing interests.

Authors' contributions

MC and MG had the idea for the study, planned it and carried it out. MOF supported the study design and MG and MOF wrote the manuscript. MAW had the idea to the study and made substantial reviews. MHG did the statistical analysis.

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