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ORIGINAL ARTICLE

Extracorporeal membrane oxygenation in coronavirus disease 2019

A nationwide cohort analysis of 4279 runs from Germany

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BACKGROUND In the context of the coronavirus disease 2019 (COVID-19) pandemic, many retrospective single-centre or specialised centre reports have shown promising mortality rates with the use of extracorporeal membrane oxygenation (ECMO) therapy. However, the mortality rate of an entire country throughout the COVID-19 pandemic remains unknown.

OBJECTIVES The primary objective is to determine the hospital mortality in COVID-19 patients receiving veno-venous ECMO (VV-ECMO) and veno-arterial ECMO (VA-ECMO) therapy. Secondary objectives are the chronological development of mortality during the pandemic, the analysis of comorbidities, age and complications.

DESIGN Cohort study.

SETTING Inpatient data from January 2020 to September 2021 of all hospitals in Germany were analysed.

PARTICIPANTS All COVID-19-positive patients who received ECMO therapy were analysed according to the appropriate international statistical classification of diseases and related health problem codes (ICDs) and process key codes (OPSs).

MAIN OUTCOME MEASURES The primary outcome was the hospital mortality.

RESULTS In total, 4279 COVID-19-positive patients who received ECMO therapy were analysed. Among 404 patients treated with VA-ECMO and 3875 treated with VV-ECMO, the hospital mortality was high: 72% ($n = 291$) for VA-ECMO and 65.9% ($n = 2552$) for VV-ECMO. A total of 43.2% ($n = 1848$) of all patients were older than 60 years with a hospital mortality rate of 72.7% ($n = 172$) for VA-ECMO and 77.6% ($n = 1301$) for VV-ECMO. CPR was performed in 44.1% ($n = 178$) of patients with VA-ECMO and 16.4% ($n = 637$) of patients with VV-ECMO. The mortality rates widely varied from 48.1 to 84.4% in individual months and worsened from March 2020 (59.2%) to September 2021 (78.4%).

CONCLUSION In Germany, a large proportion of elderly patients with COVID-19 were treated with ECMO, with an unacceptably high hospital mortality. Considering these data, the unconditional use of ECMO therapy in COVID-19 must be carefully considered and advanced age should be considered as a relative contraindication.

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KEY POINTS

- In Germany, a large proportion of elderly with COVID-19 were treated with ECMO, with an unacceptably high hospital mortality.
- During the pandemic, no reduction in mortality was observed until September 2021.
- A high rate of complications, for example, cerebral haemorrhage was observed.

Introduction

A new highly transmissible coronavirus struck the city of Wuhan in China's Hubei province in late December

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2019, representing the first known epicentre to date. The Coronavirus Study Group of the International Committee on Taxonomy of Viruses termed the virus SARS-CoV-2.[1] Infection with the SARS-CoV-2 virus, that is, the coronavirus disease, has led to a global pandemic and claimed the lives of millions of people. Although most people affected do not develop severe respiratory symptoms, COVID-19 can lead to severe respiratory failure in the setting of COVID pneumonia. The treatment of severe acute respiratory distress syndrome (ARDS) often requires the use of mechanical ventilation and prone positioning therapy. However, COVID-ARDS can cause severe gas exchange disorders that require extracorporeal membrane oxygenation (ECMO). ECMO is a technique that can reduce mortality in severe cases of ARDS. The recommendation of ECMO therapy for lung and/or heart replacement in selected COVID-19 patients has been made by several organisations.[2–4]

For the cohort of COVID-19 patients who require ECMO therapy, only observational studies are available, which reported similar results to those of ECMO therapy for non-COVID-19 ARDS.[5] Key findings are that patients with severe hypoxaemia who start ECMO therapy earlier after admission, the influence of a high-case volume in the previous year and lower age was associated with improved survival.[6,7] In a large international observational study of the ELSO registry, it was shown that for COVID-19 patients treated with ECMO after 02 May 2020, mortality increased to 53%, which illustrates that changes during the pandemic can occur and that it remains unclear, which patients benefit from ECMO therapy.[8]

This study examines the mortality in all COVID-19 patients across Germany who required ECMO therapy using data from the German Institute for Hospital Remuneration System (InEK) and assesses possible influences on mortality.

Methods

Objectives

The primary objective was to determine the hospital mortality in patients who suffer from COVID-19 and received venovenous-ECMO (VV-ECMO) and venoarterial-ECMO (VA-ECMO) therapy. The primary outcome was hospital mortality.

Secondary objectives were the chronological development of mortality during the pandemic, the analysis of comorbidities, age and complications. The secondary outcome were the hospital mortality for each month from January 2020 to September 2021 and the proportion of comorbidities, age and complications between the survivors and nonsurvivors.

Inclusion criteria

All patients with proven SARS-CoV-2 infection and ECMO therapy between 01 January 2020 and 30 September 2021 in Germany were included.

Definitions and data acquisition

In Germany, all hospitals are required by law to report the data of all inpatients in an anonymised form to the InEK for the continuing development of the DRG system. Since 2020, access to these data has been possible during the year, albeit with considerable restrictions for the public. For this observational study, we used performance data provided by InEK. As the register data were anonymised, no ethical approval was required.

SARS-CoV-2 infection was defined by ICD code U07.1. ECMO therapy was defined by procedure codes 8-852.3x for VA-ECMO and 8-852.0x for VV-ECMO. The dataset contains demographic data, procedures, diagnoses, outcomes and lengths of stay. Due to interannual access, only highly aggregated data can be retrieved, and the composition of the search query is limited.

The Patient Clinical Complexity Level (PCCL) score is calculated in a complex procedure from the secondary diagnosis values (complication or comorbidity level values – CCL) and indicates the severity of the complication or comorbidity (CC) based on results between 0 (no CC) and 6 (most severe CC). The PCCL was designed to reflect the cumulative effect of the patient's comorbidities.[9] PCCL was used in this analysis to compare the severity of the disease levels of the patients.

Statistical analysis and outcome

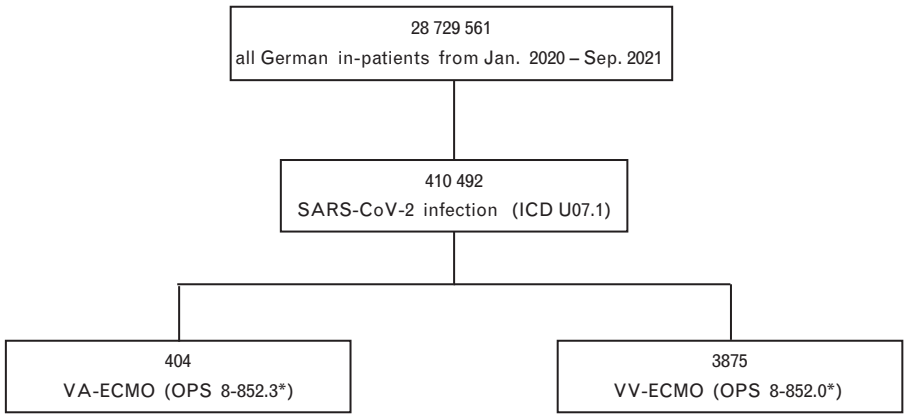
The data were descriptively analysed. The mortality rate was stratified by different ECMO modes, age groups, PCCL and hospital size. Due to the aggregated data, only group comparisons of categorical variables were possible. For this purpose, the Pearson χ^2 test was used and the relative risk was determined with the 95% confidence interval. Excel for Mac (Release 16.37, Microsoft Corp., Seattle, Washington, USA) and Python with scipy and stats Packages was used for the analyses.

Results

A total of 4279 hospital cases with confirmed COVID-19 and ECMO support were identified in Germany from 01 January 2020 to 30 September 2021 (Fig. 1). Of these, 404 received VA-ECMO, and 3875 received VV-ECMO. A total of 56.7% ($n = 2199$) of all VV-ECMO and 57.4% ($n = 232$) of all VA-ECMO patients were younger than 60 years. Men were more common with 77% ($n = 311$) and 74.6% ($n = 2892$) for VA-ECMO and VV-ECMO, respectively.

The in-hospital mortality was high at 72% ($n = 291$) and 65.9% ($n = 2552$) for VA-ECMO and VV-ECMO patients, respectively. In the individual age groups, mortality was the highest among those more than 80 years of age, with 92.9% ($n = 14$) under VV-ECMO. In the VV-ECMO group, mortality was 77.6% ($n = 1301$) for patents over 60years of age and 56.9% ($n = 1251$) for those under 60 years of age. In the VA-ECMO group, the mortality

Fig. 1 Patient flow chart



rate was 72.7% ($n = 125$) for patients over 60 years of age and 71.6% ($n = 166$) for patients under 60 years of age. The relative risk increased by 1.37 (1.31 to 1.43) for VV-ECMO in patients older than 60 years.

The mortality rate among the venoarterial and venovenous groups over the pandemic period widely varies (Fig. 2). In the venovenous group, mortality increased from 57.4% ($n = 93$) in March 2020 to over 84% ($n = 63$) in September 2021. In September 2020 ($n = 38$) and September 2021 ($n = 63$), mortality was highest at 84% for VV-ECMO and December 2020 ($n = 16$), June ($n = 4$) and August 2021 ($n = 10$) at 100% for VA-ECMO.

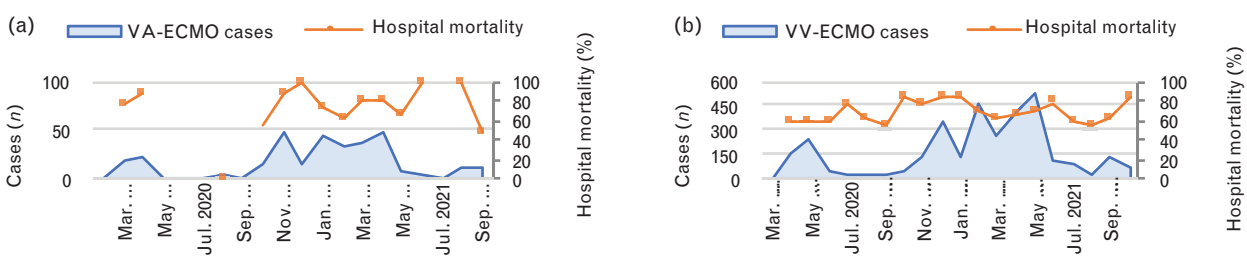
Comorbidities and complications in the patients are shown in Table 1. Although low rates of persistent renal failure are indicated, high rates of dialysis are observed, particularly in the deceased patients. The relative risk increased by 2.99 (2.25 to 3.9) in patients requiring dialysis in VA-ECMO and by 4 (3.35 to 4.77) in VV-ECMO (Table 2). Intracerebral haemorrhage occurred in 2.2% ($n = 9$) and 12.3% ($n = 476$) of VA-ECMO and VV-ECMO patients in this study. The relative risk increased by 1.5 (1.45 to 1.56) for VV-ECMO in the presence of intracerebral haemorrhage. The number of CPRs was 44.1% ($n = 178$) in the venoarterial group and 16.4% ($n = 637$) in the VV-ECMO group.

Considering the hospital size based on the number of beds, 64.5% ($n = 2\ 760$) of all ECMO patients were treated in a hospital with more than 800 beds. Combined, mortality was 67% ($n = 1\ 690$) and 78% ($n = 187$) in hospitals with more than 800 beds and 62.1% ($n = 780$) and 61% ($n = 60$) in hospitals with less than 800 beds in the VV-ECMO and VA-ECMO groups, respectively.

In hospitals with more than 800 beds, patients were younger with a proportion of 59% ($n = 1569$) in the less than 60 years group compared with 52% ($n = 757$) treated in hospitals with less than 800 beds but they were more severely ill considering the proportion of the PCCL level 4 to 6 of 65.6% ($n = 1743$) to 52.5% ($n = 764$).

The mean length of stay for survivors was 43.1 ± 38.4 days for the VA-ECMO group and 43.2 ± 27.4 days for the VV-ECMO group.

Fig. 2 Hospital mortality and case volume



Hospital mortality (%) and case volume (n) in VA-ECMO (a) and VV-ECMO (b) from January 2020 to September 2021. VA-ECMO, venoarterial extracorporeal membrane oxygenation; VV-ECMO, venovenous extracorporeal membrane oxygenation.

Table 1 Patient characteristics

		Total	VA-ECMO Survivor *n* (%)	Non-survivor *n* (%)	Total	VV-ECMO Survivor *n* (%)	Non-survivor *n* (%)
Total	n	404	113 (28)	291 (72)	3875	1323 (34.1)	2552 (65.9)
PCCL	2	23	10 (8.8)	13 (4.5)	345	127 (9.6)	218 (8.5)
	3	107	26 (23)	81 (27.8)	1039	317 (24.0)	722 (28.3)
	4	143	29 (25.7)	114 (39.2)	1328	404 (30.5)	924 (36.2)
	5	99	31 (27.4)	68 (23.4)	859	353 (26.7)	506 (19.8)
	6	22	12 (10.6)	10 (3.4)	182	70 (5.3)	112 (4.4)
Sex	Male	311	83 (73.5)	228 (78.4)	2892	945 (71.4)	1 947 (76.3)
	Female	92	30 (26.5)	62 (21.3)	983	378 (28.6)	605 (23.7)
Age-groups (years)	<18	5	1 (0.9)	4 (1.4)	4	3 (0.3)	1 (0.0)
	18 to 49	104	30 (26.5)	74 (25.4)	899	462 (34.9)	437 (17.1)
	50 to 59	123	35 (31)	88 (30.2)	1 296	483 (36.5)	813 (31.9)
	60 to 64	65	17 (15.0)	48 (16.5)	758	270 (20.4)	488 (19.1)
	>65	91	21 (18.6)	70 (24.1)	924	169 (12.8)	755 (29.6)
Hospital size (beds)	>1000	167	36 (31.9)	131 (45.0)	1808	573 (43.3)	1 235 (48.4)
	800 to 999	72	16 (14.2)	56 (19.2)	713	258 (19.5)	455 (17.8)
	600 to 799	30	12 (10.6)	18 (6.2)	406	115 (8.7)	291 (11.4)
	300 to 599	57	24 (21.2)	33 (11.3)	687	278 (21.0)	409 (16.0)
	<300	11	2 (1.8)	9 (3.1)	153	73 (5.5)	80 (3.1)
Comorbidities	Congestive heart failure	290	89 (78.8)	201 (69.1)	1111	289 (21.8)	822 (32.2)
	Hypertension	182	58 (51.3)	124 (42.6)	1 842	682 (51.5)	1 160 (45.5)
	Chronic pulmonary disease	12	0 (0.0)	12 (4.1)	493	178 (13.5)	315 (12.3)
	Diabetes	74	19 (16.8)	55 (18.9)	1045	341 (25.8)	704 (27.6)
	Renal failure	10	0 (0.0)	10 (3.4)	258	59 (4.5)	199 (7.8)
	Obesity	39	8 (7.1)	31 (10.7)	850	353 (26.7)	497 (19.5)
	Cardiac arrhythmias	250	81 (71.7)	169 (58.1)	1718	498 (37.6)	1 220 (47.8)
Complications	Intracerebral bleeding	9	0 (0.0)	9 (3.1)	476	33 (2.5)	443 (17.4)
	Ischaemic Stroke	5	0 (0.0)	5 (1.7)	79	17 (1.3)	62 (2.4)
	Arterial embolism/thrombosis	12	4 (3.5)	8 (2.7)	97	34 (2.6)	63 (2.5)
	Myocardial infarction	21	6 (5.3)	15 (5.2)	76	23 (1.7)	53 (2.1)
	Cardiac arrest	178	30 (26.5)	148 (50.9)	637	107 (8.1)	530 (20.8)
	Dialysis	285	30 (26.5)	255 (87.6)	3 322	872 (65.9)	2 450 (96.0)
	Pulmonary embolism	80	25 (22.1)	55 (18.9)	575	193 (14.6)	382 (15.0)

Patient characteristics of all COVID-19-positive patients treated with ECMO in Germany from January 2020 to September 2021. PCCL, Patient Clinical Complexity Level; VA-ECMO, venoarterial extracorporeal membrane oxygenation; VV-ECMO, venovenous extracorporeal membrane oxygenation.

Table 2 Relative risk and 95% confidence intervals for hospital mortality

		Relative risk	VA-ECMO 95% CI	*P*	Relative risk	VV-ECMO 95% CI	*P*
Sex	Female (ref.: male)	0.92	(0.79 to 1.08)	0.328	0.85	(0.73 to 0.93)	0.001
Age groups (years)	≥60 (ref.: <60)	1.01	(0.9 to 1.14)	0.921	1.37	(1.31 to 1.43)	<0.0001
Hospital size	>800 (ref.: ≤800)	1.24	(1.05 to 1.46)	0.007	1.07	(1.02 to 1.13)	0.008
Comorbidities	Congestive heart failure (ref.: no)	0.88	(0.78 to 0.99)	0.069	1.18	(1.13 to 1.24)	<0.0001
	Hypertension (ref.: no)	0.91	(0.8 to 1.03)	0.142	0.92	(0.88 to 0.96)	0.00036
	Chronic pulmonary disease (ref.: no)	-	-	0.062	0.97	(0.9 to 1.04)	0.351
	Diabetes (ref.: no)	1.04	(0.89 to 1.21)	0.731	1.03	(0.98 to 1.09)	0.243
	Renal failure (ref.: no)	-	-	0.101	1.19	(1.11 to 1.27)	<0.0001
	Obesity (ref.: no)	1.12	(0.94 to 1.33)	0.366	0.86	(0.81 to 0.92)	<0.0001
	Cardiac arrhythmias (ref.: no)	0.85	(0.76 to 0.96)	0.016	1.15	(1.1 to 1.2)	<0.0001
Complications	Intracerebral bleeding (ref.: no)	-	-	0.13	1.5	(1.45 to 1.56)	<0.0001
	Ischaemic stroke (ref.: no)	-	-	0.368	1.2	(1.06 to 1.35)	0.023
	Arterial embolism/thrombosis (ref.: no)	0.92	(0.62 to 1.38)	0.925	0.99	(0.85 to 1.14)	0.934
	Myocardial infarction (ref.: no)	0.99	(0.75 to 1.31)	0.852	1.06	(0.91 to 1.23)	0.55
	Cardiac arrest (ref.: no)	1.31	(1.17 to 1.48)	<0.0001	1.33	(1.28 to 1.39)	<0.0001
	Dialysis (ref.: no)	2.99	(2.25 to 3.9)	<0.0001	4	(3.35 to 4.77)	<0.0001
	Pulmonary embolism (ref.: no)	0.94	(0.8 to 1.11)	0.555	1.01	(0.95 to 1.08)	0.788

Relative risk of all COVID-19-positive patients treated with VA-ECMO or VV-ECMO in Germany from January 2020 to September 2021. CI, confidence interval; VA-ECMO, venoarterial extracorporeal membrane oxygenation; VV-ECMO, venovenous extracorporeal membrane oxygenation.

Discussion

This study provides the data of all ECMO therapies in COVID-19 patients in Germany from January 2020 to September 2021 with a total of 4279 patients. The main findings of this study are as follows: first, the in-hospital mortality rate was 65.9% in patients treated with VV-ECMO and as high as 72% in VA-ECMO. Second, over 43.2% ($n = 1848$) of patients were older than 60 years with an extremely high mortality of 77.2%. Third, the mortality rate significantly varied among individual months between 48.1 and 84.4% and increased from 57% in March 2020 to 84% in September 2021 in the VV-ECMO group.

A comparison of the mortality rate of 65.9% in this study with that of 54.4% in ARDS patients and VV-ECMO treatment in Germany before the pandemic shows a clear increase.[10] Our latest analysis of the claims data from 2018 shows a large discrepancy between previously published mortality rates in the literature.[10] Thus, not surprisingly, there is a difference in mortality between this study and a meta-analysis of 1896 COVID-19 ECMO patients.[5] The results from the meta-analysis show a 37% mortality rate with a median age of 51.6 years.[5] In comparison, in our analyses, only 37.3% of all VV-ECMO patients were younger than 54 years with a mortality of 52.9%, whereas this rate increased to 77.6% in patients more than 60 years. For COVID-19 disease, a higher age is one of the main risk factors of poor outcome and presumably contributes a decisive factor here.[11] In Germany, there was almost no shortage of resources during the pandemic and through ethical discussions, age was excluded as a triage criterion in an official clinical practice guideline. Perhaps therefore, patients with advanced age were treated with ECMO in relation to a new disease like COVID-19, whereas in other countries and alliances of hospitals, advanced age is seen as prognostic marker with unfavourable outcome, and consequently, limited in usage in this particular group of patients.[12,13]

Remarkably, in this study, the high number of cardiac arrests of 44.1% in VA-ECMO and 16.4% in VV-ECMO may indicate a high severity of illness, which may partly explain the increased mortality. Unfortunately, the data do not provide any information on the cause of circulatory arrest. The high number of intracerebral bleeding events of 12.3% in the VV-ECMO group, compared with 6% from the Extracorporeal Life Support Organization (ELSO) data, is also apparent.[14] Keeping the right balance of the right amount of anticoagulation was a challenge during ECMO treatment, even before COVID-19. Since COVID-19 affects coagulation, it is even more important to have centres with sufficient experience in the management of anticoagulation and complications.[15] Unfortunately, no detailed statements can be made about individual medical histories or important conditions before ECMO, which makes comparability with other studies difficult.

In addition to trying to explain the poor outcome using patient-associated factors, possible centre effects must be considered. In the retrospective data, the assessed hospitals were mostly specialised ECMO centres; in this study, all hospitals were analysed. Although over 64.5% of all treatments were performed at hospitals with more than 800 beds, the remainder were treated in smaller hospitals. In Germany, the median number of ECMO treatments per year was four in 2018, so it can be assumed that the majority of treatments have not been performed in centres fulfilling minimal criteria in terms of ECMO-runs per year.[10] In a position paper from ELSO in 2014, 20 cases per year were defined as the minimum number of cases to demonstrate an appropriate routine in the use of ECMO.[16] In a retrospective analysis from Lebreton *et al.*,[6] a statistically significant advantage for survival was found with a minimum of 30 cases per year. Although our data show a better outcome for hospitals lower than 800 beds with 61.2 and 62.6% for VA-ECMO and VV-ECMO, these patients are less severely ill compared with those in hospitals more than 800 beds, which is a fact that appears in the distribution of the proportion of the PCCL group of four to six (Table 1). Another reason for the better outcome is the transfer of severely ill patients from a mid-sized hospital to a maximum care hospital, which cannot be identified from the data.

Looking at mortality over the course of the pandemic, the picture is highly variable with a tendency to worsen, especially in VV-ECMOs, although there are guidelines and recommended therapies, such as dexamethasone or antibody therapies. Interestingly, also in specialised ELSO centres, the mortality rates starting at 36.9% significantly increased to over 50.9% in patients treated after September 2020, which also occurred in our study during 2020 but with significantly higher mortality rates.[8] Possible reasons for the increase may be the increase in noninvasive ventilation and high-flow therapy, resulting in a later initiation of ECMO, and thus involves possibly sicker patients with greater lung damage. Another possible explanation for the changes in mortality over the time is the domination of the delta variant in the second wave in December 2020 in Germany, and therefore, more severe clinical courses with unfavourable outcome. The patient demographics may have changed to older and potentially sicker patients. The indication for ECMO therapy may also have been a reason as the inclusion criteria may have been too broad and not standardised. This may be influenced by diverse reasons, such as reimbursement, resource availability, ethics, individual expert opinions or the media.

Limitations

These data are retrospective. In this case, data were collected in a very structured and representative manner, and since correct data entry affects the hospital costs, increased interest in their correct documentation is expected. Since the diagnosis U07.1 is recorded for all patients with a positive SARS-COV 2 test, patients for whom COVID 19 infection is not the cause of hospital admission are also included. In addition, the validity of the data is reduced by possible multiple countings of each patient due to inter-hospital transfers and possibly inaccurately documented conversion from VV-ECMO to VA-ECMO. These secondary data only provide case-based in-hospital mortality and cannot provide information on long-term mortality. In addition, there is a lack of accurate patient data to verify the indication and detailed information on the time of implantation and onset of symptoms. Therefore, erroneous coding is possible. Finally, due to the provision of data by the InEK during the year, only highly aggregated data are available, and no further detailed queries are possible, e.g., the median age.

Conclusion

In Germany, a large proportion of elderly with COVID-19 were treated with ECMO, with an unacceptably high hospital mortality. Due to the aggregated data, further analyses to investigate the poor outcome and possible minimum requirements for centres were not possible. The government must urgently ensure that this data is made available for scientific evaluation at an early stage. An unconditional recommendation cannot be given for COVID-19; instead, the indication and available resources must be very carefully weighed and especially regarding the elderly, a relative contraindication should be considered here. The lessons to be drawn are: 'Think before ECMO'. Uncritical use is not justified. There is an urgent need for binding regulations for the use of ECMO therapy in Germany. This applies in particular to the elderly patient group: Here, 'Do Not ECMO' applies.

Furthermore, there must be a minimum volume requirement for hospitals. This ensures a routine in the therapy and indication of ECMO.

Research in context

Previous observational studies published on ECMO in COVID-19 were conducted mostly in specialized centres and showed mortality rates of 37%, which has recently increased to 53% as the pandemic has progressed, according to analyses of the ELSO registry.[5,6] Key findings are that patients with severe hypoxemia who start ECMO therapy earlier after admission, the influence of a high case volume in the previous year and lower age was associated with improved survival.[6,7]

This analysis is based on a complete record of all COVID-19 ECMO treatments in Germany from the beginning of the pandemic until September 2021, showing a high proportion of 43.2% ($n = 1848$) for patients older than 60 years and an extremely high mortality rate of 77.6%. In Germany, there are no mandatory national regulations or guidelines that regulate ECMO therapy and during the pandemic, there was no shortage of resources, allowing the use of ECMO in older patients. Considering these high mortality rates, however, advanced age must be considered as a relative contraindication for ECMO therapy in COVID-19.

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References

1 Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. *Nat Microbiol* 2020; **5**:536–544.
2 Bartlett RH, Ogino MT, Brodie D, *et al.* Initial ELSO guidance document: ECMO for COVID-19 patients with severe cardiopulmonary failure. *ASAIO J* 2020; **66**:472–474.
3 Alhazzani W, Moller MH, Arabi YM, *et al.* Surviving sepsis campaign: guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19). *Crit Care Med* 2020; **48**:e440–e469.
4 World Health Organization. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected: interim guidance, 13 March 2020. Geneva: World Health Organization; 2020 2020. Contract No.: WHO/2019-nCoV/clinical/2020.4
5 Ramanathan K, Shekar K, Ling RR, *et al.* Extracorporeal membrane oxygenation for COVID-19: a systematic review and meta-analysis. *Crit Care* 2021; **25**:211.
6 Lebreton G, Schmidt M, Ponnaiah M, *et al. Paris ECMO-COVID-19 investigators.* Extracorporeal membrane oxygenation network organisation and clinical outcomes during the COVID-19 pandemic in Greater Paris, France: a multicentre cohort study. Lancet Respir Med 2021; **9**:851–862.
7 Shaefi S, Brenner SK, Gupta S, *et al.* STOP-COVID Investigators. Extracorporeal membrane oxygenation in patients with severe respiratory failure from COVID-19. *Intensive Care Med* 2021; **47**:208–221.
8 Barbaro RP, MacLaren G, Boonstra PS, *et al.* Extracorporeal Life Support Organization. Extracorporeal membrane oxygenation for COVID-19: evolving outcomes from the international Extracorporeal Life Support Organization Registry. *Lancet* 2021; **398**:1230–1238.
9 Kim S, Choi B, Lee K, *et al.* Assessing the performance of a method for case-mix adjustment in the Korean Diagnosis-Related Groups (KDRG) system and its policy implications. *Health Res Policy Syst* 2021; **19**:98.
10 Friedrichson B, Mutlak H, Zacharowski K, Piekarski F. Insight into ECMO, mortality and ARDS: a nationwide analysis of 45,647 ECMO runs. *Crit Care* 2021; **25**:38.
11 Williamson EJ, Walker AJ, Bhaskaran K, *et al.* Factors associated with COVID-1 9-related death using OpenSAFELY. *Nature* 2020; **584**:430–436.
12 Schmidt M, Hajage D, Lebreton G, *et al.* Groupe de Recherche Clinique en REanimation et Soins intensifs du Patient en Insuffisance Respiratoire aiguE (GRC-RESPIRE) Sorbonne Universite, Paris-Sorbonne ECMO-COVID investigators. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome associated with COVID-19: a retrospective cohort study. *Lancet Respir Med* 2020; **8**:1121–1131.

13 Fiske A, McLennan S, Buyx A. Ethical insights from the COVID-19 pandemic in Germany: considerations for building resilient healthcare systems in Europe. *Lancet Reg Health Eur* 2021; **9**:100213.
14 Barbaro RP, MacLaren G, Boonstra PS, *et al.*, Extracorporeal Life Support Organization. Extracorporeal membrane oxygenation support in COVID-19: an international cohort study of the Extracorporeal Life Support Organization registry. *Lancet* 2020; **396**:1071–1078.
15 Masi P, Hekimian G, Lejeune M, *et al.* Systemic inflammatory response syndrome is a major contributor to COVID-19-associated coagulopathy: insights from a prospective, single-center cohort study. *Circulation* 2020; **142**:611–614.
16 Barbaro RP, Odetola FO, Kidwell KM, *et al.* Association of hospital-level volume of extracorporeal membrane oxygenation cases and mortality. Analysis of the extracorporeal life support organization registry. *Am J Respir Crit Care Med* 2015; **191**:894–901.