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Early View

Editorial

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ECMO during the COVID19 pandemic: Moving from rescue therapy to more reasonable indications

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COVID19 led to an unprecedented number of patients on mechanical ventilation, many of them presenting with severe acute respiratory distress syndrome (ARDS) [1-4]. Depending on the resources of national health care systems, extracorporeal membrane oxygenation (ECMO) was frequently applied during the pandemic [3, 5-7]. While ICU experience improved with this new disease, various forms of drug therapies were introduced in living guidelines, resulting in a dynamic development in outcome of COVID19 [8, 9]. Particularly and noteworthy is the introduction of dexamethasone in the summer of 2020 and 2021 the additional administration of tocilizumab in the early severe phase of the disease [10]. The third important factor that had had a significant impact on the outcome of severe respiratory failure was the start of vaccination programs, depending on national strategies primarily for risk groups, followed by the general public.

Depending on the phase of the pandemic, different studies showed a variable outcome for COVID19 patients treated with extracorporeal membrane oxygenation (ECMO). While in the first wave the in-hospital mortality remained below 40% [11], after the summer 2020 a significant mortality increase was seen in many centers [5]. The latest data from the international ECMO registry (ELSO) showed a significant increase in hospital mortality of about 15% during the pandemic [12]. In addition, in the

German health care system without significant limitations to access (no governmental restrictions, high reimbursement of invasive procedures), there was a higher in-hospital mortality of about 70% over the entire pandemic. The main questions that therefore arise are a.) why mortality increased in the later phases of the pandemic and b.) why some health care systems such as Germany's had such a high mortality.

Riera and colleagues analyzed some major risk factors in this issue of the ERJ [13]. Hereby substantial factors were identified being congruent world-wide whereas some remain a matter of debate. Almost all studies show the most beneficial survival in patients under 50 years of age with a significant increase in mortality above 60 years of age. This is also evident in data from Germany, but age stratified comparisons show again significant differences, so that not the age alone seems to play a major role. Furthermore, the work of Riera et al. as well as data from the greater Paris area [14] or from the last ELSO analysis [7] show that a high center-associated experience, measured by the number of ECMO runs greater or less than 30 per year, has a significant influence on mortality. Experience and high-level routine thus seem to be one of the essential factors to reduce overall mortality. Somewhat incongruent also in the present work is the timing of ECMO initiation in relation to intubation, here it can be concluded from all available data that a very early initiation of the system in the first three days showed at least the best survival rates, while very late ECMO initiation showed a significantly higher mortality. However, the timing alone cannot be used as a criterion for indication, other parameters such as the stiffness of the lung or CT morphological changes are needed. Furthermore, this raises the question if ECMO is still a rescue therapy or more or less the most invasive option to treat most severe hypoxemic ARDS patients within its evidence-based indication.

In more detail, according to the values of medical ethics physicians' activities must be guided by two main principles: the *indication* and the *patient's will*. The indication to perform a diagnostic or therapeutic procedure (or to do not!) is based on the careful assessment of a realistic rehabilitation of the patient in association with such a measure (e.g. ECMO) to allow the patient for continuing life with a certain quality

and to achieve a well-defined therapeutic goal coordinated with the values and wishes of the individual patient. Since many guidelines claim the indication for ECMO as ‘rescue’ or ‘ultima ratio’ the above introduced definition of ‘indication’ may be levered out (figure 1). ‘Ultima ratio’ (a phrase created in the Thirty Years War) could justify the use of ECMO under neglect of a careful and ethically valued indication. We assume that ‘resuce’ and ‘ultima ratio’ motivations may have contributed to a high mortality in patients treated with ECMO in some health care systems such as Germany [4]. Thus, taken all current evidence into account, the indication for ECMO should be based on a careful assessment of several anamnestic, biographic, medical, and prognostic parameters (table 1) in each individual patient to avoid futile treatments as well as a high in-hospital mortality.

In summary, the main risk factors for poor survival are particularly the age of the patient, but also the previous experience in ECMO centers and of course the pre-existing concomitant diseases. Hereby the indication for ECMO therapy moves more and more into focus, away from a rescue therapy to an extended standard therapy, which requires a high expertise and an ethically based careful indication, and it has to be used with a sense of proportion. Even if the initiation remains an individual case-based decision, work such as that of Riera and others [13] should be taken as an opportunity to develop dedicated criteria.

Conflict of Interest

C.K. reported advisory fees for Xenios and lecture fees for Xenios and Getinge, T.B. reported no conflicts of interest, T.W. reported reported advisory fees for Xenios.

Table 1: A gradual assessment of indications for implementation of ECMO in critical acute respiratory distress syndrome. *For the graded indication all aspects of the column should be fulfilled.*

Justified and strongly recommended	**Perhaps indicated under individual conditions**	**No indication (high probability)**
Age < 60 years	Age 60 – 69 years	Age > 70 years
Good-moderate prognosis on acceptable quality of life	Uncertain prognosis on acceptable quality of life	Unacceptable quality of life probable (e.g. continuous dependency on organ replacement therapies (artificial ventilation, hemodynamic support) and/or chronic immobility
No additional organ failure (except lung)	Mild additional organ insufficiency (except lung)	Additional multi-organ failure with low probability of recovery (except lung)
Onset of severe ARDS < 3 days	Onset of severe ARDS 4- 7 days	Onset of severe ARDS > 7 days with concomitant signs of fibrosis of the lung
No considerable comorbidities, good general health status	Moderate comorbidities without necessity for organ replacement (e.g. dialysis)	Severe comorbidities requiring continuous support (e.g. dialysis, inotropes), high frailty, poor general health status

A declared or presumed patient's will: pro	Patient's will unclear, next of kin undecided	A declared or presumed patient's will: contra
No chronic illness with expectancy of life shortening	Chronic illness with uncertainty of life shortening	Chronic illness with clear reduction of life expectancy

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