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Editorial

Decision-making in response to respiratory veno-venous extracorporeal membrane oxygenation referrals: is current practice precise enough?

Veno-venous extracorporeal membrane oxygenation (VV-ECMO) is accepted as part of a treatment bundle for selected patients with severe acute respiratory distress syndrome (ARDS) [1, 2]. Though there have been many comparisons of VV-ECMO and conventional management [3–5], decision-making for referrals to severe respiratory failure centres (SRFC) has not been examined. In this issue of the journal, Gillon et al. report a retrospective analysis of decision-making for patients referred to a SRFC in central London [6]. They compared physiological parameters at the point of referral and 6-month survival thereafter with four discrete decision

outcomes. The finding that 6-month survival was 72.8% for those accepted to the service and 72.1% for those retrieved with VV-ECMO, which is higher than previously reported [7], appears to support decision making and clinical practice at the study site. Nevertheless, 16.6% of those declined admission survived to six months and 28.9% who were accepted but not retrieved did not. This begs the question, do we need

to increase the precision of practice by better differentiating those who will survive from those that will not? In order to answer this question, the themes of decision-making for SRFC referrals require careful analysis in the context of the conclusions drawn by Gillon et al. [6].

Prognostication

Decision-making processes for VV-ECMO and critical care referrals have many similarities. Bed capacity and resource limitations likely influence decisions though they are usually superseded by clinical factors [6, 8]. The inability to correctly predict mortality is also common to both scenarios [9]. The question, therefore, is can objective systems or rules be used to increase precision, reduce bias and enhance consistency? For SRFC referrals, no validated tool exists and Gillon et al. demonstrate that the retrospective application of the Respiratory ECMO Survival Prediction (RESP) score [10] to the study cohort significantly underestimates survival [6]. Rather than the RESP score being erroneous [11], it is more likely, as the authors clearly state, that such systems were not designed for the purpose of SRFC referrals.

How then should we set standards for decisions with respect to mortality? We could, of course, aim for survival to be 0% for those declined and 100% for those accepted. On balance, however, to strive for perfection in terms of predicted and actual mortality may prove to be unachievable and may even cause harm to patients [11, 12]. Predicating the future is an art of medicine but the associated

science is imprecise, particularly when the stakes are high, with a heterogeneous patient population, at the extremes of pathology and physiology and when there is limited literature to support and guide such decisions. Currently, therefore, prognosticating for patients referred to a SRFC comes with a high risk of miscalculation.

Subjectivity

'Reversibility', 'severity' and 'reserve' were found to strongly influence decision-making. While we all understand their meaning, such terms are difficult to express quantitatively and, therefore, measure. Gillon et al. begin with the perception that reversibility and reserve influence the decision to accept or decline whereas severity influences the decision to retrieve and/or initiate VV-ECMO [6]. Perceived disease severity was found to closely resemble commonly-used VV-ECMO indication criteria as described by the Extracorporeal Life Support Organization (ELSO) guidelines [13], the CESAR trial [3] and the Murray Score [14]. These parameters together with arterial carbon dioxide and pH, may be surrogates for the degree of physiological derangement as can be measured with scores such as APACHE [15], but this is not reported.

Reversibility and reserve are somewhat more difficult to cross-examine. By comparison, the CESAR trial included patients that were judged to have reversible pathology '*based on the clinical opinion of one of three duty ECMO consultants*' [3]. Through analysis of their data, Gillon et al. reveal this

perceived reversibility and reserve to be a function of age, immuno-compromise, serum lactate concentration, duration of mechanical ventilation and the presence of cardiac failure [6]. Serum lactate does not fit comfortably under this heading, though some explanations for this are provided. If precision is to be improved through objectifying decision-making processes, it follows that the definition of reversibility, severity and reserve must be precisely established through a further enquiry.

Processing

We often take heuristic short-cuts when aiming to make effective and timely decisions in less than ideal circumstances [16, 17]. Such an approach to problem solving is never guaranteed to be perfect, as precision and accuracy are traded against the speed and efficiency at which a satisfactory solution can be found. Many will be unfamiliar with the term 'heuristics', but all will understand the concept of a 'rule of thumb', a 'guestimate' or 'common sense'. Most medical decisions require the heuristic input of experienced clinicians. We may perceive our decisions to be analytical and based on statistics, probability and slow deliberative abstract thinking, namely a type-2 process. Despite these perceptions, it is likely that we use instinct, experience and heuristics to make quick, automatic, intuitive and sometimes affect based decisions, in keeping with a type-1 process [18]. Imagine seeing a patient pre-operatively or during a critical care assessment. Despite possessing a wealth of information,

the brain may employ a type-1 process due to difficulties processing all the data, some of which may be missing. It could be argued that Gillon et al. use a type-2 process through careful and deliberate retrospective analysis as a means to challenge past type-1 decisions [6]. It may be unreasonable to expect that all such decisions will be correct all of the time, as heuristics and bias introduce error that may reduce precision.

Alternatively, and more likely the case, as clinicians we use a combination of type-1 and -2 processes in our daily practices. To categorise medical decisions under a binary framework of decision-making may be too simplistic given the degree of associated complexity [19]. For anaesthetic and critical care clinicians, these practices involve assessing the immediate patient, and there is immense value assigned to the tacit picture from the end of the bed [20]. Decisions made at a physical distance from the patient may remove type-1 processes and the outcome may be slightly different compared with conducting an assessment of the patient in person. Whether this is the case and the resultant effect on precision is unclear and yet to be studied. During the decision-making process for remote patient assessments, this is often combatted by asking the referrer for their overall impression of the patient from the end of the bed. Despite this, our ability to understand our own decision-making processes for SRFC referrals must keep pace with advances in our understanding of VV-ECMO and its associated

technology [21]. This study adds greatly to that understanding.

Survival

Using 6-month survival as an endpoint may not tell the whole story. The strengths and limitations of reporting and comparing mortality as a function of the lunar orbit cycle have been articulated by Carlisle [22]. When performing a retrospective analysis, investigators are limited by the available data. Mortality as a function of time is commonly reported for retrospective studies as it is well understood, of fixed length, and reliably recorded. While this helps us compare the patients triaged to four discrete decision outcomes in this study [6], its meaningfulness for patients and their relatives is unclear. There are many examples from elsewhere in the literature where a numerical effect may be mistaken for genuine one [23]. Of the 16.6% of patients declined by the SRFC that survived beyond six months, perhaps many died soon after or survived for many years with severe physiological limitations.

Under the surface of survival data lies uncaptured quality of life and functional capacity narrative in addition to other outcomes that may be of importance to patients. We cannot assume those who survived in all four groups are equal in these terms. With this in mind, the survival of those denied acceptance by the SRFC may not necessarily represent a lack of precision, as acceptance may not have improved quality of life. On the other hand, little is also known of those who survived following VV-ECMO. Should the incidence of long-term

severe complications be high, the consequences to the patient, significant though they are, will remain uncaptured.

Collaboration

When patients are referred to a SRFC for consideration of VV-ECMO, we have no validated tools to assist us; we use subjective factors to guide us; we are unsure with regards the influence of instinct, heuristics or our own biases; and we are recording outcomes that are of little importance to patients. Collaboration and consensus could act as countermeasures to these problems. Again, using the example of critical care referrals, consensus was revealed to be a strong moderator of decision-making for the good of the patient [8], though elsewhere it has been shown to cause problems [24]. Whilst collaboration and consensus may increase precision through the reduction of inconsistency, it may not necessarily result in the correct decision [25]. On balance, it is our belief that expert clinical assessment must incorporate collaboration with those at the referring centre and consensus amongst those at the VV-ECMO centre. This surely enhances both the precision and accuracy of practice when expert clinical assessment is used as a means to make decisions for those referred to a SRFC.

Heterogeneity

There is another important question that needs to be asked of this study. Why was survival similar for those managed with VV-ECMO as compared to those managed conventionally? Some may argue

that VV-ECMO is now no better than optimal conventional management, given the recent advances in ventilatory and non-ventilatory strategies for severe ARDS [26]. The benefit from high-level expertise at SRFCs may therefore outweigh the use of advanced equipment such as VV-ECMO. This view is supported by a recent Cochrane systematic review that reported an inconclusive verdict with regards to the use of VV-ECMO in patients with severe respiratory failure [4], though this may simply reflect a lack of good quality evidence. The alternative view is there was no randomisation in this study and patients at the severe/refractory end of the ARDS spectrum were selected for VV-ECMO [6]. As the severity of respiratory failure increases, so too does the support given; from telephone management to retrieval and then to VV-ECMO. To achieve equipoise for all those accepted by the SRFC may simply demonstrate appropriate patient selection. Although the CESAR trial demonstrated VV-ECMO to be superior to conventional management for ARDS [3], the limitations of this evidence have been discussed at length [27–29]. The debate will no doubt continue and the results of an ongoing international multicentre RCT are eagerly awaited [30].

This heterogeneity between the four groups of this study could be further compounded by the different 'types' of referral. From our own experience, these can be broadly classified as:

1 Unsuitable – we continue to receive referrals for patients that are outside our well-publicised criteria for VV-ECMO [13];

2 For completion – these patients are referred from centres with extensive experience in managing severe acute respiratory failure. They may wish to refer the patient despite both parties having recognised there being no requirement for a change in management;

3 For advice – some patients can be managed remotely with telephone advice, though referrers are becoming more knowledgeable with regards to optimisation measures such as prone positioning neuromuscluar blockade and haemofiltration;

4 For action – these patients are young, sick and refractory to optimisation strategies. They clearly fit the criteria for VV-ECMO. A team is dispatched and they are established on VV-ECMO at the referring centre or following conventional retrieval.

Of course, not every patient fits satisfactorily into the above categories and it is these 'borderline' decisions that we find the most challenging.

Geography

From our own experience, the characteristics of the referring centre may affect decisions regarding VV-ECMO referrals. The threshold for retrieving a patient from a critical care unit with limited experience of severe refractory respiratory failure could be lower than for somewhere with extensive experience. Again, this is yet to be studied, so it is unclear whether or not our perception is correct. In addition to the geography of referral sites, the geography of SRFCs may play a role in the precision of national practice. The five SRFCs in the England may have dissimilar cultures and practices due to variable workloads, resources, capacity, experience and expertise. Practices at individual SRFCs and the threshold for acceptance may, therefore, vary. For example, our centre rarely retrieves patients for assessment or conventional management of acute severe respiratory failure, instead basing decision-making on the criteria for VV-ECMO [3, 13]. This is somewhat different to the practices described by the study centre [6, 31]. Furthermore, the CESAR trial on which we base much of our practice was a single centre study with respect to the VV-ECMO arm of the trial [3].

Conclusion

The conclusions of retrospective studies must always be interpreted with caution [32]. Despite this, the general message seems to be that expert collaborative clinical assessment is, at present, an acceptable way to manage referrals to a SRFC for the consideration of VV-ECMO. As cumulative experience and expertise increase, so too will our understanding of patient selection, though boundaries will understandably shift with time. New scoring systems may emerge but we are a long way from increasing the precision of practice by incorporating these into clinical decision-making. The pace at which VV-ECMO technology is improving, together with advances in our understanding of patient care, may limit the utility of past research as a

means to prognosticate for patients of the future [33]. With regards to the future, it is likely that improvements will continue, demand will increase, there will be a need for more SRFCs and VV-ECMO may become more widely available in the UK [1, 34]. Our understanding of decision-making for such patients must keep with the pace of these advances. Is current practice for respiratory VV-ECMO referrals precise enough? That of course depends on your subjective opinion of how precise it should be and how this should be judged, but in the absence of our ability to make perfect decisions or substitute clinicians for computers, there will always be scope for further improvement.

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