Let us be cautious and prevent unnecessary patient harm

Sejamos cuidadosos prevenindo danos desnecessários aos pacientes

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In the current issue of the Brazilian Journal of Pulmonology, Azevedo et al. discuss the case of a patient with severe hypoxemia whom they supported with extracorporeal membrane oxygenation (ECMO).[1] They used a modern ECMO technique, and their patient survived. It is clear that ECMO is a dramatic support technique, and survival of a patient felt likely to die can easily lead clinicians to become believers in the efficacy of the technique. However, human cognition and human belief are complex processes that have important limits and frequently lead to incorrect conclusions.[2-4] The recent novel H1N1 influenza epidemic was associated with many patients with severe hypoxemia and led to renewed application of ECMO support. ECMO was used during patient transport[5] and for treatment of patients with acute respiratory distress syndrome (ARDS) secondary to infection with novel H1N1 influenza virus.[6]

Proponents of ECMO have claimed that the modern advances in technology have led to a favorable impact on patient survival.[7,8] However, others have argued that the survival of patients with novel H1N1 influenza-induced ARDS and severe hypoxemia who are treated with ECMO is equivalent to that of patients treated without ECMO.[9,10] In response, MacLaren identified three crucial issues: ECMO must be correctly applied; ECMO must be applied to the appropriate patient; and, finally, that we need to define when, how, and in whom we can optimally use the technique.[11] I believe these issues can be resolved only with scientifically rigorous clinical trials that include detailed methods for selection of patients, conduct of extracorporeal support, and management of important clinical co-interventions. Short of this, clinicians cannot know when, how, or in whom ECMO can be optimally applied. For example, MacLaren et al. recently indicated that patient complications continue to occur, that uncertainties remain, and that ". . . there are no effective means of confidently predicting recovery or death."[12]

The only two scientifically rigorous randomized clinical trials failed to demonstrate a survival benefit of extracorporeal support.[13,14] I believe these scientifically rigorous results should be supplanted only by new scientifically rigorous randomized clinical trial results obtained with modern ECMO technology. I believe, as do others, that ECMO should not be widely used for adult ARDS patients until such new data clearly demonstrate the efficacy of ECMO in ARDS.[15,16]

Recent technical advances in ECMO support are obvious.[12] New extracorporeal circuits are simpler, are easier to use, and appear to be safer than are those used in the randomized clinical trials of the 1970s and 1980s.[13,14] Legitimate questions can be raised about the current value of these early clinical trial results. It is likely that compelling answers will be provided only by new clinical trials that adhere to accepted experimental standards. New and rigorous clinical trials using modern technology should provide results that illuminate the crucial issues articulated by MacLaren et al. (in whom, how, and when ECMO should be applied).[12]

We currently have no better data to guide decisions about ECMO than those provided by the two early clinical trials.[13,14] Many hold strong beliefs about the efficacy of ECMO support for patients with severe ARDS. Such strong beliefs are not new. In 1984, Gattinoni et al. reported a dramatic increase in survival with low frequency positive pressure ventilation-extracorporeal CO_2 removal (LFPPV-ECCO2R) using veno-venous support.[17] Thereafter, my colleagues and I completed a randomized controlled clinical trial of LFPPV-ECCO2R. We expected LFPPV-ECCO2R to be a significant treatment advance. In our published discussion, we stated the following: "we concluded from published reports that there was about a 0.5 prior probability that LFPPV-ECCO2R was a superior therapy for ARDS."[14] However, our trial results failed to indicate a survival advantage of LFPPV-ECCO2R. In a letter to the editor, one group of authors claimed that LFPPV-ECCO2R was not yet optimized and the technique not yet ready for a clinical trial.[18] We replied and asked how it could be known that the LFPPV-ECCO2R technique was beneficial

(the conclusion of the strong believers) when it was not yet adequately evolved to allow a clinical trial? These past published exchanges indicate that uncertainty about the role of extracorporeal support has been a longstanding issue. Strong believers have made claims about the efficacy of ECMO ever since the first report of survival after the use of ECMO with a membrane lung.[19] We will not likely encounter observational results more compelling than those of Gattinoni et al.,[17] who, in 1984, reported a 77% survival of patients meeting the 1970s ECMO criteria. This contrasted with the consistent 10% survival of such patients at the Boston and Salt Lake City centers, two of the original National Institutes of Health ECMO clinical trial centers.[13] I do not believe that current observational studies, case reports, or strongly articulated beliefs will be more compelling than those past results of Gattinoni et al.[17]

I cannot avoid the conclusion that we need new scientifically rigorous clinical trials carried out with current ECMO technology. Unfortunately, the recent clinical trial conducted in the United Kingdom, while impressive, did not adhere to accepted experimental standards and did not produce scientifically rigorous data.[20,21]

The alternative to credible clinical trial results is to accept at face value the claim of experts that their experience "managing adult patients on ECMO for refractory respiratory failure" or similar expressions, demonstrates, documents, and validates the efficacy of ECMO.[11] Unfortunately, such beliefs, no matter how strongly and sincerely held, are frequently proven to be invalid.[4] Experience can easily mislead due to the selective emphasis and recollection that characterize human cognition. Many past treatments were enthusiastically supported and widely disseminated but then shown to be of no value—or even harmful. These include avoiding beta blockers in heart failure treatment; using insulin for schizophrenia; using vitamin K for myocardial infarction; using hormone replacement therapy to prevent cardiovascular disease; using flecainide for ventricular tachycardia; and immobilizing scaphoid bone fractures.[22]

Twenty-five years ago, Roger Bone discussed issues that made observational studies of extracorporeal support difficult to interpret.[23] These issues remain part of the current controversy surrounding extracorporeal support. Although extracorporeal support is a promising technique, its clinical application in ARDS requires a firmer scientific foundation than currently exists. I hope that new and compelling evidence from scientifically rigorous clinical trials with new ECMO technology will eventually indicate that the new ECMO technology has realized the promised benefits of extracorporeal support. Until these new data are published, we are left with no clear indication of the role of ECMO in adults with severe ARDS.

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