Improved survival in ARDS: chance, technology or experience?

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Randomised, clinical controlled trials in ARDS have shown that the use of historical control groups can produce misleading results.[1] If , for example, the 90% mortality of the 1979 National Heart and Lung Institute ARDS Extracorporeal Membrane Oxygenation (ECMO) trial[2] is used as a baseline, then all subsequent studies of ARDS would demonstrate an apparent increase in survival. Examination of the entry criteria and case mix of this study highlights many of the potential pitfalls in examining changes in mortality from ARDS over time. Abnormalities of gas exchange were the major entry criteria whilst no adjustment was made for the fact that many patients were admitted with severe, atypical pneumonia. Subsequent work has shown that the initial severity of gas exchange is not a strong predictor of survival in ARDS while case mix (in terms of patient selection, severity of disease, patient age and predisposing factors) is very important.[3]

Problems with patient selection have, to some extent, been overcome by the adoption of recent European/North American consensus conference definitions of ARDS.[4] Gas exchange, plain chest radiology and, if available, haemodynamic data define ARDS in the context of an "at risk" patient. However, the ease of use of these criteria does not guarantee the selection of a homogeneous population. The two major hallmarks of the pathophysiology of ARDS—the increase in lung permeability and the inflammatory nature of the injury—are not included in the definition.[5] The unknown relationship between the clinical syndrome and pathophysiology creates problems when attempts are made to adjust the case mix for disease severity. No clinical method of assessing lung injury correlates well with recovery and the most popular method, the Murray lung injury scoring system,[6] has never been validated as an indicator of outcome. The lack of a gold standard for the measurement of severity of lung injury therefore poses great problems when comparing survival in ARDS.

ARDS does not occur in isolation. Many patients have an admitting diagnosis of sepsis, trauma, or massive tissue injury and the outcome differs depending on the original cause of lung injury.[7 8] Many studies have demonstrated that ARDS associated with malignancy has a very poor outcome whilst lung injury following major trauma has a much better prognosis. The European collaborative ARDS study reported a 65% survival in trauma patients compared with only a 20% survival in patients with pneumonia.[7] A single centre study of 215 patients with ARDS reported a 4% survival in a subgroup with cancer compared with an overall survival of 54% for all patients.[8]

The complications of the underlying illness are also important in determining outcome in ARDS. Subtle signs of organ dysfunction occur in almost all cases and there are a number of reports showing a strong correlation between outcome and the number of failed organ systems.[9 10] Hypoxaemia is a relatively unusual cause of death in ARDS and most patients who die do so of multi-organ failure and intractable sepsis.[11]

These questions of patient selection, severity of disease, and predisposing factors form the background for judging recent reports on improved survival over time in ARDS. Groups from both North America[12] and the UK (in this issue of *Thorax*[13]) report a fall in mortality when comparing recent outcome with past performance from their institutions. The North American group examined yearly ARDS mortality from 1983 to 1993. Overall mortality was constant up to 1988 (approximately 60%) but then showed a marked and significant decline to 36% in 1993. The figures from the UK group are strikingly similar although the time periods are different. From mid 1990 to 1993 mortality was 66% and this fell to 34% in the period from 1993 to 1997.

A key issue is the comparability of the groups. The North American report made a survival subanalysis based on the admitting diagnosis of either sepsis, trauma, or other conditions. Fatality rates were also adjusted for age and sex and, where appropriate, for injury severity in the trauma patients. Following adjustment the mortality of the patients with sepsis and those with other risks still showed a substantial fall over time. The changes in the trauma group were much less marked. Case mix adjustments were not performed by the UK group but patients seemed well matched in terms of age, diagnosis, and severity of illness in the two time periods. These results suggest that the outcome from ARDS may be improving but a more sophisticated case mix adjustment model is needed to confirm the findings. The model should be specifically developed for patients meeting the American/European consensus criteria for ARDS and would need prospective validation. It is likely that a sufficiently large ARDS database exists to develop such a model retrospectively using information that the two groups and others have already obtained.

Real changes in mortality require an explanation. Improved treatment of acute lung injury is possible but no large randomised controlled trial has shown any benefit for a specific therapy.[14] However, a shifting philosophy in ventilation support has occurred over the time period of the reports and could explain the changes.[15] Low pressure/low volume approaches, aimed at minimising the destructive effects of barotrauma, are now common as typified by the more recent North American ECMO study[16] where inverse ratio pressure-controlled ventilation with permissive hypercapnia was the standard treatment.

Better management of the underlying conditions causing ARDS could explain the improved survival. A large number of sepsis trials have been conducted in the last decade but again no single treatment has been shown to be effective.[17] It is also interesting to note that the improved survival reported in ARDS has occurred during the period when supernormalisation of oxygen delivery was popular. This approach has recently been shown to be ineffective or even harmful[18] and further improvement in survival could occur now that the approach has been abandoned.

Could clinical effectiveness explain the changes in mortality? There is a significant variation in outcome between intensive care units in both the UK and North America.[19] Over the time period of the survival studies the discipline of intensive care has gradually established itself with dedicated training schemes and practitioners. It would be disappointing if this effort, and the expertise gained over time, did not translate into better patient outcomes. Perhaps the current papers demonstrate that concentrating

groups of complex, critically ill patients into experienced centres improves survival?

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