

Management of Severe Refractory Hypoxia in
Critical Care in the UK in 2010

Report from UK Expert Group

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Executive Summary

The 2009/10 Influenza A H1N1 pandemic in the UK required a national strategy to be developed for Critical Care. This involved the formation of a number of committees with a DH remit to assist the National DH `flu team to develop policy and provide guidance to the service. The clinical advice was provided by a group chaired by Dr Judith Hulf. This committee have since detailed their contribution to the Critical Care Strategy ^[1]. A recommendation was made, following the experience of this group, to develop clinical guidance for the management of severe respiratory failure with particular reference to refractory hypoxia.

Following publication of Dr Hulf's report a working party with members from the relevant Stakeholders was commissioned by DH (appendix 1). The objectives of this group were:

1. To define severe respiratory failure in the context of the critically ill adult patient.
2. To agree guiding principles for clinicians in the management of patients with severe respiratory failure.
3. To describe a clinical pathway for patients with severe respiratory failure.

This report describes the consensus of professional opinion received from the working party and acknowledges the recent publication from the Scottish Government's Health Directorates Report "The provision of non-H1N1 Adult Respiratory Extra Corporeal Membrane Oxygenation (ECMO) in the medium and longer term for Scotland ^[2].

The expert group provides as an interim document consensus advice for the immediate short term (winter 2010) to guide Critical Care Networks in their commissioning and delivery of critical care services for adult patients with severe respiratory failure within the currently developing tiered framework of services for the critically ill. Clinical principles of therapy are described and an illustrative

pathway is proposed. The expert group envisage a tiered approach with escalation to specialist respiratory centres for additional respiratory management. Such centres will assist the ECMO centres in identification of appropriate patients who would benefit from extracorporeal treatment. In addition these centres in the immediate short term will need to undertake repatriation and deliver ongoing care to patients who successfully come off ECMO.

This proposed pathway provides clinicians and commissioners with a platform for collaborative audit of both the pathway effectiveness and ultimate outcomes at local and national level.

Introduction

Clinical Background and Epidemiology

Acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) are life threatening conditions initiated by a large array of clinical diagnoses but as distinct entities are characterised by acute lung inflammation causing pulmonary oedema, refractory hypoxia and reduced lung compliance. As a consequence the population is not homogeneous.

Acute lung injury is common and is associated with substantial mortality, morbidity and costs^[3]. It is estimated to affect approximately 200,000 patients annually in the United States and accounts for 10-15% of intensive care unit admissions^[3]. It is commonly stated that the associated mortality has reduced with time. In fact a discrepancy still exists between outcomes associated with patients recruited into randomised controlled trials (RCT) and observational studies. Mortality in observational studies remains above 40%.

In contrast Erickson et al^[4] studied 2,451 patients who were enrolled in the ARDS Network clinical trials from 1996 to 2005. Crude 60 day mortality was 35% in 1996-7 and declined over the period to a low of 26% in 2004-5. Crude mortality was higher for patients who received higher tidal volume ventilation compared with those who received lower tidal volume and the temporal trend toward decreased mortality persisted after adjustment for age, gender, receipt of low tidal volume ventilation, and P/F ratio. Similarly, Zamboni et al reported a reduction in mortality over the period 1994 to 2006^[5] at a rate equivalent to approximately 1.1% reduction per year.

The attributable reasons for these improved outcomes in RCT as compared with observational studies will be multi-factorial but the role played by the increasing use of protocol-guided therapy in Intensive Care and the pathway assurance this provides should not be understated^[6].

Estimation and agreement of the prevalence of both ALI and ARDS is fraught with inconsistencies. The recent Scottish Government's publication^[2] reviewed the evidence base till the end of 2009 and reported worldwide estimates to vary from 58.7 cases per 100,000 in one study in the US to values less than a tenth of this (3.5 to 5.0 per 100,000). The variation in incidence is partly due to the differing criteria used for defining ARDS. The gold standard however incorporates clinical, radiological criteria and the relationship between arterial partial pressure of oxygen and inspired oxygen fraction (P/F ratio ≤ 300 and 200mmHg or 40 and 26.7kPa).

Comparison with other Intensive Care databases in the UK (ICNARC'S Case Mix Programme (CMP) and a single unit database from the University Hospital of Wales) identified a cohort of 64,796 patients who met the ARDS definition (January 2007 to December 2009) in the CMP and a prevalence for ARDS in Wales of 106 per 100,000 (personal communication from Dr Findlay). This comparison utilised the worst P/F ratio in the first 24hrs following admission to categorise patients. Such an approach has limitations. The group's consensus however was to estimate the prevalence of ARDS in the UK to be approximately 70 cases per 100,000.

Correlating and comparing outcomes solely on the P/F ratio as an indicator of mortality is inappropriate as other factors exert major influences on outcome but the use of the ratio to categorise the severity of respiratory failure and selection of appropriate interventional strategies is in line with clinical practice in the UK. Although most deaths in ARDS patients occur from multiple organ failure it is estimated that a significant number are attributable solely to acute respiratory failure^[7].

Estimating the number of patients who die from potentially reversible respiratory failure is difficult due to the heterogeneity of the ARDS population. Nevertheless assessment of ICNARC'S CMP database would support the hypothesis of improved outcomes for centres who treat a large number of such patients. Survival benefit was observed for both ARDS and ALI in units which treated annually >180 and > 350 patients with P/F ratios of ≤ 26.7 and 40 KPa respectively.

This relationship between volume and outcome has been documented previously^[8] when assessing outcomes associated with mechanical ventilation. The underlying clinical reasons will without a doubt be complex and will be inter-related. One potential reason may lie in the use of protocol-guided pathways^[6] which have in the US been shown to offer both reduction in ALI and survival benefit.

Preventing iatrogenic ARDS and adjuvants to conventional management

Within Intensive Care Medicine in the UK comparative audit of the ventilatory strategies for the management of ARDS patients has not been carried out, but the ARDSnet group from the US have published extensively on their proposed protective lung ventilation strategy^[9] which seeks to limit alveolar distension, recruit non-aerated alveoli, prevent further alveolar collapse and minimise secondary injury to the lung consequent on mechanical ventilation. Peak airway pressure is limited and associated permissive hypercapnia is common as a consequence of the strategy.

This mode of ventilation is the gold standard in patients with or at risk of ALI and has demonstrated improved survival^[9] but disappointingly despite this, adherence to the technique remains poor.

The CESAR study^[10] reported that almost 20% of severe non-cardiac respiratory failure patients referred into the National ECMO Centre for non-cardiac respiratory failure (Glenfield) and randomised to Extra Corporeal Membrane Oxygenation (ECMO) only required modification of conventional treatment. Similar management patterns were observed at another specialist ECMO centre during the H1N1 pandemic (personal communication from Dr Mark Griffiths). Controversy and extensive debate followed publication of the CESAR study but it is acknowledged by this expert group that despite limitations in the trial the CESAR trial provides sufficient evidence to indicate that in selected patients ECMO can be a clinically effective treatment. Additional evidence of efficacy and safety within this highly selected patient population with H1N1 associated ARDS was acquired from Australia /New Zealand^[11].

Other observations made during the H1N1 pandemic related to significant intravascular fluid therapy prior to admission to an ECMO centre (personal

communication from Mr Richard Firmin and Dr Mark Griffiths) and the need for adjuvant inhalational strategies such as nitric oxide, other modes of ventilation such as high frequency oscillatory ventilation or adjustments to positioning (proning) both before and subsequent to ECMO. In addition other extracorporeal strategies were utilised during the pandemic. Such technology is developing rapidly and scientific evaluation will be urgently required to identify survival benefits.

High frequency oscillatory ventilation (HFOV) was one such therapy. As a technique it has been widely used to ventilate neonatal and paediatric patients for more than 2 decades. Its use in adults for ALI or ARDS is however relatively new. HFOV delivers small tidal volumes at high frequencies (3-15HZ) with a diaphragm pump^[12]. HFOV meets the goals of a strategy of lung protective ventilation with extremely small tidal volumes (1-4ml/kg) and constant lung recruitment. Several observational studies and a meta-analysis in ARDS patients have shown improved oxygenation in patients with refractory hypoxaemia^[11], but survival benefit awaits the outcome of a randomised multicentre UK study (OSCAR)^[13] comparing conventional protective lung strategy ventilation with HFOV, and a similar multicentre Canadian study..

In addition other strategies which have proven useful in avoidance of secondary lung injury relate to the avoidance of ventilator associated pneumonia and transfusion related injury.

The availability of many of these adjuvant therapies are limited to a few sites in each Critical Care Network, thereby focusing expertise and competency in a limited number of ITUs. Access to these facilities is not always easy and often relies on personal or professional relationships rather than predictable and reliable clinical pathways. As a consequence access is unpredictable. The expert group have developed a proposed pathway which should increase reliability of the referral pathway and facilitate Critical Care Networks designing, with clinicians and commissioners, bespoke networks for the management of severe respiratory failure. Such a pathway will focus the auditing of clinical practice and outcomes at both local and national level and sits neatly within the tiered specialist services currently commissioned and delivered by Critical Care Networks. In addition weaning from long term ventilation and specialist rehabilitation following prolonged critical care are

frequently required for this subset of patients and provision for this must be included in the design of the pathway at a Network level.

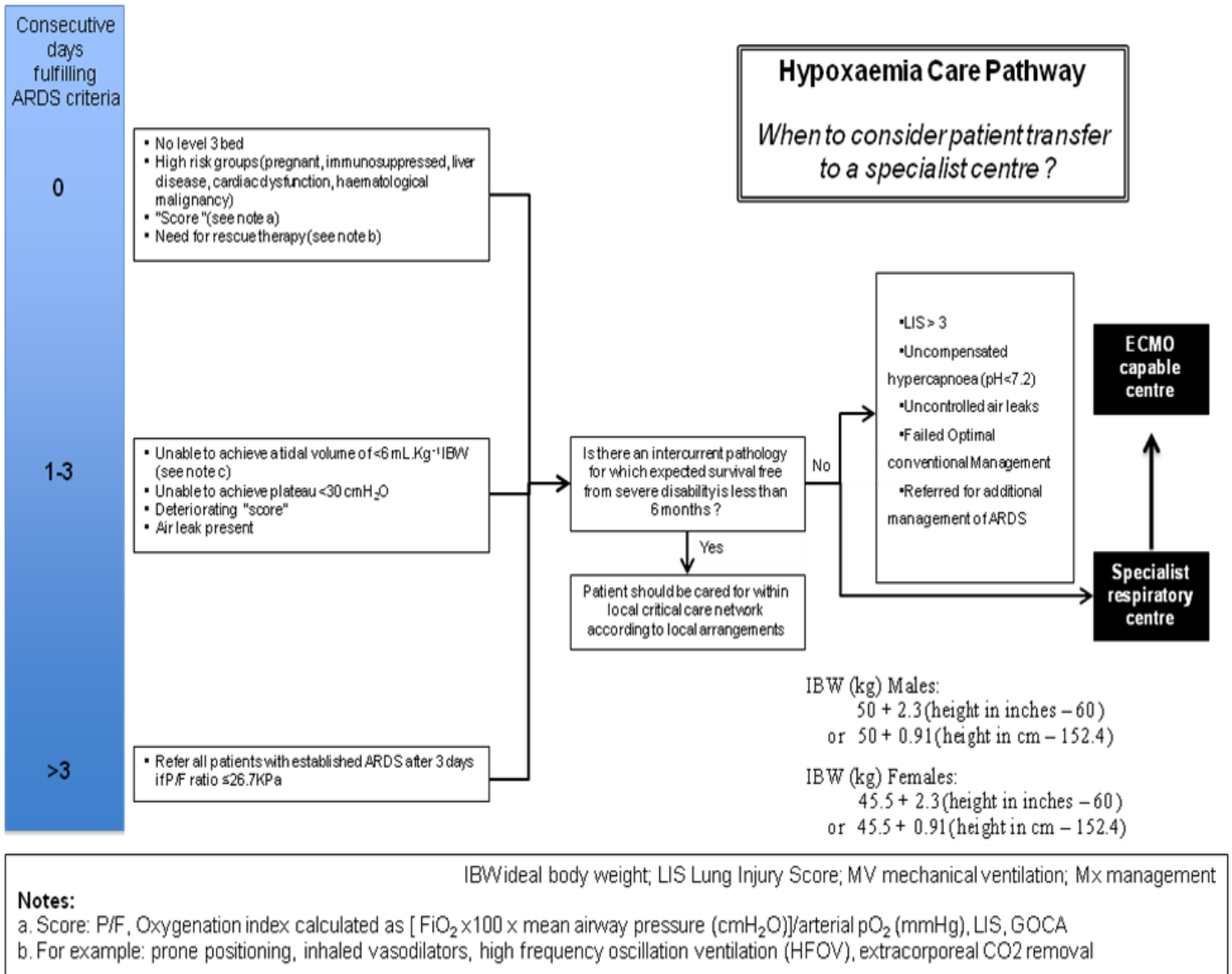
Proposed Clinical Pathway

The expert group envisage a tiered approach with escalation to specialist respiratory centres for additional respiratory management. Such centres will assist the ECMO centres in identification of appropriate patients who would benefit from extracorporeal treatment. These centres will also place an invaluable role in the repatriation pathway from ECMO centres.

All level 3 units will offer lung protective ventilation, ventilator care bundles, prone ventilation, weaning from short term mechanical ventilation and associated rehabilitation following critical illness . Specialist centres who have a higher volume of patients who fulfill the definition of severe respiratory failure, P/F ratio ≤ 26.7 KPa (>180 patients per year) should offer from a menu of more specialised techniques such as inhaled therapies and oscillation with a few centres nationally offering extra-corporeal support therapies. The pathway as developed at a Network level should clearly identify the transport arrangements for moving these highly complex patients between hospitals.

In addition all hospitals undertaking ventilation of ALI and ARDS patients should meet the professional standards for Intensive Care as determined by the Intensive Care Societies Professional Standards Groups and participate in local and national collaborative audit. The higher volume centres should in addition undertake collaborative research at a national level in this patient population.

The expert group have illustrated these principles in a proposed clinical pathway for patients with ARDS and details the clinical features which clinicians and Network teams should find valuable in designing their referral pathway. Transfer of patients to specialist centres will require planning and accompanying resourcing and should be included in the design of the pathway.



Proposed Clinical Outcome Standards

Development of the clinical pathway should be accompanied by the selection of appropriate outcome measures. Such measures for severe respiratory failure will need to encompass more than merely mortality and utilisation of critical care resources due to the heterogeneity of the patient population. Indeed measures should be developed to reflect; timing of diagnosis; time to implement and evidence of adoption to protective lung ventilation, and ultimately effectiveness of the pathway both in terms of choice of therapy and successful weaning/rehabilitation following the acute reversible lung injury.

Recommendations

The expert group recommend:

- the use of the P/F ratio in all patients in Critical Care with respiratory failure as a measure of respiratory compromise
- the adoption of a protective lung strategy for all patients at risk of ALI and ARDS
- the development by Critical Care Networks of clearly defined auditable pathways within a tiered framework of adult critical care services for patients with a P/F ratio ≤ 26.7 KPa
- Additional research should be pursued to understand more clearly why the higher volume centres have better outcomes as compared with the smaller sites when adjusted for case mix. This should include the publication of outcome data from the designated specialist respiratory centres.
- Participation in ICNARC's Case Mix Programme or SICSAG for all sites offering level 3 care.

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Appendix 1 : Membership of the Group

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Dr Geoff Bellingham	University College Hospital London, Royal College of Physicians
Dr Tom Clutton-Brock	Queen Elizabeth Hospital Birmingham Royal College of Anaesthetists
Dr Jane Eddleston	Manchester Royal Infirmary, Clinical Advisor to the Department of Health (chair)
Dr George Findlay	University Hospital of Wales, representative of the Welsh Assembly Government
Mr Richard Firmin	Glenfield Hospital Leicester (National ECMO centre)
Dr Mark Griffiths	Brompton Hospital London, Royal College of Physicians
Heather Livingston	Senior Medical Officer Department of Health, Social Services and Public Safety
Dr Simon MacKenzie	Edinburgh Royal Infirmary, representative of the Scottish Government Health Directorate
Dr Kathy Rowan	ICNARC
Dr Bob Winter	Queen's Medical Centre, Nottingham, President of the Intensive Care Society

