Conventional Ventilation or
ECMO for
Severe
Adult
Respiratory Failure

Summary Protocol

ISRCTN47279827

Background

Approximately 350 adults develop severe, but potentially reversible respiratory failure in the UK every year. Whilst intensive care of these patients is improving in specialist centres the mortality for the majority of these severely ill patients has changed little in the last 20 years, and is approximately 70%. Extracorporeal membrane oxygenation (ECMO) provides gas exchange whilst the lungs are rested and allowed to recover, thereby reducing the effects of ventilator lung injury, an approach proven to result in improved survival in the NIH ARDS Network study. ECMO is an evidence-based treatment in severe *neonatal* respiratory failure, resulting in improved outcome compared to conventional ventilation. The Glenfield Hospital group has treated over 200 adults with ECMO since 1989. A detailed study of the first 50 patients revealed a hospital mortality of 34% for patients with a mean PaO_2/FIO_2 ratio of 65 mmHg and Murray score of 3.4.

We now aim to perform a randomised controlled trial (RCT) where adults with severe, but potentially reversible, respiratory failure are randomised for consideration of ECMO or continuing conventional ventilation.

Primary hypotheses:

For patients with severe, but potentially reversible, respiratory failure, ECMO:

(a) Will increase the rate of survival without severe disability by six months post randomisation.

(b) Will be cost effective from the viewpoints of the NHS and society, compared to conventional ventilatory support.

Inclusion Criteria:

(i) Centres:

(a) ECMO: This will be provided in the Glenfield Hospital, Leicester, which has 12 years of experience and is the only ELSO-recognised adult ECMO centre in the UK.

(b) Conventional treatment centres (CTC): These are centres acknowledged by their Network Director to provide an appropriately high standard of conventional care for ECMO-eligible patients. In areas where Networks are not yet operational this level of care has been defined, for the purposes of this protocol, as units which treat $\geq$ 350 patients per year, and can provide pressure controlled ventilation and veno-venous haemofiltration.

(c) Referral hospitals (RH): In addition to the centres described under (b) above, patients meeting ECMO entry criteria may be entered into the trial from a small number of other hospitals, if these hospitals are prepared to transfer the patient to a designated CTC should the allocation be to conventional management.

ii) Patients:

- Adult patients (18-65 years)
- Severe, but potentially reversible respiratory failure.
- Murray score $\geq$3.0, or uncompensated hypercapnoea with a pH <7.20

Exclusion Criteria Prior to Trial Entry:

- Duration of high pressure and/or high FIO_2 ventilation > 7 days.
- Intra-cranial bleeding.
- Any other contra-indication to limited heparinisation.
- Patients who are moribund and have any contra-indication to continuation of active treatment.

Outcome measures

Primary:

Death or severe disability at six months (defined as death by 6 months or before discharge from hospital at any time to end of data collection, or answering EQ5D first two questions as 'confined to bed' and 'unable to wash or dress yourself').

Secondary:

I) Hospital Indices: duration of ventilation, use of high frequency/oscillation/jet ventilation, use of nitric oxide, prone positioning, use of steroids, length of ICU stay, length of hospital stay. Some data will be recorded daily (see "Economic issues", below). For ECMO patients only, data will be collected on mode (VV/VA), duration of ECMO, blood flow and sweep flow.

II) Health status 6 months after randomisation. This will include activities of daily living, quality of life, respiratory symptoms, cognitive psychological state and lung function. Where applicable carer strain will also be assessed.

III) Surviving patients will be asked to give agreement for information to be held by the General Register Office. If appropriate, further funding may be requested later for longer-term follow-up including lung function tests.

It is not possible to completely blind this study, as the treatments are very different. However, one component of the primary outcome (death) is unlikely to be susceptible to assessment bias, and for the assessment of disability, patients and their relatives will be instructed not to reveal which treatment was used, and patients will wear a special scarf to cover the neck, masking the presence or absence of cannulation wounds.