Risk factors for and economic implications of prolonged ventilation after cardiac surgery

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The use of prolonged ventilation (PV) in patients undergoing cardiac surgery was assessed. PV was defined as ventilation for 96 hours or more.

Type of intervention
Secondary prevention. Rehabilitation following cardiac surgery.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients undergoing cardiac surgery. No further inclusion or exclusion criteria were reported.

Setting
The setting was secondary care. The economic study was carried out in Bristol, UK.

Dates to which data relate
The effectiveness and resource use data related to patients who underwent surgery between April 1996 and March 2003. A price year was not reported.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients as that used in the effectiveness study.

Study sample
The sample was selected by considering all patients receiving cardiac surgery in the study setting between the dates of the study for inclusion. The authors did not carry out power calculations to assess the influence of chance on the results. However, the sample size was very large (i.e. 7,553) and should have minimised the influence of chance. Seventy patients were excluded because they died within 96 hours of surgery, or they had at least three items of baseline demographic or clinical data missing. The PV group comprised 197 patients (2.6%) of which 29.9% were female. The mean age was 68 years (Interquartile range, IQR: 62 to 73) and the mean body mass index was 24.8 kg/m2 (21.1 to 27.7). The control group comprised 7,356 patients (97.4%), of which 24.2% were female. The mean age was 65 years (IQR: 58 to 71) and the mean body mass index was 26.4 kg/m2 (23.8 to 29.2).
Study design
The authors designed a prospective cohort study with groups defined by exposure to PV. The analysis was based at a single centre, the British Heart Institute, Bristol Royal Infirmary, UK. The design of the study aimed to identify those factors that were predictors of PV using backward stepwise logistic regression. The analysis was based on the actual length of ventilation received by a patient, and the consultant anaesthetist made the decision to extubate a patient. Blinded assessment and loss to follow-up were not reported.

Analysis of effectiveness
The analysis was conducted on an intention to treat basis. The primary health outcomes were in-hospital death, survival to 5 years, and patient characteristics identified as risk factors for PV. The authors estimated 5-year survival from the date of surgery until 31 July 2004. Survival time for patients who were lost to follow-up was censored at hospital discharge. Five-year survival was estimated using Kaplan-Meier survival curve and Cox proportional hazards regression.

Patients in the PV group were older and more likely to have had a recent myocardial infarction, cardiac surgery, an ejection fraction less than 50%, congestive heart failure, renal dysfunction, and advanced New York Heart Association (NYHA) class and Canadian Cardiovascular Society score. The control patients were more likely to have hypercholesterolaemia, a smoking history, and more extensive coronary artery disease. The characteristics of the patients were analysed without adjustment for confounding factors, with adjustment for confounding factors, and after being propensity matched between the groups.

Effectiveness results
The risk of in-hospital death for PV patients was 28.7 (95% confidence interval, CI: 20.3 to 40.6) before adjustment, 7.48 (95% CI: 4.56 to 12.3) after adjustment, and 8.06 (95% CI: 4.27 to 15.2) after propensity matching, (p<0.001).

The risk of death after hospital discharge was 5.13 (95% CI: 3.70 to 7.11) before adjustment, 2.48 (95% CI: 2.02 to 3.02) after adjustment, and 2.39 (95% CI: 1.75 to 3.27) after propensity matching, (p<0.001).

The 5-year survival (excluding in-hospital deaths) was significantly lower in the PV group (56.1%, 95% CI: 46.6 to 64.6 versus 88.8%, 95% CI: 87.9 to 89.6) also after adjustment for imbalances and when comparing propensity-matched patients (hazard ratio 2.39, 95% CI: 1.75 to 3.27; p<0.001 for propensity-matched group).

The following factors were found to be independent predictors of PV: older age, New York Heart Association class, ejection fraction less than 50%, renal dysfunction, cardiopulmonary bypass time more than 90 minutes, multiple valve replacement aortic procedures, use of preoperative inotropes and intra-aortic balloon pump, operative priority and reoperation for bleeding.

Clinical conclusions
The authors concluded that PV is associated with high in-hospital morbidity and mortality, and it significantly reduced 5-year survival. The independent predictors of PV identified may help to optimise the preoperative and postoperative clinical treatment of such patients.

Measure of benefits used in the economic analysis
The authors did not estimate a summary measure of benefit. Therefore, the study is classified as a cost-consequences analysis.

Direct costs
A perspective for the cost analysis was not reported, but it seems to have been that of the health care provider (e.g. hospital). The authors focused on the direct costs associated with a stay in hospital and accounted for the difference in intensity of care by estimating the length of time spent in intensive care, high dependency units and ward beds. The unit costs were compared between the PV and control groups.
cost also accounted for nurse time. There was no report that discounting was carried out, but this was not relevant as the stay in hospital was relatively short and broader costs over a longer time horizon were not considered. The resource use estimates were based on the actual length of time spent in hospital by the patients in the effectiveness study. A price year was not reported.

**Statistical analysis of costs**
The authors reported that 95% CIs for the mean costs were estimated using 100 bootstrap samples and were based on percentiles of the bootstrap estimates. This method was chosen to account for the skewed nature of the cost estimates.

**Indirect Costs**
Indirect costs, such as the broader economic costs of lost production, were not estimated. This may have been due to the significant implications identified for mortality and morbidity.

**Currency**
US dollars ($).

**Sensitivity analysis**
The authors did not report that any sensitivity analyses were carried out.

**Estimated benefits used in the economic analysis**
See the Effectiveness Results- section.

**Cost results**
The mean total bed occupancy costs were $14,286 (95% CI: 12,731 to 15,690) for PV and $2,761 (95% CI: 2,705 to 2,814) for the control group, (p<0.001).

Patients in the PV group on average had higher intensive care unit costs and high dependency unit costs, (p<0.0001), but similar ward costs, (p=0.35).

The 197 PV patients represented 2.6% of the entire population but accounted for 12.2% of the total bed occupancy costs.

**Synthesis of costs and benefits**
Not relevant.

**Authors' conclusions**
The authors drew three main conclusions: prolonged ventilation (PV) patients have significantly higher in-hospital morbidity and mortality and worse 5-year survival; there were several independent predictors of PV; and a very small percentage of the treated population account for a large percentage of the total costs.

**CRD COMMENTARY - Selection of comparators**
To identify risk factors for PV, the authors compared a cohort of cardiac surgery patients who received PV and a cohort of cardiac surgery patients who did not receive PV. The technology of interest and comparator technology were natural choices given the clinical question addressed.
Validity of estimate of measure of effectiveness
The study design, a prospective cohort analysis, was an appropriate study design to address the study question. The authors selected factors to consider as predictors of PV in advance of the study, thus avoiding potential internal biases. The authors were very thorough in their results, reporting details both unadjusted and adjusted for confounding factors. In addition, the patients were propensity-matched to try to diminish the influence of confounding. The study sample was representative of the study population as it included patients who had undergone cardiac surgery and received ventilation, and no further exclusion criteria were reported.

Validity of estimate of measure of benefit
The authors did not estimate a summary measure of health benefit. The study was therefore categorised as a cost-consequences analysis.

Validity of estimate of costs
The authors did not report the perspective from which the costing was carried out, although a hospital perspective seems to have been adopted. An explicit statement of the perspective would help readers to interpret and decide whether the cost results are generalisable to alternative settings. The analysis might have been improved with the consideration of indirect costs, as the study population comprised patients whose economic productivity was diminished and treatment and recovery times may influence future productivity. The unit costs and the quantities were reported separately, thus enhancing the reproducibility of the results in other settings. The resource use and price data were specific to the study setting. A statistical analysis of the quantities was conducted using appropriate bootstrap samples. The study would have benefited had the price year been reported. Aside from these points, the analysis was clear to understand and well reported, giving a basic idea of the comparison in costs between the two study groups.

Other issues
The authors compared their own findings and those of others, particularly with reference to survival rates. Generalisability to other settings was not addressed and, in addition to the points mentioned previously, the ability to generalise is limited by the institution-specific costs. The effectiveness results are more likely to be generalisable as there were no inclusion and exclusion criteria. The study enrolled patients undergoing cardiac surgery and this was reflected in the authors’ conclusions. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. The authors presented some limitations of their study. These focused on preoperative differences between the groups, although the authors made extensive efforts to control for such differences.

Implications of the study
The authors highlighted numerous implications of their study, most notably, predicting the occurrence of PV might help optimize the preoperative patient information and consenting process, patient management, and case-mix scheduling. Further work to explore the impact of the degree of lung dysfunction was suggested, which the authors felt warranted a dedicated study.

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