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Cost of treating ventilator-associated pneumonia post cardiac surgery in the National Health Service: Results from a propensity-matched cohort study

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Abstract

Background: Ventilator-associated pneumonia is associated with significant morbidity, mortality and healthcare costs. Most of the cost data that are available relate to general intensive care patients in privately remunerated institutions. This study assessed the cost of managing ventilator-associated pneumonia in a cardiac intensive care unit in the National Health Service in the United Kingdom.

Methods: Propensity-matched study of prospectively collected data from the cardiac surgical database between April 2011 and December 2014 in all patients undergoing cardiac surgery (n = 3416). Patients who were diagnosed as developing ventilator-associated pneumonia, as per the surveillance definition for ventilator-associated pneumonia (n = 338), were propensity score matched with those who did not (n = 338). Costs of treating post-op cardiac surgery patients in intensive care and cost difference if ventilator-associated pneumonia occurred based on Healthcare Resource Group categories were assessed. Secondary outcomes included differences in morbidity, mortality and cardiac intensive care unit and in-hospital length of stay.

Results: There were no significant differences in the pre-operative characteristics or procedures between the groups. Ventilator-associated pneumonia developed in 10% of post-cardiac surgery patients. Post-operatively, the ventilator-associated pneumonia group required longer ventilation ($p < 0.01$), more respiratory support, longer cardiac intensive care unit (8 vs 3, $p < 0.001$) and in-hospital stay (16 vs 9) days. The overall cost for post-operative recovery after cardiac surgery for ventilator-associated pneumonia patients was £15,124 compared to £6295 for non-ventilator-associated pneumonia ($p < 0.01$). The additional cost of treating patients with ventilator-associated pneumonia was £8829.

Conclusion: Ventilator-associated pneumonia was associated with significant morbidity to the patients, generating significant costs. This cost was nearer to the lower end for the cost for general intensive care unit patients in privately reimbursed systems.

Keywords

Ventilator-associated pneumonia, cost of ventilator-associated pneumonia, National Health Service costs, cardiac surgery

Introduction

Ventilator-associated pneumonia (VAP) is associated with significant patient morbidity and mortality.[1–3] It has also been suggested that there are significant cost implications when treating patients with VAP.[4–6] VAP is recognised as one of the healthcare-associated infections (HAI) along with surgical site infection (SSI), central line-associated blood stream infection (CLABSI), catheter-associated urinary tract infection (CAUTI) and clostridium difficile infection (CDI),[7]

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which bears heavily on the health system and are very preventable.

A number of studies have attempted to estimate the economic burden of VAP and have reported costs ranging from $10,000 to $40,000 per patient treated.[7–10] However, most of these studies were based in general intensive care unit (ICU) patients within healthcare systems such as in the USA where the hospitals were reimbursed by a private health insurer. VAP can develop within any group of patients who are ventilated for a period of time even when this period is less than 24 h, such as in patients undergoing cardiac surgery.[11] As the management of VAP is the same whether the patient is a general ICU patient or a cardiac surgical patient on cardiac intensive care unit (CICU), similar cost implications may apply.

In the UK, the healthcare system is provided mostly by the government funded National Health Service (NHS) and hospitals are remunerated via a payment by results (PbR) system using nationally agreed tariffs. The latter is calculated using clinical codes grouped together by the Healthcare Resource Group (HRG).[12] Each HRG is assigned a cost, which reflects the required expenditure for providing a specified package of care, and there are specific HRG costs for intensive care stay depending on the number of body organs being supported. When patients develop VAP, these costs can escalate to a significant sum.[7–10] This increase in costs reflects the additional need for manpower, equipment use and drug treatments. The HRG costs based on specific HRG codes are listed in Table 1.

The aim of this study is to assess the costs to the NHS when treating VAP in a cardiac surgical population using the HRG codes given to healthcare providers in England.

Table 1. HRG activity classification.

HRG code	Code description	Per diem cost (£)
XC01Z	Adult Critical Care – 6 Organs supported	1886
XC02Z	Adult Critical Care – 5 Organs supported	1712
XC03Z	Adult Critical Care – 4 Organs supported	1594
XC04Z	Adult Critical Care – 3 Organs supported	1449
XC05Z	Adult Critical Care – 2 Organs supported	1266
XC06Z	Adult Critical Care – 1 Organs supported	890
XC07Z	Adult Critical Care – 0 Organs supported	643
	One day Cardiothoracic Ward stay	383

HRG: Healthcare Resource Group.

Material and methods

All patients undergoing cardiac surgery at our centre during the period of April 2011 to December 2014 were initially selected (n = 3416). Patients who were diagnosed to have developed definite VAP were included in the VAP group (n = 342). VAP was diagnosed using the CDC definition[13] as well as the HELICS clinical criteria.[14] Two definitions were used in conjunction with each other, as the VAP criteria are regularly updated and these two definitions were active during the study period. The diagnosis of VAP included patients who demonstrated new and/or progressive pulmonary infiltrates on a chest radiograph, along with two or more of the following: fever (>38.5°C) or hypothermia (<36°C), leukocytosis ($>12 \times 10^9$/L), purulent tracheobronchial secretions or a reduction in PaO_2/FiO_2 (partial pressure of arterial oxygen/fraction of inspired oxygen) of 15% or more in the previous 48 h. Patients also had positive bacteriologic cultures.[14] As per the CDC definition, patients were diagnosed as having VAP irrespective of the duration of intubation.[13] Based on these definitions, only patients who were classed as having definite VAP were included in the study. Moreover, only patients who developed a pneumonia as their first main complication were included. Thus, patients who developed another complication, e.g. low renal output and then developed a pneumonia, were excluded. Complete data needed for patient matching and data analysis were available for 338 VAP patients (99%) (study group). Patients in the VAP group were then matched according to propensity score to create a non-VAP patient group (control, n = 338). Prospectively collected data for the patients were then retrieved from our databases (Dendrite Cardiac surgery and Medtrack Intensive Care). This study was agreed by the Hospital's Research and Development Department. Ethical approval for this study (Ethical Committee REC reference number: 15/WS/0142).

Our antibiotic prophylaxis includes intravenous gentamicin and flucloxacillin prior to skin incision followed by flucloxacillin 6-hourly for 24-h post-op. Patients allergic to penicillin are given teicoplanin (single dose).

Patients are extubated when they fulfil the following criteria:

- They are adequately warm
- They do not require high ventilatory/FiO2 support
- They are haemodynamically stable and are unlikely to need to return to the operating room
- They are awake and co-operative enough to maintain their airway and obey simple commands

Our VAP prevention bundles include appropriate hand hygiene, changing of ventilator circuits when soiled, or at 7 days whichever was sooner, semi

recumbent positioning whenever clinically possible and Chlorhexidine 2% oral mouth wash 6 hourly whilst intubated. All patients routinely received gastric stress ulcer prophylaxis with Ranitidine 50 mg I.V. 8 hourly.

A logistic regression model was used to generate a propensity score for each patient. This can be considered as the probability of contracting a chest infection and is based on patient and procedure characteristics. The following variables were considered for the propensity score model: age, sex, ethnicity, BMI, smoking history, diabetes management, operation year, CABG, other cardiac procedure, major aortic procedure, valve surgery, urgency, ejection fraction, extra cardiac arteriopathy, history of pulmonary disease, renal function, bypass time, pre-operative haemoglobin, creatinine and Euroscore. Cardiopulmonary bypass time, pre-operative haemoglobin, creatinine and Euroscore were log transformed prior to entry into the model. For each patient in the VAP group, an individual was selected in the non-VAP group by matching on the log of the estimated propensity score, using a nearest neighbour matching algorithm with callipers (an interval) of maximum width of 0.2 standard deviations (SDs). The distribution of all model factors was compared in the two groups to assess the success of the propensity score model. In line with recommendations, the balance in the covariates across the two groups was considered achieved if the standardised differences were less than 10%.[15] The first model for the propensity score containing all the above variables was considered a success as all standardised differences were less than 10%. Hence, no further models were considered.

In order to estimate the cost for treating VAP, resource use associated with each patient was retrieved from the hospital's database. This contained two pieces of information: (a) the various HRGs incurred by each patient and (b) the number of days spent at each HRG. Unit costs were taken from 2013 to 2014 Reference Costs (National Schedule of Reference Costs, 2014) and total patient cost was obtained by multiplying resource use by the unit costs. Finally, the cost of VAP was calculated as the difference in the cost between the VAP and non-VAP cohorts.

As the cost data were right skewed, they were analysed using the non-parametric bootstrap statistical technique.[16,17] The 95% bias-corrected accelerated (BCa) confidence intervals around the means were calculated by running 10,000 sampling replications. All bootstrap computations were performed in R.[18]

Categorical data are expressed as percentage and differences between the two groups assessed using the chi square (χ^2) test of independence. Continuous variables are expressed as mean (SD) or median (range) for Gaussian and skewed distributed data, respectively. Likewise, group comparisons were carried out using the t-test or non-parametric (Mann–Whitney U) test accordingly. Tests were considered significant at $p \leqslant 0.05$. Statistical analyses were carried out in SPSS version 20 (IBM, SPSS package) and STATA 12 (StataCorp).

Table 2. Pre-operative patient characteristics.

	VAP (n = 338)	No VAP (n = 338)
Age[a], years	65.9 (10.9)	65.6 (10.8)
Males, n (%)	269 (80%)	281 (83%)
Caucasian, n (%)	289 (86%)	284 (84%)
Diabetics, n (%)	95 (28%)	96 (28%)
Lung disease, n (%)	83 (25%)	80 (24%)
Smokers, n (%)	64 (19%)	68 (20%)
PVD, n (%)	71 (21%)	77 (23%)
Elective, n (%)	183 (54%)	172 (51%)
Impaired LV, n (%)	108 (32%)	120 (35%)
Isolated CABG, n (%)	168 (50%)	176 (52%)
Isolated valve, n (%)	38 (11%)	40 (12%)
Log EuroScore[a]	7.85 (8.54)	7.54 (8.29)

[a]Data expressed as mean (SD).
VAP: ventilator-associated pneumonia; PVD: peripheral vascular disease; LV: left ventricular function; CABG: coronary artery bypass grafting; SD: standard deviation.

Results

Ten percent (342/3416) of patients undergoing cardiac surgery during the study period developed VAP. There were no significant differences between the two groups in terms of patients' pre-op characteristics (Table 2). The types of surgery and the priority for the need for surgery were also not significantly different (Table 2). The median intubation times were 16 h (8,1680) for the VAP and 16 h (8,1008) for the non-VAP groups ($p < 0.01$). Only 3% (105/3416) of patients required ventilation for more than 48 h. Post-operatively patients in the VAP group required longer ventilation period ($p < 0.01$) and additional respiratory support ($p < 0.01$) such as facial CPAP (continuous positive airway pressure), re-intubation and tracheostomy (Table 3). Positive bacteriological cultures were obtained in VAP patients from either BAL or sputum samples. The various pathogens identified included: Gram-negative bacteria (GNB) in 43% (*Haemophilus influenzae* being most common – 34%, *Klebsiella pneumoniae* – 13%, Coliform species – 10%, *Pseudomonas aeruginosa* – 10%, *Escherichia coli* – 10% and others – 23%), Gram-positive bacteria in 7% (*Staphylococcus aureus* – 69%, *Streptococcus* species – 31%) and a fungal component (mostly *Candida albicans*) in 21%. Of note, given that these samples were obtained from a combination of BALs and sputum culture, 51% had a mixed growth pattern on microscopy.

In all, 10.4% (35 patients) in the VAP group required a tracheostomy as part of their ventilator wean.

The median ICU stay was significantly different between VAP and non-VAP patients, being 7.8 (0,74) and 2.9 days (0,46) respectively ($p < 0.01$) as was the in-hospital stay 16.2 days (4,137) and 8.6 days (4, 64), respectively ($p < 0.01$). However, there were no significant differences in mortality (4.7% vs 3.3%, $p = 0.2$).

The cost of treating VAP patients was significantly higher than for non-VAP patients (Table 4). This amounted to an additional cost of £8829 (BCa 95% CI = 6937–11,189) per patient when VAP occurred.

Discussion

This is the first UK-based study (where HealthCare delivery is essentially free) assessing the cost of treating VAP in cardiac surgical patients. It confirmed the significant morbidity, prolonged ICU and in-hospital stays, which have been previously described[3,11] and provides a realistic estimate of the cost for treating VAP in a non-profit making medical institution.

The duration of mechanical ventilation was not included in the propensity score matching (PSM) model, because it is well recognised that VAP patients usually require longer ventilation as compared to non-VAP patients. This current study was set up to assess the cost of VAP rather than its causes and if duration of mechanical ventilation was used in the PSM model, then there would have been a large number of patients in the VAP group who would not be matched and would have been excluded from the study group and would not have provided a true clinical progress picture. Thus, it would have defeated the purpose of the cost calculations, as it is the longer duration of mechanical ventilation along with its ensuing complications such as sepsis and renal failure, which generates the high cost of treating patients with VAP.

The costs were calculated as the difference between the VAP and the non-VAP cohorts. This comparative method of calculating the cost of VAP has also been used by most other authors who have reported a cost of VAP, and certainly by authors who conducted primary data analysis (as opposed to systematic reviews).[7–9] In accordance with best practice, the confidence intervals of the cost of VAP were computed using bootstrapping.[16,19] Being a Monte Carlo-based, non-parametric technique, the bootstrap does not make any assumption about the underlying distribution of the data and it has therefore the ability to generate more realistic estimates of the uncertainty around the mean than would be the case with standard parametric statistical procedures.[16]

It is widely acknowledged that VAP leads to morbidity and use of resources, which could have been deployed elsewhere. Despite this, there is a lack of accurate estimates of the cost of VAP in the UK. In this study, a combination of the CDC definition[13] and HELICS clinical criteria were used.[14] It is recognised that other definitions are in use, e.g. CPIS,[20] and the varied definitions used in other studies might account for the differences in the VAP rates reported, the differing bacteriological agents and the mortality associated with VAP.[20,21] Over the last decade, the VAP definitions have been ever-changing and newer

Table 3. Intra- and post-operative data.

	VAP (n = 338)	No VAP (n = 338)	p-Value
Number of CABG grafts[a]	2.4 (1.7)	2.4 (1.6)	0.7
Atrial fibrillation[+]	154 (46%)	86 (25%)	<0.001
Facial CPAP[b]	47 (14%)	6 (2%)	<0.001
Re-intubation[b]	44 (13%)	8 (2%)	<0.001
Tracheostomy[b]	35 (10%)	5 (2%)	<0.001
CVA/TIA[b]	11 (3%)	8 (2%)	0.6
Confusion[b]	67 (20%)	24 (7%)	<0.001
CVVHF[b]	69 (20%)	17 (5%)	<0.001
Re-admission to CICU[b]	25 (7%)	10 (3%)	<0.01
Survival[b]	322 (95.3%)	327 (96.7%)	0.3

For the percentages of patients requiring facial CPAP, re-intubation and tracheostomy, patients were classed according to the highest level of ventilatory support required.
[a]Mean (SD)
[b]Data expressed as n (%).
VAP: ventilator-associated pneumonia; CPAP: continuous positive airway pressure; CVA/TIA: transient or permanent neurological dysfunction; CVVHF: continuous veno-venous haemofiltration; CICU: Cardiac Intensive Care Unit.

Table 4. Cost of VAP based using the HRG.

	VAP		no VAP				
Cost category	Mean (£)	SD (£)	Mean (£)	SD (£)	Difference (£)	BCa 95% CI (£)	
ICU stay	12,117	17,400	4178	5953	7939	6222	10,071
Ward stay	3007	3322	2117	1905	890	521	1336
Total	15,124	18,993	6295	6787	8829	6937	11,189

VAP: ventilator-associated pneumonia; HRG: Healthcare Resource Group; ICU: intensive care unit.

concepts such as ventilator-associated complications (VAC) are becoming more popular.[22] During the period of this study, the HELICS definitions used were the most topical. However, from a clinical perspective, irrespective of the definition, patients experience significant morbidity when a chest infection ensues after a period of intubation. The infection can develop even after a few hours of intubation as reported by Gopal et al., when VAP was seen in patients undergoing cardiac surgery after a median intubation time of 15 h,[11] further supporting the notion that the endotracheal tube is a recognised modifiable risk factor, that can reduce the risk of VAP.[23]

With £8829, the cost of VAP calculated in this study is lower than that generally reported in the literature. In a systematic review, Safdar et al.[10] present the pooled cost estimate from their literature survey. They report a mean cost between $10,019 and $13,647 (in 2005 US Dollars), which did not include physician charges and is therefore likely to be conservative. They also report a mean increase in ICU LOS of 6.1 days. Patients had to have been on ventilation for at least 48 h. Restrepo et al.,[9] in a retrospective analysis of the NASCENT clinical trial, report a median cost of approximately $20,000 (in 2010 US Dollars), which is also an underestimate of the average cost, given that costs are generally right skewed with the consequence that the mean is always greater than the median. The median incremental LOS was 10.5 days for ICU stay and 12.5 for total hospital stay. VAP diagnostic was microbiologically confirmed and patients had to be intubated for at least 24 h. Kollef et al.,[3] in a large observational hospital database study published in 2012, present a mean cost of VAP of $39,828. The reported increase in mean LOS was 8.9 days in the ICU and 13.1 days for total hospitalisation. VAP was identified via the ICD-9 code 997-31 and only patients with at least 48 h of mechanical ventilation were included in the analysis. Finally, based on a systematic review, Zimlichman et al.[7] report a mean cost of $40,144 (in 2012 US Dollars). The additional mean ICU LOS was 8.4 days and it was 13.1 days for hospitalisation overall. The diagnosis of VAP followed the CDC definition.

In our study, the mean additional LOS due to VAP was 4.8 days for ICU stay and 7.6 for overall hospitalisation. These incremental LOS values are smaller than those of the literature cited above and this may partly explain the lower cost of VAP found in this study. However, it should also be considered that in a private health care system, as is the case for the American setting, costs may have been more closely monitored for reimbursement purposes. This could also account for some of the difference between the cost of VAP presented here and previously published data. Also, in this study, the HRG codes were used to calculate the costs, whereas in other reports, both direct and indirect costs were included when the economic implication of VAP was assessed.[8] However, these costs may still be an under-estimate as the indirect costs to the patients and their caregivers were not taken into consideration.

The incidence of VAP has been estimated to up to 30% in general ICU patients.[20] Furthermore, in cardiac surgery, the mortality associated with VAP has been reported to be around 40%.[24,25] In this study, the VAP incidence in a post-op cardiac surgery patient was 10% with a mortality of 4.7%. The latter although higher than when VAP did not occur, was still well below what was previously thought to be the mortality rate associated with VAP, considering that the current population (post-op cardiac surgery patients) was different from the other reports (general ICU patients).[1] Moreover, this low mortality may also reflect a very pro-active management of any complication when it does arise in our service, which is fully consultant-based be it in cardiac surgery, cardiac anaesthesiology or cardiac intensive care. Generally survival after cardiac surgery in the UK is very good.

According to He et al.'s meta-analysis, the most common pathogen causing VAP belongs to the gram-negative bacteria (GNB) group with *Pseudomonas* being a leading pathogen. The current study also confirms GNB to be the leading cause of VAP, but in this series *Haemophilus* species was the major pathogen. This, most likely, reflects the fact that in the current series, the intubation times were much shorter. Gram-positive bacteria also caused VAP and could have been introduced during the process of intubation. A recent publication that reviewed BAL samples in 240 patients showed that most VAP are due to aspiration of pooled secretions around the endotracheal tube cuff (usually gastric content based), translocation of bacteria along the inner lining of the ET tube or direct contamination during intubation.[11,26]

Prevention is the best strategy against VAP as treatment of VAP is limited and VAP is associated with poor outcomes. Efforts such as early extubation, strict hand hygiene and enforcement of Institute of Healthcare Improvement (IHE) recommended infection prevention 'ventilator bundles' help towards reducing the risk of VAP. Furthermore, some will also advocate chlorhexidene mouthcare[27] and selective gut decontamination[28] to reduce the risk of VAP. ET tubes with better cuff management systems provide a good seal and thereby prevent micro-aspirations.[2,29,30] Early administration of antibiotics at clinical suspicion of VAP is appropriate as delay in starting antibiotics is associated with poor outcomes. Adopting the above measures in clinical practice may come at a cost. In this study, the cost of treating VAP per patient undergoing cardiac surgery was calculated at £8829. Hence, any change in managing this issue will be cost-beneficial as long as it is cheaper than £8829.

The limitations include those of a retrospective review of prospectively collected data. The CDC VAP definition and the HELICS clinical categorisation were used for VAP diagnosis. Although these three diagnoses were confirmed as definite VAP, there could have been some bias in categorising patients as having VAP. Other VAP definitions were not considered during this study, e.g. the CPIS. We do recognise this limitation of an appropriate definition but given that the VAP definitions were constantly being updated, we have used these two definitions, which were in practice during the period of the study. Moreover, although the patients were propensity matched, as in all studies using this method, selection bias cannot be completely excluded. Ventilation time was not entered in the propensity model as only a minority of patients were ventilated for more than 48 h (3%) and most of these patients were those in the VAP group. This would have excluded a good proportion of VAP patients and would not have provided a true reflection of the actual cost of treating patients who develop VAP as most of this cost would include the increased ventilation time, increased ICU stay and the ensuing complications. Likewise, post-op complications were not used in the propensity model, as only patients who developed VAP as their first main complication, were included in the VAP group. However, it might have been possible that these patients were already having sub-clinical complications, which had not as yet been the prime problem in their management. Finally, this is a single centre based study with its inherent limitations.

From a UK perspective, future studies will need to assess the cost–benefit of proposed interventions to reduce VAP and prove that introducing and adopting such interventions represents an efficient use of available health care resources. In conclusion, VAP after cardiac surgery is associated with significant morbidity. Its treatment amounts to significant costs to any type of healthcare system whether direct or indirect costs or both are included. Prevention strategies should be evaluated for cost-effectiveness and could represent the best option for improving patients' outcome and hospitalisation costs.

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