Evaluating the Direct Economic Burden of Prolonged Mechanical Ventilation Among Patients With Acute Type A Aortic Dissection: a Propensity Score-matched Cohort Analysis

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Abstract

Background: Prolonged mechanical ventilation (PMV) among acute type A aortic dissection (AAAD) may affect the prognosis, but poorly known about the direct economic burden of PMV in patients with AAAD. The present study was contributing to filling this knowledge gap.

Methods: This present study was a retrospective cohort study. Age, gender, payment methods, and postoperative complications were matched at a 1:1 ratio by using a propensity score analysis of AAAD patients. The direct economic burden was expressed as the median 1:1 differences of various hospital costs and length of stay (LOS). The Wilcoxon signed-rank tests were used to compare the difference of direct economic burden at mechanical ventilation (MV) and PMV patients.

Results: A total of 464 patients, PMV occurred in 142 (30.6%) patients, and 218 patients were enrolled in the matched analysis. The estimated total direct economic burden of PMV was $4970.28 (P < 0.05). Among different hospital costs, western medicine ($3183.23) accounted for the highest category in the economic burden, followed by blood transfusion ($250.81) and materials fees ($207.43). The median hospital and Intensive Care Unit LOS in PMV groups were prolonged 5 days than those in MV groups (P < 0.05).

Conclusions: Postoperative PMV was associated with increased economic burden among AAAD patients. This study emphasizes the need for early detection and management of PMV to reduce the economic burden.

Background

The incidence of aortic dissection is approximately 3.5-6.0/10,000/year [1], among them, acute type A aortic dissection (AAAD) is a type characterized by high mortality, medical therapy for AAAD is associated with a 60% 30-day mortality, thus surgical repair is indicated for most AAAD patients [2, 3]. Compared with other cardiovascular diseases, AAAD patients are more prone to perioperative hemodynamic instability and postoperative complications. For example, postoperative respiratory dysfunction is common, usually caused by systemic inflammation [4] and ischemia-reperfusion injury [5]. Thus, some patients require prolonged mechanical ventilation (PMV).

PMV can not only increase the risk of death but also accumulate more hospital costs and length of stay (LOS) [6–7]. According to reports, PMV patients with myocardial infarction had nearly three times more medical expenses and four times the hospital LOS than MV patients in the United States [8]. Moreover, the median cost of PMV patients was over $42,784 in Canada [9], while the MV patients were only $13,005. It can be seen that even in developed countries such as the United States, PMV has imposed a heavy economic burden on patients. Studies have shown that the incidence of PMV in AAAD patients is 28.9%-44.5% [10–12]. It is higher than other cardiac surgery patients [13–14].
At present, there is a dearth of knowledge on the economic burden of PMV among AAAD patients. Considering that the incidence of PMV in AAAD patients is higher than that in other cardiac surgery patients, and along with an increase in the aging population and the determined incidence of aortic dissection has continued to rise in China [15], the economic burden caused by PMV on AAAD patients is worth quantifying, providing clinical and policy decisions for reducing the economic burden of such patients in developing countries. To this aim, we conducted a retrospective cohort study to provide definitive evidence for the direct economic burden that PMV may cause that allows the hospital to make decisions about the cost-effective allocation of limited resources.

Methods

Study location and participants

The present study was performed in a tertiary public hospital in Fujian Province, China. In 2017, the annual disposable income of per capita residents was $4,836.15 in Fujian Province. About 96% of the population has national basic health insurance, which can cover 60% of the patient's total hospitalization expenses among AAAD patients. Between January 2017 and May 2020, patients with AAAD who were diagnosed by computed tomography angiography were recruited to our study. The inclusion criteria were based on the following approaches: (1) Age \( \geq 18 \) years; (2) Required mechanical ventilation; (3) Underwent AAAD surgery after admission. When it's come to the exclusion criteria, we excluded the following conditions: (1) All-cause readmission; (2) With incomplete data; (3) Chest pain or other related symptoms occur more than 14 days before surgery; (4) History of cancer. This study was approved by the ethics committee of the aforementioned hospital, informed consent was not necessary because this was a retrospective study.

Matching Procedure

We assessed the economic burden of PMV by using a 1:1 matched sample to compare all-cause hospitalization costs between MV and PMV patients. According to previous studies [16] and combined with logistic regression model included covariates of related factors for PMV, factors correlated with hospital costs include gender, age, payment methods, and postoperative complications. Thus, our study was based on the same matching method of age, gender, payment methods, and postoperative complications to estimate the increased hospital costs and LOS among patients with baseline demographic characteristics similar to those without PMV.

Perioperative management

The open triple-branched stent-graft placement technique was to repair the total arch instead of direct surgical repair, surgical strategies and intraoperative management apply to all patients, and the above procedures were reported in our previous study [17]. All patients were admitted to the cardiac surgery Intensive Care Unit (ICU) after the operation and received mechanical ventilation under an appropriate fraction of inspired oxygen to maintain postoperative arterial oxygen saturation > 95%. During mechanical ventilation, all patients selectively used midafenazole, dexmedetomidine, and morphine as
analgesia and sedation regimens. Extubation guidelines [18] for cardiac surgery included: hemodynamic stability with minimal inotropic support; awake and follow simple commands; adequate muscle strength; tidal volume greater than 5 ml/kg, end-tidal CO$_2$ < 50 mmHg; no significant metabolic acidosis, normothermia; absence of significant coagulopathy. If the patient develops hypoxemia after extubation, non-invasive positive pressure ventilation or high flux oxygen inhalation was applied.

**Data collection and definitions**

The data of all patients were collected retrospectively by searching the electronic medical record of our hospital. The demographic data including gender, age, marital status, admission type, payment methods, and place of residence. At the same time, the preoperative comorbidities and postoperative complications of patients were collected. Hypertension, diabetes, and coronary heart disease were comorbidities in our study, complications included pulmonary infection, renal insufficiency, and gastrointestinal bleeding, comorbidities, and complications were determined through history taking or documentation in the medical records.

Apart from this, according to the necessary data of medical insurance reimbursement in China, we collected the various hospitalization costs, including western medicine, materials, diagnosis, bed charge, nursing, examination, treatment, blood transfusion, and surgery, and we also extracted the costs of mechanical ventilation. In our study, medicine is mainly composed of antibiotics, vasoactive drugs, and sedatives, etc. Materials mainly include surgical supplies and surgical incision packages. The diagnosis is the cost of health examination, such as computed tomography angiography (CTA), B-ultrasound, color doppler ultrasound. Treatment cost refers to the medical services rendered to patients and the required medical supplies. The examination is the cost of dynamically monitoring the patient's condition, such as ECG monitoring and arterial blood pressure. The increase of total hospitalization costs related to PMV is our primary outcome, while the various increased costs and LOS related to PMV are our secondary outcomes.

Direct economic burden refers to the cost of providing medical services, such as hospital costs, medicine, surgical, etc. PMV was defined as endotracheal intubation and ventilation requiring more than 48 hours during the postoperative stay, starting from the cardiac ICU admission to the time in which patients were tracheal extubated. While for patients who were detached repeatedly from the ventilator, a total of these episodes should be required at least 48 hours or more were also included. However, there is no standardized definition of delayed extubation following AAAD surgery. Therefore, we adopted this current definition according to previously conducted studies [10–12].

**Statistical analysis**

Demographic data with normality distributed variables are presented as mean values ± standard deviation, and non-normally distributed data were presented as median (interquartile range). All categorical variables were shown in the form of frequencies and percentages, and the $\chi^2$ test was calculated for the differences of categorical variables such as admission type and insurance. An
independent sample t-test was utilized to compare the continuous variables normally distributed, and the Mann-Whitney U test was used for non-normally distributed data such as hospital LOS.

For the analysis of the direct economic burden, we used the Wilcoxon signed-rank tests to evaluate the differences between MV and PMV patients. The various direct economic burden was presented by the median of the pair differences of costs or LOS (PMV group minus MV group). All statistical calculations were performed with SPSS IBM version 24.0, a $P$-value of less than 0.05 was considered to be statistically significant. The exchange rate (USD/CNY) was set at 0.15, approximate.

Results

Patient characteristics

We identified 464 patients between January 2017 and May 2020, prolonged mechanical ventilation occurred in 142 (30.6%) of these patients. After propensity score matching, out of 109 pairs patients were included in the matched analysis. The selection of study participants is shown in Fig. 1. Among them, in the MV group, 34 (31.2%) were female and 75 (68.8%) were male; while in the PMV group, 102 (71.6%) were male and 31 (28.4%) were female. Patients aged $\geq$ 45 were 89 (81.7%) in the PMV group, and in the MV group was 81 (74.3%). The MV group and the PMV group were comparable between age, gender, payment methods, and postoperative complications ($P$> 0.05). A comparison characteristic of the matched cohorts is shown in Table 1.
Table 1
A matched cohort of demographic and postoperative complications data between MV group and PMV group

| Characteristic                        | MV group (n = 109) | PMV group (n = 109) | P-value |
|---------------------------------------|-------------------|---------------------|---------|
| Age (y), mean (SD)                    | 53.98 ± 11.70     | 53.07 ± 11.68       | 0.859   |
| Marital status, n (%)                 |                   |                     | 0.553   |
| Married                               | 104 (95.4)        | 102 (93.6)          |         |
| others                                | 5 (4.6)           | 7 (6.4)             |         |
| Gender, n (%)                         |                   |                     | 0.657   |
| Male                                  | 75 (68.8)         | 78 (71.6)           |         |
| Female                                | 34 (31.2)         | 31 (28.4)           |         |
| Admission type, n (%)                 |                   |                     | 0.681   |
| Emergency                             | 45 (41.3)         | 48 (44.0)           |         |
| Outpatient                            | 64 (58.7)         | 61 (56.0)           |         |
| Insurance, n (%)                      |                   |                     | 0.621   |
| Insurance covered                     | 84 (77.1)         | 87 (79.8)           |         |
| Self-paid                             | 25 (22.9)         | 22 (20.2)           |         |
| Address, n (%)                        |                   |                     | 1.000   |
| Rural                                 | 44 (40.4)         | 44 (40.4)           |         |
| Urban                                 | 65 (59.6)         | 65 (59.6)           |         |
| Comorbidity, n (%)                    |                   |                     |         |
| Hypertension                          | 10 (92.7)         | 102 (93.6)          | 0.789   |
| Diabetes                              | 13 (11.9)         | 7 (6.4)             | 0.159   |
| Coronary heart disease                | 21 (19.3)         | 13 (11.9)           | 0.135   |
| In-hospital complications, n (%)      |                   |                     |         |
| Lung infection                        | 13 (11.9)         | 11 (10.1)           | 0.665   |
| Gastrointestinal bleeding             | 5 (4.6)           | 7 (6.4)             | 0.553   |
| Renal insufficiency                   | 24 (22.0)         | 26 (23.9)           | 0.747   |

MV, mechanical ventilation; PMV, prolonged mechanical ventilation.
Comparison of various hospital costs between MV and PMV groups

A comparison of various hospital costs of the matched cohorts is shown in Table 2. Each type of hospital cost showed that the PMV group was higher than that in the MV group except for diagnosis and surgery costs, additional details of various hospital costs are shown in Fig. 2. The total economic burden of the PMV group is $4,970.28. As for various stratified hospital costs, western medicine ($3183.23) accounted for the highest category in the economic burden, followed by blood transfusion ($250.81), mechanical ventilation costs ($80.00), and treatment costs ($40.52). Statistically significant differences were observed between the two groups ($P< 0.05$). Other item costs, such as bed charge ($36.44$), nursing ($28.15$), examination ($3.56$), and laboratory ($17.63$) account for only a relatively small share of the economic burden. However, statistically, significant differences were observed between these two groups ($P< 0.05$).
Table 2
A matched cohort of direct economic burden stratified by various hospital costs between MV group and PMV group

| Expenses category       | MV group (n = 109)           | PMV group (n = 109)           | Direct economic burden* | \( P \)-value |
|-------------------------|------------------------------|------------------------------|-------------------------|---------------|
| Medicine ($) (IQR)      | 4034.13 (2979.27, 6627.37)   | 7217.36 (4811.76, 10759.11)  | 3183.23                | < 0.001       |
| Diagnosis ($) (IQR)     | 79.11 (70.52, 155.56)        | 79.11 (60.00, 130.07)        | 0.00                    | 0.465         |
| Materials ($) (IQR)     | 1871.73 (1605.74, 6710.11)   | 2079.16 (1711.37, 6593.32)   | 207.43                  | 0.142         |
| Bed charge ($) (IQR)    | 30.67 (17.78, 74.00)         | 67.11 (39.56, 152.59)        | 36.44                   | < 0.001       |
| Nursing ($) (IQR)       | 26.81 (19.19, 78.37)         | 54.96 (30.37, 154.00)        | 28.15                   | < 0.001       |
| Laboratory ($) (IQR)    | 23.85 (8.92, 121.97)         | 41.48 (19.11, 132.88)        | 17.63                   | 0.002         |
| Examination ($) (IQR)   | 7.11 (7.11, 18.50)           | 10.67 (7.11, 21.92)          | 3.56                    | 0.035         |
| Treatment ($) (IQR)     | 3.54 (2.20, 191.42)          | 44.06 (3.73, 260.62)         | 40.52                   | 0.001         |
| Blood transfusion ($) (IQR) | 601.78 (510.38, 821.71)    | 852.59 (595.04, 1354.30)    | 250.81                  | < 0.001       |
| Surgery ($) (IQR)       | 0.00 (0.00, 171.85)          | 0.00 (0.00, 194.07)          | 0.00                    | 0.207         |
| MV ($) (IQR)            | 45.93 (27.04, 60.00)         | 125.93 (92.22, 241.48)       | 80.00                   | < 0.001       |
| Total ($) (IQR)         | 7438.00 (5373.69, 18935.84)  | 12408.28 (8220.19, 20647.16)| 4970.28                 | < 0.001       |

MV, mechanical ventilation; PMV, prolonged mechanical ventilation.

*Direct economic burden was expressed by the median pair of various costs (PMV group minus MV group).

Comparison of the hospital and Intensive Care Unit LOS between MV and PMV groups

A comparison of the LOS of the matched cohorts is shown in Table 3. Both the median of the paired hospital and Intensive Care Unit LOS was five days, a statistically significant difference was found between the two groups (\( P < 0.05 \)). In other words, the median total duration of hospitalization and Intensive Care Unit was five days longer for the PMV group.
Table 3
A matched cohort of differences in LOS between MV group and PMV group

| Length of stay | MV group (n = 109) | PMV group (n = 109) | Direct economic burden* | P-value |
|----------------|-------------------|-------------------|------------------------|---------|
| ICU, median (IQR) | 3 (2, 4) | 8 (5, 11) | 5 | < 0.001 |
| hospital, median (IQR) | 18 (13, 24) | 23 (15.5, 27.5) | 5 | 0.002 |

MV, mechanical ventilation; PMV, prolonged mechanical ventilation; LOS, length of stay; ICU, Intensive Care Unit.

*Direct economic burden was expressed by the median pair of LOS (PMV group minus MV group).

Discussion

It is widely believed that prolonged mechanical ventilation imposes a heavy economic burden on patients, healthcare systems, and society. American scholar Zilberberg estimates the aggregate bill for their hospital care alone would be over $64 billion annually after adjusting for the age and inflation of PMV patients across the country [19]. Based on our results, the economic burden of PMV among AAAD patients was considerably high with a median hospitalization cost was up to $12,408.28 in China, and each of them paid $4,970.28 for additional costs. To our knowledge, this study was the first domestic study to quantify the direct economic burden among AAAD patients associated with PMV. It should be reminded that the high level of economic burden caused by PMV among these patients for the local government and hospitals, this study provided solid evidence for the importance of future PMV Intervention and management.

From our results, the median total hospitalization costs per PMV patients were $12408.28 compared with those of the non-PMV group, which were $7438.00. In developed countries, Canadian scholar Zilberberg et al [20] showed that the median hospitalization cost of PMV patients was as high as $55,014, while in the non-PMV group it was $20,120. The results of Vallabhajosyula et al [21] showed that the long-term use of MV with acute myocardial infarction patients costs $247,169 ± 227,047, and this cost is 3 times than that of non-PMV patients. What's more, PMV will also increase the financial burden of patients one year after discharge. In Hill et al's [9] study, it was found that the median cost of patients who received PMV was $42,784, while the median cost of patients who did not receive PMV was $13,005. In contrast, the disposable income of per capita residents in Fujian Province, Canada, and the United States were $4,451.56, $45,100, and $57,700 in 2017, respectively [22, 23]. These differences could be attributable to the level of national economic development, various health insurance systems, differential epidemiology, and objects or methods used between different studies. In short, whether in developed or developing countries, PMV will bring a huge economic burden to patients.
In our study, PMV developed in 30.6% of AAAD patients, and each of them paid $4,970.28 for additional costs, the extra cost could be partly due to some interventions. For example, they may need a tracheostomy and place a feeding tube for continuous care. They were confronted with ventilator-associated complications (such as ventilator-associated pneumonia), but also at increased risk of other hospital complications, such as Clostridium difficile infection (CDI), which caused disproportionate distress to patients. Besides, PMV patients are more likely to visit county-level medical institutions or take healthcare services home [24, 25]. In brief, PMV patients represent unique critically ill patients who consume disproportionate medical resources, they shoulder more than 60% of all costs related to the entire MV population [19]. It shows that a moderate reduction in MV and hospital stay can also limit medical expenditures and hospital economic losses in different proportions. For example, daily spontaneous awakening trials (SAT), a pilot project funded by the Centers for Disease Control and Prevention adopted these technologies, which not only nearly doubled the pairing of SAT but also reduced the number of MV, ICU, and hospital stays [19]. Clinical intervention based on Six Sigma reduced the median length of stay by 27% and the direct cost by 27% in PMV patients [26].

Another unique point of our research is the spread of cost categories. Through stratified analysis by costs, the western medicine was the highest direct economic burden amount to an average of $3183.23 per patient, followed by blood transfusion and materials, the increased cost per patient was $250.81 and $207.43. Others studies have shown that western medicine accounted for approximately 36.9% and 37.9% of medical costs and constituted a major of patients' additional medical costs in China [27], it demonstrates that the usage of western medicine was a general phenomenon. While the cost of surgery, treatment, and nursing, which is a good reflection of labor value, is lower than the basic cost, particularly the nursing cost is even significant in the total hospitalization costs. In our study, the cost of treatment, examination, Laboratory, and nursing are statistically significant in the two groups of patients, reflecting that the PMV group paid more extra costs than the MV group. However, it only accounts for a small part of the total economic burden.

Furthermore, our team developed implements triple-branched stent-graft placement and applied to all AAAD patients [28], there was no statistically significant difference in surgical and material costs between the two groups. It’s not difficult to see that medical insurance reimburses almost all the surgical fees, a significant proportion of patients still pay the material costs. It is worth mentioning that the material cost is second only to the cost of western medicine in the total cost. The median material cost of the MV group is $1871.73, and the PMV group is $2079.16. This indicated that although China initiated a new medical reform to reduce the cost of medicines to increase labor costs in 2010. However, this issue needs to be further resolved by relevant government agencies and personnel. The future medical reform may try to increase the scope of reimbursement of material cost, and when purchasing high-value medical consumables, under the premise of ensuring medical quality, comparative procurement should be carried out based on the principles of reasonable prices and clinical needs. These measures may be expected to reduce the economic burden of AAAD patients.
Due to the same surgery, which reduces postoperative hospital mortality [16] and postoperative complications [29]. Still, the impact of extracorporeal circulation and poor coagulation function of patients, nearly all patients required blood transfusions postoperatively. According to our research, the cost of blood transfusions among PMV groups paid an extra $250.81 to the MV group. The same conclusion was drawn in Newcomb’s study [30], post-cardiac bleeding contributes to increased hospital costs by 1.76 times. Blood is a limited resource. Therefore, under the context of the current medical reimbursement system, blood products, as a nutrition and health care category, are not included in the medical reimbursement. However, governments introduce new national policies to reduce the blood transfusion for blood donors [31], which will save a large number of patients from the huge economic burden.

The findings also suggest that PMV can cause an increase significantly in the hospital and ICU LOS among patients. It is estimated that PMV patients with AAAD were prolonged by five days both in hospital and ICU LOS. Similar conclusions have been confirmed in several other studies [10–12]. It is well-known that hospitalization costs increased gradually with the increase of hospitalization days, and the relationship between costs and LOS has been confirmed in many studies. Previous studies have displayed those additional costs related to hospital LOS were the main drivers of medical costs [33–35]. Prolonging the LOS not only increases the direct economic burden but also the indirect economic burden, it is due to patients have to be absent from work. If the exact indirect economic burden is needed, the rigorous economic data requires a detailed manual calculation of specific time and resource usage and cost, which is not feasible at the scale of such study, thus, we did not evaluate the indirect economic burden among these patients.

We acknowledge several limitations in this study. First of all, all patients were recruited from a single hospital in southeast China, the findings of this study may not be extended to other hospitals with different regions and economic conditions, Thus, our findings have limited generalizability. Secondly, given the small sample size may be biased of the results. Given this, future studies with an increased sample size should be performed to improve the accuracy of results from different hospitals or even different countries. Third, due to the limited information, we were unable to evaluate the indirect economic burden related to extended sick leave duration. Thus, further study and the collection of more data (a type of job, monthly salary) are required to assess the indirect economic burdens. Finally, we did not conduct follow-up and evaluate unplanned readmission for AAAD patients after discharge from the hospital, which implies that we are likely to have underestimated the actual additional costs.

**Conclusions**

We have quantified the direct economic burden associated with PMV among AAAD patients who need MV greater than 48h or longer. Further studies with an increased sample size should be performed to provide profound results in different hospitals among various countries.

**Abbreviations**
AAAD: Type A aortic dissection; PMV: Prolonged mechanical ventilation; LOS: Length of stay; MV: Mechanical ventilation; CTA: Computed tomography angiography; ICU: Intensive Care Unit; CDI: Clostridium difficile infection; SAT: Spontaneous awakening trials.

Declarations

Authors’ contributions

S-LL and X-ZH collected socio-demographic and clinical data; QC and Y-CP analyzed and interpreted the data; XZ and L-WC drafted the manuscript; Y-JL assessed the subjects. All authors critically revised the manuscript. All authors read and approved the final manuscript.

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Ethics approval and consent to participate

This study was approved by the Ethics Committee of Fujian Medical University Union Hospital (approval number:2013002), informed consent was waived because of the retrospective nature of this study.

Consent for publication

Not applicable.

Availability of data and materials

Full data set available from the corresponding author on reasonable request. Besides, the full data need to be approved by Fujian Medical University Union Hospital.

Competing interests

The Authors declare that there is no conflict of interest.

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Figures
601 patients identified acute aortic dissection undergoing surgery

137 patients were excluded:
- Patients have a history of cancer (n=7),
- Patients symptom onset time $\geq$ 14 days (n=25),
- Patients have a history of Re-admission (n=97),
- Patients with a grossly incomplete medical record (n=8).

464 patients, 142 patients with PMV

1:1 propensity score analysis

218 patients included in final study cohort

109 patients with PMV 109 patients without PMV

**Figure 1**

Flow diagrams for the selection of study participants.
Figure 2

Various hospital costs between MV group and PMV group. Each item of hospital cost showed that the PMV group was higher than that in the MV group (P<0.05), except for diagnosis and materials. MV, mechanical ventilation; PMV, prolonged mechanical ventilation.