Characterization of Patients who were Mechanically Ventilated in General Medicine Wards

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ABSTRACT: Background: In Israel, where the “Do not resuscitate code” and “advanced directives” are not yet universally practiced, physicians are frequently ‘forced’ to mechanically ventilate patients despite an upfront unfavorable prognosis. Due to the shortage of intensive care unit (ICU) beds, patients are mostly hospitalized in general medicine wards.

Objectives: To differentiate between patients with particularly grim prognoses and those with good prognoses, in order to inform the potential decision-making process regarding whether or not to offer aggressive medical care.

Methods: This retrospective study included all mechanically ventilated patients hospitalized exclusively in one of the six general internal medicine wards at the Assaf Harofeh Medical Center during 2009–2010. Demographic and ventilation-related data, laboratory values and main medical diagnoses were correlated to in-hospital mortality.

Results: The study group comprised 437 patients with a median age of 83 years. Mortality was 72%. Initiation of mechanical ventilation out of the hospital or in the emergency room improved outcome. Age, anemia, leukocytosis and renal failure correlated negatively to outcome. In-hospital mortality was 80% in patients after in-hospital resuscitation, 90% in patients ventilated due to infections, but 50% in patients ventilated for cardiac or respiratory failure.

Conclusions: The prognosis of mechanically ventilated patients can be foreseen, which could help in deciding whether aggressive life support would be in the interest of the patient.

KEY WORDS: mechanical ventilation, patient characterization, proxy/ family decision making

Critically ill patients require medical treatment in intensive care units (ICUs). Furthermore, as life expectancy increases, more elderly patients with critical diseases will need intensive care, which has led to a shortage of ICU beds, a well-recognized problem. In Britain, for instance, patients await transfer to ICUs for as long as 8 days after having been mechanically ventilated on the regular floor [1]. In Israel, most elderly mechanically ventilated patients are hospitalized in general medicine wards [2-5]. The mortality rate of elderly mechanically ventilated patients hospitalized in intensive care is around 34–40%, significantly higher than in younger subjects [6,7]. In general medical wards, as reported from three tertiary referral hospitals in Israel, it ranges between 67% and 80% [2-5]. Mortality can be reduced by transferring patients to the ICU within a ‘critical window of time’ [2,8].

In view of the extremely high in-hospital mortality in general medicine wards and the shortage of both ICU beds and personnel, it is crucial to provide maximal available treatment to patients with a reasonable prognosis and to desist from practicing “futile” medicine aimed at extending the life of patients with no chance of survival.

We report here characteristics of mechanically ventilated elderly patients hospitalized in general medicine wards only. It is the purpose of this paper to differentiate patients with particularly grim prognoses from patients with good prognoses in order to provide adequate medical care.

PATIENTS AND METHODS

Assaf Harofeh Medical Center is a university-affiliated hospital with 900 beds. Close to 250 patients are hospitalized in seven general internal medicine departments. Non-surgical and non-traumatic mechanically ventilated patients when not admitted to the ICU are hospitalized in six of the seven general medical wards in a room dedicated for mechanical ventilation. Generally, a maximum of five ventilated patients are hospitalized in one general ward at the same time. The patients are ventilated with VELA® ventilators (USA) and kept supine at an angle of 30 degrees; patients lie on air-filled mattresses and positional changes are routinely performed to prevent pressure sores. One exclusively dedicated nurse and one staff physician who performs additional patient care duty during his shift attend those patients. The patients are under continuous electrocardiographic monitoring and vital sign surveillance. Central venous lines are inserted when indicated, but arterial lines and Swan-Ganz catheters are not used.

This was a retrospective study. Patients who were mechanically ventilated in one of the six internal medicine wards during the years 2009–2010 were included in the study if mechanical ventilation was administered in the internal medical wards for the entire period. We excluded patients who were initially...
admitted to one of the ICUs and then transferred to the medical wards or vice versa. We likewise excluded patients who were admitted with pre-existing tracheostomy and those who underwent tracheal intubation and mechanical ventilation and survived for less than 4 hours after cardiopulmonary resuscitation.

**DATA COLLECTED**

Demographic data, the indication for mechanical ventilation, the timing of intubation (before hospitalization, during, and on which day of hospitalization), the length of hospitalization and of mechanical ventilation, date of death, blood pressure and body temperature were collected. Laboratory values included white blood cell count, hemoglobin and creatinine level.

Mechanically ventilated patients were classified into seven main medical diagnoses according to the ICS: infections, respiratory diseases (chronic obstructive pulmonary disease exacerbation, acute respiratory failure), cardiac diseases (arrhythmia, acute coronary syndrome, acute heart failure, cardiogenic shock), oncological diseases (active cancer and/or metastatic disease), status post-cardiopulmonary resuscitation, neurological diseases (ischemic or hemorrhagic stroke), and others.

**STATISTICAL ANALYSIS**

The data were analyzed using BMDP [9]. Continuous variables were compared using analysis of variance (ANOVA). Discrete variables were compared using Pearson's chi-square test or Fisher's exact test, as appropriate. To determine the variables most significantly associated with death we included all the univariate parameters that were significant at the 0.10 level, in a stepwise logistic regression. A P value ≤ 0.05 was considered significant.

**RESULTS**

A total of 806 patients were mechanically ventilated in six internal medicine wards during the study period; 359 were excluded for reasons shown in Figure 1. The characteristics of the remaining 437 patients are presented in Table 1. The median age was 83 years (range 45–103) with 67% being older than 80 years. Almost 60% of the patients were admitted from home, 20% from old age homes and 20% from nursing facilities.

**PARAMETERS ASSOCIATED WITH SURVIVAL**

A total of 316 patients (72%) died during hospitalization. Table 1 demonstrates the parameters associated with survival when evaluated by univariate analysis. Gender, length of mechanical ventilation and length of hospitalization were not associated with decreased survival.

- **Age**

  Patients who survived were younger than those who died (78.8 vs. 81.7 years, P = 0.008), and mortality increased by 4% for each additional year of age. Of patients over age 80, 75% died whereas only 65% of those below 80 did not survive.

- **Initiation of mechanical ventilation**

  Mechanical ventilation was initiated in the ambulance on the day of hospitalization in 256 patients and during hospitalization in 181 patients. Mortality was significantly higher in the latter group, 78.5% compared to 68% in the former group (P = 0.02). Moreover, mortality increased by 14% per day of hospitalization prior to initiation of mechanical ventilation. We also investigated whether re-intubation after successful extubation jeopardized prognosis: 43 patients needed re-intubation after successful extubation and 36 died during hospitalization (84%). Mortality was lower, 64%, in the patients intubated only once, but this difference was not statistically significant (P = 0.08).

- **Laboratory**

  An increased survival rate was found in patients with a higher hemoglobin level at admission when compared to those who died. White blood cell count was also lower, as was plasma creatinine.

**Table 1. Patient characterization by univariate analysis**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Survived</th>
<th>Died</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>121</td>
<td>316</td>
<td></td>
</tr>
<tr>
<td>Age (years ± SD)</td>
<td>78.8 ± 10.6</td>
<td>81.7 ± 10.2</td>
<td><strong>0.008</strong></td>
</tr>
<tr>
<td>The day of initiation of mechanical ventilation (days ± SD)</td>
<td>1.3 ± 2.8</td>
<td>2.4 ± 4.4</td>
<td><strong>0.002</strong></td>
</tr>
<tr>
<td>Hemoglobin on first day of admission (g/L ± SD)</td>
<td>12.1 ± 1.9</td>
<td>11.5 ± 2</td>
<td><strong>0.007</strong></td>
</tr>
<tr>
<td>WBC count on first day of admission (103 ± SD)</td>
<td>12.6 ± 5.9</td>
<td>14.4 ± 8.3</td>
<td><strong>0.012</strong></td>
</tr>
<tr>
<td>Creatinine on first day of admission (mg/dl ± SD)</td>
<td>1.3 ± 0.8</td>
<td>1.8 ± 1.5</td>
<td><strong>&lt; 0.001</strong></td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg ± SD)</td>
<td>134.8 ± 28.2</td>
<td>121.5 ± 30.4</td>
<td><strong>&lt; 0.001</strong></td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg ± SD)</td>
<td>73.6 ± 16.3</td>
<td>67.2 ± 17.9</td>
<td><strong>&lt; 0.001</strong></td>
</tr>
</tbody>
</table>
• **Main clinical diagnosis at time of mechanical ventilation**
  Most of the mechanically ventilated patients (58%) suffered from infections or respiratory insufficiency. Mortality reached almost 80% in patients with infectious diseases and 90% in those who underwent cardiopulmonary resuscitation, but less than 50% in patients ventilated due to cardiac or respiratory failure. This difference was statistically significant ($P < 0.001$). A stepwise logistic regression analysis of factors affecting mortality independently is shown in Table 2.

• **Residence previous to hospitalization**
  Mortality was 78% in patients admitted from nursing homes, 66% in those admitted from old age homes, and 42% in patients living at home before hospital admission. Of the 121 patients surviving, 73 (60%) were discharged to their homes, 46 of whom had previously been residents of a nursing or old age home; and 48 patients were discharged to a nursing facility, 28 of whom had been living at home prior to the index hospitalization.

### DISCUSSION

We report the in-hospital mortality rates of mechanically ventilated patients who were treated solely in general medicine wards. Four findings characterize our study: Firstly, only one-fourth of all mechanically ventilated patients survived hospitalization. Secondly, survival in patients ventilated due to cardiac or respiratory conditions was better than in those with underlying cancer or those with severe infections. Thirdly, mortality was extremely high in patients who underwent in-hospital cardiorespiratory resuscitation or were admitted from nursing homes. Fourthly, more than half the survivors were discharged home and did not require transfer to a nursing care facility.

Our finding of a 28% in-hospital survival rate is similar to previous reports from tertiary referral Israeli hospitals (20–38%), but our population included significantly more octogenarians [3,4]. Analyzing the data of those reports indicates that the survival in their octogenarians was similar to ours (approximately 25%).

Improved outcome for cardiac or respiratory events as compared to those ventilated for infectious diseases confirms previous findings [10]. It has been shown that hospitalization in intensive care units reduces mortality in the latter group, especially regarding pneumonia [11]. It is standard care at our hospital to refer all mechanically ventilated patients to the ICU to assess whether transfer to that unit would be appropriate. It is doubtful that outcome would have improved if ICU could have accommodated additional patients. Arrhythmias, MI or acute respiratory problems without multiorgan failure, on the other hand, can be managed relatively well in the internal medical wards due to their generally good prognosis. There was a tendency for decreased survival in patients who needed to be re-intubated; however, perhaps because of the small number of patients the difference was not statistically significant when compared to patients with a single intubation.

The chance for survival was better for patients who were intubated prior to or upon arrival at the emergency room than for those who were intubated later during hospitalization. We hypothesize that mechanical ventilation at the onset of hospitalization is usually required because of a critical event in an acutely ill patient. Patients who need to be ventilated while already hospitalized suffer from severe underlying diseases; the additional deterioration of their conditions decreases the likelihood of survival.

Functional capacity deteriorates in ventilated patients, as previously described [4]. We did not have access to the status of pre-admission functional capacities of the patients included in the study. Yet, we were able to compare the need for a nursing care facility before and after the index hospitalization. To our surprise, although mortality was high in patients admitted from a nursing care facility, a significant number of survivors who resided in nursing homes prior to their hospital admission were discharged to their homes. This may not necessarily shed light on the functional capacity of the discharged patients. For example, some families may have decided to nurse their loved one at home, having been exposed to a nursing home experience before.

Medical guidelines dictate hospitalization of mechanically ventilated patients in intensive care units by default unless their prognosis is grave [12]. Patients with good prognoses should obviously receive all possible treatment resources. Patients with extremely poor prognoses, on the other hand, should be offered medical help that preserves their dignity but does not prolong life unnecessarily.

In a country like Israel, where the “do not resuscitate code” and “advanced directives” are not (yet) universally practiced, physicians are frequently ‘forced’ into practicing aggressive medicine causing sorrow and suffering to the patients and the
families. Israeli law allows respecting the will of a patient or his/her proxy not to prolong life in a situation where his/her life expectancy is naturally short (less than 6 months). Our data can contribute to an educated dialogue among the medical staff, the patient and the family. Patients with an extremely poor prognosis as described earlier, or their proxies, should be informed about the prognosis the same way terminal oncological diseases are discussed, as recently suggested [13,14]. This will help them to decide whether aggressive life support would be in the interest of the patient and would concur with his/her intentions. According to our calculation, a significant proportion of the nursing staff could be freed from practicing futile medicine to treat patients with good prognoses and even improve their outcome.

Our study has several weak points: It could not evaluate underlying medical conditions other than those causing acute deterioration necessitating mechanical ventilation. Almost one-third of the patients were mechanically ventilated due to infections; we did not subdivide them into subgroups that would have resulted in groups too small for statistical analysis. We could not obtain functional scores of the patients before hospitalization; we tried partially to compensate for the lack of this information by incorporating patients’ location prior to this hospitalization. Also, we do not have data on readmission and mortality after discharge, and whether the recent hospitalization had an impact upon quality of life.

In conclusion, we characterized patient groups with good prognoses and with poor prognoses when ventilated in general medicine wards. Courageous ethical decisions are required regarding whether the latter should be treated less invasively in order to prevent unnecessary suffering of the patients and their families. Moreover, such a decision will free medical personnel to improve the care of those with good prognoses.

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References

Capsule

Diabetes primes neutrophils to undergo NETosis, which impairs wound healing

Wound healing is impaired in diabetes, resulting in significant morbidity and mortality. Neutrophils are the main leukocytes involved in the early phase of healing. As part of their antimicrobial defense, neutrophils form extracellular traps (NETs) by releasing condensed chromatin lined with cytotoxic proteins. NETs, however, can also induce tissue damage. Wong et al. show that neutrophils isolated from type 1 and type 2 diabetic humans and mice were primed to produce NETs (a process termed NETosis). Expression of peptidylarginine deiminase 4 (Padi4, encoded by Padi4 in mice), an enzyme important in chromatin decondensation, was elevated in neutrophils from individuals with diabetes. When subjected to excisional skin wounds, wild-type (WT) mice produced large quantities of NETs in wounds, but this was not observed in Padi4−/− mice. In diabetic mice, higher levels of citrullinated histone H3 (H3Cit, a NET marker) were found in their wounds than in normoglycemic mice and healing was delayed. Wound healing was accelerated in Padi4−/− mice as compared to WT mice, and it was not compromised by diabetes. DNase 1, which disrupts NETs, accelerated wound healing in diabetic and normoglycemic WT mice. Thus, NETs impair wound healing, particularly in diabetes, in which neutrophils are more susceptible to NETosis. Inhibiting NETosis or clearing NETs may improve wound healing and reduce NET-driven chronic inflammation in diabetes.