Sex and Mortality of Hospitalized Adults After Admission to an Intensive Care Unit

By Jed Lipes, MD, FRCPC, Louay Mardini, MD, and Dev Jayaraman, MD, MPh, FRCPC

Background After admission to intensive care, women have higher mortality rates than do men. The reasons for the greater mortality in women are not fully understood.

Objective To determine if increased mortality in women was due to delays in the recognition of critical illness or to delays in timely admission to intensive care.

Methods A total of 241 consecutive admissions to intensive care from medical and surgical units during a 12-month period were analyzed retrospectively. Patients’ demographics, illness severity, and delay between the time the patients would have fulfilled criteria for calling a medical emergency team and consultation with and admission to intensive care were analyzed.

Results Delay from fulfillment of criteria for calling a medical emergency team and consultation with intensive care and from consultation to admission to intensive care did not differ between sexes. Despite similar delays in admission to intensive care, women had a higher 30-day mortality than did men (44.9% vs 30.5%; \( P = .02 \)). The increased mortality was more pronounced in the medical patients (53% vs 34%; \( P = .02 \)). Multivariate analysis of mortality data yielded a mortality odds ratio of 0.35 (95% CI, 0.16-0.74) for men, significantly different from values for women (\( P = .006 \)).

Conclusion After admission to intensive care from medical or surgical units, women had higher mortality rates than did men, and the difference was more pronounced in medical patients. The difference in mortality between sexes was not explained by delayed recognition of critical illness or delayed admission to intensive care. (American Journal of Critical Care. 2013;22: 314-319)
Evidence indicates that women have a higher mortality after admission to an intensive care unit (ICU) than do men. The reasons for this difference are poorly understood, and many questions remain unanswered. Women are likely to receive less aggressive treatment than do men during an ICU admission, are likely to be discharged earlier from critical care units, and are more likely to have a longer hospital length of stay. Moreover, Pietropaoli et al suggest that delayed recognition of worsening of physiological status in women may explain the increased mortality, but this topic has not been explicitly studied. Delay in recognition that a patient is critically ill and in timely treatment has been associated with increased morbidity and mortality.

We hypothesized that differences between sexes are important in the timely transfer of critically ill patients to the ICU and that this difference results in a higher mortality among women. We conducted a retrospective study to determine if delays in ICU admission and severity of illness before ICU admission differed between men and women who were already hospitalized and if ICU mortality differed according to sex between medical and surgical patients. We also sought to confirm previous reports that differences in mortality between the sexes are more pronounced in younger patients and in patients who were less severely ill.

Methods

A structured retrospective chart review was conducted at 2 tertiary care academic centers in Montreal, Canada. Both centers have closed 20-bed mixed medical-surgical ICUs and do not use medical emergency teams (METS). All ICU admissions from medical and surgical units during a 12-month period were screened at both centers. Because of administrative limitations (the hospital at 1 center was switching to electronic charts), the time points in the 2 hospitals differed (March 2008 to March 2009 for one and September 2007 to November 2008 for the other). Patients were included if they were admitted to the ICU after being on an inpatient unit for more than 48 hours. Patients were excluded if they were admitted within 48 hours from the emergency department or less than 48 hours after surgery because the time of worsening of physiological status might have preceded admission to the inpatient unit. All patients readmitted within 30 days of ICU admission were also excluded. Patients admitted to the ICU from inpatient units who had not reached any pre-specified criteria for request for an MET or who were transferred from another critical care area such as the coronary care unit or postanesthesia recovery units were also excluded. The study was approved by the ethics committees of both hospitals.

Data Collection

Time data were collected via a retrospective review of medical charts and our prospectively collected ICU database. The MET criterion was defined as the first occurrence of one or more of the following physiological abnormalities that are often use as a basis for use of METs: heart rate 120/min or greater or 40/min or less, respiratory rate 30/min or greater or 10/min or less, systolic blood pressure 200 mm Hg or greater or 100 mm Hg or less, temperature 39.5°C or greater or less than 35.5°C, or new change in mental status. The time of ICU consultation and the time of ICU admission were recorded, and the durations from meeting the MET criterion to consultation and admission were then calculated.

All chart reviews were performed by 2 of the investigators (J.L. and L.M.). A random sample of 10% of the charts were then independently examined by the other investigator (D.J.) to evaluate the reliability of time assessments for delay from meeting the MET criterion to consultation and admission were then calculated.

About the Authors

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Data Analysis

All significance testing was 2-tailed, and the significance level was set at .05. Proportions or percentages, means and standard deviations, or medians and interquartile ranges were used when appropriate to describe clinical and demographic characteristics. A t test and the Mann-Whitney test were used for parametric and nonparametric continuous variables, respectively. Categorical variables were compared by using \( \chi^2 \) analysis or the Fisher exact test when appropriate. Univariate analyses were used to test age, sex, MEWS and APACHE II scores, presence of markers of poor prognosis, time between meeting the MET criterion and ICU consultation and between ICU consultation and ICU admission, and if ICU consultation or when patients reached the MET criterion occurred during the day or night as predictors of 30-day mortality or ICU length of stay. Predictors with \( P < .30 \) were included in multivariate models. A stepwise backward elimination process was used, and all covariates with \( P > .10 \) were excluded from the final model. Goodness of fit was evaluated by using the Hosmer-Lemeshow goodness-of-fit test.

Results

Data on 241 patients (144 medical patients and 97 surgical patients; Figure 1) were analyzed. Baseline characteristics, including the origin of admission, presence of markers of poor prognosis, and diagnoses at admission did not differ between the sexes (Table 1). Women had a significantly higher (\( P = .02 \)) 30-day mortality rate (44.9%; 95% CI, 35.1%-54.7%) than did men (30.5%; 95% CI, 23.1%-37.8%; Figure 2). ICU mortality did not differ significantly (\( P = .54 \)) between women (24.4%; 95% CI, 15.8%-33.1%) and men (21.1%; 95% CI, 14.6%-27.8%). The time between reaching the MET criterion and ICU consultation and between ICU consultation and ICU admission did not differ between the sexes (Table 2). Men and women also did not differ in severity of illness before ICU admission or at the time of ICU admission, as reflected by MEWS and APACHE II scores, respectively (Table 3). Women had a higher mortality rate than did men in both medical and surgical subgroups, but this difference was significant only for medical patients (Figure 2). Multivariate analysis yielded a mortality odds ratio of 0.42 (95% CI 0.24-0.74) for men compared with women (\( P = .003 \)). The final multivariate analysis included delay to ICU admission on a natural log scale, sex, and APACHE II score at admission (Table 4).

Mortality rates differed significantly (\( P = .009 \)) between women (49.4%; 95% CI, 38.6%-60.1%) and
men (31.5% [95% CI, 23.6%-39.5%]) for patients more than 50 years old. In contrast, mortality rates for women (20.0%; 95% CI, 0%-40.2%) and men (23.8; 95% CI, 5.6%-42.0%) did not differ significantly ($P = .78$) among patients less than 50 years old. Stratifying patients into low (≤24) and high (>24) APACHE II scores revealed more than double the mortality rate in women than in men in the low APACHE II group (Figure 3).

**Discussion**

Women can manifest critical illness differently than men do and often have atypical signs and symptoms. We hypothesized that these differences result in delayed recognition of critical illness in women and in delays in subsequent ICU consultation and timely transfer to the ICU. Despite a significantly higher 30-day mortality rate in women, we found no significant difference in delays in ICU consultation or ICU admission between the sexes.

Furthermore, we used MEWS as a marker of critical illness became this scoring system has been validated as a simple tool that yields values predictive of the risk for death and need for admission to an ICU or a high-dependency unit. The men and women in our study had similar MEWS at the time the patients met the MET criterion and at the time of ICU consultation. In addition, indices of severity of illness before ICU admission were similar between women and men as indicated by MEWS and APACHE II scores.

Our findings confirmed that women have a higher mortality than men do, especially among patients admitted to the ICU from medical units. Similar findings have been reported previously, although some controversy remains. The reasons women may have a higher mortality than men during a critical illness are poorly understood, and clinical studies have shown that women have higher mortality rates than men do despite biological evidence of the protective effect of estrogens on both immune function and cardiovascular responses. In the largest study on sex and the critically ill, Mahmood et al found that overall women had higher mortality rates than men did. However, when the data were stratified according to age less than 50 years, women actually had a survival advantage, a finding that may support the physiological evidence for the protective role of estrogens in both immune function and cardiovascular responses. We did not find a survival advantage for women less than 50 years old, although the number of patients in this age group was small in our sample.

Interestingly, mortality was significantly higher in women than in men among patients who had lower APACHE II scores.

![Figure 2](http://ajcc.aacnjournals.org/) Difference in overall mortality between women and men and divided into surgical and medical subgroups.

### Table 2

<table>
<thead>
<tr>
<th>Delay from</th>
<th>Median (interquartile range), h</th>
<th>Women</th>
<th>Men</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concern to consultation</td>
<td>2.1 (0.4-8.6)</td>
<td>2.0 (0.7-7.5)</td>
<td>.97</td>
<td></td>
</tr>
<tr>
<td>Consultation to admission</td>
<td>1.6 (1.0-3.3)</td>
<td>2.0 (1.0-3.5)</td>
<td>.25</td>
<td></td>
</tr>
</tbody>
</table>

### Table 3

<table>
<thead>
<tr>
<th>Measure of severity</th>
<th>Mean (95% CI)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modified early warning score at time of concern</td>
<td>4.1 (4.0-4.8)</td>
<td>4.0 (3.6-4.3)</td>
</tr>
<tr>
<td>Modified early warning score at time of consultation</td>
<td>4.4 (4.0-4.8)</td>
<td>4.5 (4.1-4.9)</td>
</tr>
<tr>
<td>Score on Acute Physiology and Chronic Health Evaluation II at time of admission to intensive care</td>
<td>22.5 (20.8-24.2)</td>
<td>23.6 (22.2-24.9)</td>
</tr>
</tbody>
</table>

### Table 4

<table>
<thead>
<tr>
<th>Delay</th>
<th>Odds ratio for death</th>
<th>$P$</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score on Acute Physiology and Chronic Health Evaluation II</td>
<td>1.07</td>
<td>&lt;.001</td>
<td>1.04-1.12</td>
</tr>
<tr>
<td>Male sex</td>
<td>0.42</td>
<td>.003</td>
<td>0.24-0.74</td>
</tr>
<tr>
<td>Concern to admission time</td>
<td>1.22</td>
<td>.08</td>
<td>0.98-1.53</td>
</tr>
</tbody>
</table>

*a* Hosmer-Lemeshow statistic: $P = .74$. 

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only in medical patients. Because the overall mortality rate was also lower in the surgical cohort, our study might have been underpowered to detect a significant difference between men and women among the surgical patients. In addition, although standard vital signs are assessed in the inpatient units once per shift (ie, every 8 hours), physicians or nurses can use their clinical judgment and increase the frequency of recording vital signs, leading to earlier diagnosis and interventions. Depending on nurse to patient ratios and level of acuity on the units, difference in clinical judgment may explain the difference in outcomes between the medical and surgical patients. We did not analyze the treatments our patients received before and during their ICU admission, and we therefore cannot determine if women were treated less aggressively or less appropriately than were men. Larger studies have shown that compared with men, women are treated more conservatively (ie, fewer invasive procedures, fewer intubations, more code status limitations). However, in our cohort of patients, MEWS before ICU admission, APACHE II scores at the time of ICU admission, and code status limitations did not differ between men and women.

**Conclusion**

As shown in previous studies, in our study, women admitted to the ICU from inpatient units had a higher mortality rate than did men. However, the increased mortality did not appear to be associated with delays in timely transfer from the other units to the ICU or with severity markers before ICU admission or at the time of ICU admission. The increased mortality rate of women seemed to be more pronounced among patients transferred from medical units than among patients transferred from surgical units and among patients who were older than 50 years or who had lower APACHE II scores. Further studies will be required to determine if inherent physiological differences influence the higher mortality rates for women or if differences physicians’ behavior and treatment between the sexes after ICU admission are responsible for the observed differences in mortality.

**Financial Disclosures**

None reported.
REFERENCES

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