eg, amiodarone for rhythm control), tobacco use [doubled], race [doubled]] score1 to predict international normalized ratio control in a cohort of 182 patients with excellent quality anticoagulation (time in therapeutic range [TTR] \( \geq 76\% \)). The mean TTR of their patients with \( \text{SAMeTT}_2 R_2 \) score \( \geq 2 \) was the same as those with a \( \text{SAMeTT}_2 R_2 \) score of 0 to 1.

Although we value the authors’ input, we have to underscore some important limitations of their study. First, \( \text{SAMeTT}_2 R_2 \) was not developed to “predict” TTR, as the authors suggest, but was developed to identify anticoagulation control “outliers” within an anticoagulated population. In our cohort, the \( \text{SAMeTT}_2 R_2 \) score performed optimally in identifying patients with average TTRs below the fifth or the 10th percentile of the center’s average. We would encourage the authors to measure the predictive performance of the \( \text{SAMeTT}_2 R_2 \) score in identifying patients with TTR less than the fifth or the 10th percentile of their center’s average, notwithstanding their small sample size.

Also, the study by Dr Skov and colleagues may be profoundly underpowered to detect differences in TTR among subpopulations. This is reflected by some “controversial” observations—for instance, they suggest that female sex is associated with numerically better TTR. Similar to our study, the Veterans Affairs Study to Improve Anticoagulation (VARIA) investigators concluded in a much larger cohort that female sex, minority status, and multiple comorbidities negatively affected TTR.2

Our other studies (unpublished data) in substantially larger populations (N > 1,000) show usefulness of the \( \text{SAMeTT}_2 R_2 \) score even in cohorts with overall median TTR of 75%, as well as the relation of a high \( \text{SAMeTT}_2 R_2 \) score (> 2) to thromboembolism and bleeding (reflecting likely poor TTR).2

In conclusion, the \( \text{SAMeTT}_2 R_2 \) was derived from a cohort with a “realistic” anticoagulation control. The average TTR was approximately 0.63, but there was also a wide range of TTR, with 10% of the population having TTR < 0.40, which is typical of the real world practice. In such populations, the \( \text{SAMeTT}_2 R_2 \) score will be a valuable tool to guide treatment. We fully agree with the authors’ conclusion that in exceptionally “super-efficient” centers with average TTR of 75%, the use of \( \text{SAMeTT}_2 R_2 \) score to help decision-making is probably less likely to be required.

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REFERENCES


Incidence, Length of Stay, and Prognosis of Hospitalized Patients With Pleural Empyema

A 15-Year Danish Nationwide Cohort Study

To the Editor:

Empyema hospitalization rates appear to be increasing in western populations, but updated population-based data are sparse. The few existing population-based studies of adult empyema have reported increases between 30% and 97% over the past decades in the United States and Canada.4,5 Most of these studies were conducted in large referral centers only.

We examined health registries covering all Danish hospitals for temporal changes in nationwide incidence, length of hospital stay, and 30-day mortality associated with empyema-related hospitalizations during 1997 to 2011. We included all patients aged \( \geq 15 \) years receiving a first-time diagnosis of empyema (International Classification of Diseases, 10th Revision, codes J86.0 and J86.9). The positive predictive value of these empyema codes is approximately 90%.5

In total, 6,878 hospitalized patients had empyema in Denmark during 1997 to 2011. More than 40% had preexisting comorbidities, and this proportion increased over time (Table 1). The median length of hospital stay decreased from 22 days (interquartile range, 12-43 days) to 17 days (interquartile range, 10-28 days). The age- and sex-standardized incidence rate (IR) increased by 26% from 8.7 per 100,000 person-years in 1997 to 11.8 per 100,000 person-years in 2011. The IR increased the most among people aged 40 to 64 years (27.8% [from 10.7 per 100,000 in 1997 to 12.6 per 100,000 in 2011]) compared with people aged 15 to 39 years (87.3% [from 20.4 per 100,000 in 1997 to 38.2 per 100,000 in 2011]) compared with people aged 40 to 64 years (27.8% [from 10.7 per 100,000 in 1997 to 12.6 per 100,000 in 2011]) (Fig 1). Rates among those aged 15 to 39 years fluctuated around 2.5 to 3.5 per 100,000 person-years. Rates were 1.7- to 3.1-fold higher in men than in women, and the IR rose sharply with increasing age. The crude 30-day mortality improved modestly from 10.5% from 1997 to 2001 to 9.0% from 2007 to 2011, corresponding to an adjusted 30-day mortality rate ratio of 0.69 (95% CI, 0.57-0.84) (Table 1). Thirty-day mortality ranged from only 1.2% in patients aged 15 to 39 years to 20.2% in those aged \( \geq 80 \) years. Mortality also varied substantially according to level of comorbidity.
Table 1—Temporal Trends in Crude and Adjusted Mortality Within 30 d Among Patients With a First-Time Hospitalization for Empyema

<table>
<thead>
<tr>
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<tbody>
<tr>
<td></td>
<td>Patients</td>
<td>Deaths</td>
<td>Patients</td>
</tr>
<tr>
<td></td>
<td>Crude MRR (95% CI)</td>
<td>Adjusted MRR (95% CI)</td>
<td>Crude MRR (95% CI)</td>
</tr>
<tr>
<td>Overall</td>
<td>1,841 (100)</td>
<td>193 (10.5)</td>
<td>1.0</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>565 (30.7)</td>
<td>57 (10.1)</td>
<td>1.0</td>
</tr>
<tr>
<td>Male</td>
<td>1,276 (69.3)</td>
<td>136 (10.7)</td>
<td>1.0</td>
</tr>
<tr>
<td>Age group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15-39 y</td>
<td>241 (13.1)</td>
<td>0</td>
<td>1.0</td>
</tr>
<tr>
<td>40-64 y</td>
<td>829 (45.0)</td>
<td>64 (7.7)</td>
<td>1.0</td>
</tr>
<tr>
<td>65-79 y</td>
<td>594 (32.3)</td>
<td>78 (13.1)</td>
<td>1.0</td>
</tr>
<tr>
<td>≥ 80 y</td>
<td>177 (9.6)</td>
<td>51 (28.8)</td>
<td>1.0</td>
</tr>
<tr>
<td>CCI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low (0)</td>
<td>1,046 (56.8)</td>
<td>63 (6.0)</td>
<td>1.0</td>
</tr>
<tr>
<td>Medium (1-2)</td>
<td>583 (31.7)</td>
<td>82 (14.1)</td>
<td>1.0</td>
</tr>
<tr>
<td>High (&gt; 2)</td>
<td>212 (11.5)</td>
<td>48 (22.6)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Data are presented as No. (%) unless otherwise indicated. CCI = Charlson Comorbidity Index; MRR = mortality rate ratio; ref = reference.

*a Adjusted for age, sex, comorbidity, and alcoholism-related conditions.
Figure 1. A, B. Incidence rates of first-time hospitalization with empyema in women (A) and men (B) according to age group in Denmark, 1997 to 2011.

The finding of an increasing empyema incidence over the past 15 years is in-line with previous studies\(^1\); however, the present study may be the first to examine nationwide trends in 30-day mortality following empyema. Short-term mortality is likely to be closely related to the infection, and it is notable that comorbidity had such a strong influence on 30-day mortality. Importantly, we found improvements in empyema survival over time, in particular when taking increasing patient comorbidity into account. Advanced age and comorbidity are strong prognostic factors, and empyema remains a serious condition requiring a long hospital stay.
The hypothesis introduced by the authors was that distinct phenotypes of PGD are associated with different prognoses identified by latent class analysis. However, the results may be produced by the evolution of PGD per se and the risk factors for exacerbation of PGD rather than by the distinct phenotypes. By analogy, it is not difficult to recognize that individuals with the same stage of non-small cell lung cancer often have disparate manifestations of the disease and different prognoses. The authors compared different characteristics among classes in the three-class model to identify risk factors for severe PGD. However, if all the factors were included in multivariable logistic regression, independent risk factors for PGD may be discriminated from those presented by the authors (donor age, donor smoking, donor mode of death, cardiopulmonary bypass, intraoperative crystalloids, tidal volume, packed RBC use, pulmonary artery pressure). Previous studies have demonstrated more risk factors, including FIO₂ during allograft reperfusion, single lung transplant, recipient BMI indicating overweight or obesity, preoperative sarcoidosis, or pulmonary arterial hypertension and black donors and female donors. PGD was a significant predictor for lung transplant outcomes. Thus, patients could benefit from preventive strategies aimed at reducing reperfusion injury and decreasing the hazard of risk factors for PGD.

PGD has a reported incidence of between 11% and 57% and accounts for 26% of causes of death within the first 30 days after lung transplant and for 17% within 1 year. Extracorporeal membrane oxygenation (ECMO) provides reliable support for PGD, with acceptable outcomes during the postoperative period. Analysis of the Extracorporeal Life Support Organization registry (January 1987-December 2005) showed that PGD requiring postoperative ECMO support developed in 151 patients, of whom 93 (61.6%) were weaned from ECMO as a result of lung recovery. However, the authors did not provide data on ECMO for all patients with PGD from the 10 participating centers. Such data are important because ECMO can facilitate lung recovery from severe PGD, and ECMO as a confounding factor complicated latent class analysis in the study.

PGD as a form of ischemia/reperfusion injury can present immediately postoperatively and 48 to 72 h later. In the latent class analysis, the authors divided 361 patients with PGD into three classes, with the same morbidity onset time, time zero; however, PGD developed at other time points after 24 h and up to 72 h postoperatively may be omitted. Thus, we argue that PGD developing at different time points should be taken into account when planning the latent class analysis.

Distinct Phenotypes of Primary Graft Dysfunction After Lung Transplantation

To the Editor:

We read with great interest the article by Shah et al in a recent issue of CHEST (August 2013). Three distinct phenotypes of grade 3 primary graft dysfunction (PGD) were identified by latent class analysis, bringing new insights into the mechanism and treatment of severe PGD. However, a few issues need to be clarified after deeper analysis of the article.

REFERENCES


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