Influence of Psychiatric Comorbidity on Surgical Mortality

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Objective: To examine the potential effect of 5 existing psychiatric comorbidities on postsurgical mortality.

Design: Retrospective cohort.

Setting: Intensive care units of all Veterans Health Administration hospitals designated as providing acute care.

Patients: We studied 35,539 surgical patients admitted to intensive care units from October 1, 2003, through September 30, 2006.

Main Outcome Measures: Psychiatric comorbidity (depression, anxiety, posttraumatic stress disorder, bipolar disease, and schizophrenia) was identified using outpatient encounters in the 12 months preceding the index admission. End points included in-hospital and 30-day mortality. Generalized estimating equations accounted for hospital clustering and adjusted mortality for demographics, type of surgery, medical comorbidity, and disease severity.

Results: We identified 8,922 patients (25.1%) with an existing psychiatric comorbidity on admission. Unadjusted 30-day mortality rates were similar among patients with and without psychiatric comorbidity (3.8% vs 4.0%, P = .36). After adjustment, 30-day mortality was higher for patients with psychiatric comorbidity (odds ratio, 1.21; 95% confidence interval, 1.07-1.37; P = .003). In individual analyses, patients with depression and anxiety had higher odds of 30-day mortality (P = .01 and P = .02, respectively) but the odds were similar for the other conditions.

Conclusion: Existing psychiatric comorbidity was associated with a modest increased risk of death among postsurgical patients. Estimates of the increased risk across the individual conditions were highest for anxiety and depression. The higher mortality may reflect higher unmeasured severity or unique management issues in patients with psychiatric comorbidity.

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Psychiatric comorbidities, such as depression and anxiety disorders, are common among hospitalized patients, with prior studies estimating a prevalence of 5% to 40% in federal and nonfederal hospitals. Moreover, the presence of a psychiatric comorbidity is independently associated with an increased risk of morbidity and mortality.

Associations between psychiatric comorbidity and mortality have largely been limited to patients admitted for the treatment of medical (ie, nonsurgical) conditions; thus, making valid inferences regarding associations between surgical outcomes and psychiatric comorbidity is limited by the paucity and heterogeneity of available research. For example, studies examining associations between psychiatric comorbidity and surgical mortality are limited to a few studies of surgical patients with schizophrenia or depression. Studies on a broader range of psychiatric conditions, such as bipolar illness, posttraumatic stress disorder, and/or anxiety illness, among surgical patients are nonexistent, to our knowledge.

In addition, no known analyses have considered multiple psychiatric conditions separately in a single surgical cohort. Indeed, the need for further work in this area was highlighted in a recent systematic review.

Because of this gap in the literature, we conducted the current study in a large national cohort of veterans who underwent a broad range of surgical procedures and were subsequently admitted to intensive care units (ICUs). Specifically, we sought to examine associations between the presence of several common psychiatric comorbidities and postsurgical mortality and the degree to which such associations varied across individual psychiatric conditions. We studied an ICU population because existing evidence indicates that such patients are known to be at higher risk for developing psychiatric comorbidities and have higher rates of mortality. Furthermore, on the basis of prior work, we hypothesized that patients with such comorbidity before an ICU admission would interact with the surgical care process, thus increasing the risk of mortality. Our primary objective was to specifically exami...
ine the effects of existing psychiatric comorbidity on postsurgical-related mortality.

**METHODS**

**DATA SOURCES**

This study used the Veterans Health Administration (VHA) centralized databases, which include administrative and clinical data. The specific sources of data used have been previously described.7,22

**PATIENT POPULATION**

Using the bed section files, we identified 59,638 consecutive admissions to a VHA ICU from October 1, 2003, through September 30, 2006, with a primary surgical diagnostic related group (DRG) code. We excluded 4488 admissions with DRG codes for percutaneous endovascular procedures (eg, percutaneous catheterization with drug-eluting stent [DRG codes 526 and 527] or other vascular angioplasty and stenting [DRG codes 553, 557, and 558]) and 9020 admissions that represented additional ICU admissions during the study period for individual patients. To ensure that the study sample had been eligible for VHA care for 1 full year preceding the index admission, we excluded patients (n=10,591) without any VHA outpatient visits during months 13 to 24 before admission. This left us with a final study sample of 35,539 patients. This final exclusion criterion was applied to reduce bias introduced into the analysis from nonregular users of the VHA system and to ensure that patients were eligible for prior outpatient care for a full 12 months.7

**STUDY VARIABLES**

The dependent variables of interest were in-hospital and 30-day mortality after the index admission. Primary independent variables were the presence of 5 psychiatric comorbid conditions, considered separately and in aggregate, identified by International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)23 diagnosis codes captured during 1 or more outpatient encounters during the 12 months before admission. The selected psychiatric conditions have been previously described.7,22

To adjust mortality for other potential confounders, we identified a number of other covariates, including principal surgical procedure (as measured by DRG), principal admitting medical condition, age, race (categorized as white, black, Hispanic, or missing), sex, marital status, comorbid medical conditions unlikely to reflect hospital complications (as defined using ICD-9-CM codes24), presence of mechanical ventilation on day of admission, receipt of blood transfusion within 48 hours of admission, and results of 8 selected laboratory tests (serum creatinine, blood urea nitrogen, albumin, total bilirubin, glucose, sodium, white blood cell count, and hemoglobin) performed within a 48-hour window surrounding the index admission. Principal admitting medical conditions were categorized using the Clinical Classifications Software, developed by the Agency for Healthcare Research and Quality.25 The Clinical Classifications Software uses principal and secondary ICD-9-CM codes to group patients into 281 clinically meaningful and mutually exclusive classes for hospitalization. For the subsequent analyses, separate indicator variables for each primary Clinical Classifications Software admitting medical condition were created.

Regarding the laboratory scores, the most abnormal value was selected and assigned a point score using similar weights according to the Acute Physiology and Chronic Disease Health Evaluation III method.26 The laboratory severity score and risk adjustment for the laboratory severity score have been previously described.7,22

**STATISTICAL ANALYSIS**

The statistical analysis was completed in several steps. First, we determined the proportions of veterans who were identified with existing individual psychiatric comorbidities or with any of the 5 comorbidities, in aggregate. Second, we identified demographic (eg, age and race) and clinical factors (eg, comorbid medical conditions, laboratory score, and Clinical Classifications Software principal admitting medical diagnoses) associated (P < .05) with in-hospital and 30-day mortality in bivariate analyses using the χ² or Wilcoxon signed rank tests.

Third, variables associated with either mortality end point (with the exception of psychiatric comorbidities) were entered into stepwise multivariate logistic regression models to identify and retain those variables independently associated with each mortality end point (P < .01). The models adjusted for surgical procedure by incorporating DRG as a class variable. Variables included in the risk-adjustment models for in-hospital and 30-day mortality are available from the authors on request.

Fourth, these variables were then entered into separate generalized estimating equation (GEE) models that included DRG in the class statement and indicator variables for the psychiatric comorbidities. To examine the effects of individual psychiatric comorbidities, additional GEE models were developed that included indicator variables for individual conditions in lieu of the aggregate psychiatric comorbidity variable. The categories for all these models were patients without the selected psychiatric condition. All GEE models used an exchangeable working correlation matrix in accounting for the clustering of patients within hospitals. Coefficients associated with the psychiatric comorbidity indicator variables were used to estimate adjusted odds of death.

Additional analyses examined associations between existing psychiatric comorbidity and mortality within subgroups of patients categorized according to the 5 most common major diagnostic category groups. Finally, additional GEE analyses included interaction effects among the 3 most prevalent individual psychiatric conditions (depression, anxiety, and PTSD).

All analyses were conducted using SAS statistical software, version 9.1 (SAS Institute Inc, Cary, North Carolina). The study was approved by the University of Iowa Institutional Review Board and the Research and Development Committee at the Iowa City VHA Medical Center.

**RESULTS**

Overall, study participants had a mean (SD) age of 65.0 (10.8) years; 34,402 (96.8%) were male. A total of 27,656 (77.8%) patients were white and 5232 (14.7%) were black; information on race was missing or was classified as other in 2137 patients (6.0%). The 10 most common surgical DRG codes are presented in Table 1. Existing psychiatric comorbidity was identified in 8922 patients (29.1%) using outpatient claims during the prior 12 months. Among individual conditions, depression was most common (5500; 15.5%), followed by PTSD (2913; 8.2%), anxiety (2473; 7.0%), bipolar disorder (793; 2.2%), and psychosis (621; 1.8%).

Patients with psychiatric comorbidity tended to be younger, were less likely to be black, and were less likely...
to be married (Table 2). Patients with psychiatric comorbidity had lower rates of congestive heart failure, higher rates of obesity, and lower mean laboratory severity scores and predicted risk of death. In contrast, patients with psychiatric comorbidity had higher rates of chronic obstructive pulmonary disease.

Patients identified with any psychiatric comorbidity had similar unadjusted in-hospital and 30-day mortality rates compared with patients without psychiatric comorbidity (4.0% vs 4.1%, P=.57, and 3.8% vs 4.0%, P=.36, respectively). Among individual psychiatric conditions, the unadjusted 30-day mortality rate was similar in patients with and without the condition for depression (3.9% vs 3.9%, P=.86), anxiety (4.0% vs 3.9%, P=.73), and psychosis (4.7% vs 3.9%, P=.33). In contrast, patients with PTSD and bipolar disorders had lower unadjusted rates of 30-day mortality (3.0% vs 4.0%, P=.009; and 2.5% vs 4.0%, P=.04, respectively). Results were similar for in-hospital mortality.

In GEE analyses, the adjusted odds of in-hospital and 30-day mortality were higher for patients with psychiatric comorbidity. The odds of in-hospital death for those with psychiatric comorbidity were 1.15 (95% confidence interval, 1.02-1.30, P=.02), and the odds of 30-day death were 1.21 (1.07-1.37, P=.003). In GEE analyses of individual psychiatric conditions, patients with depression and anxiety had higher odds of death, whereas odds of death were similar for patients with PTSD, bipolar disorder, and psychosis (Table 3). In analyses examining potential interaction effects among the 3 most common conditions, none of the interaction terms (depression × anxiety, anxiety × PTSD, and PTSD × depression) were significant (P > .10 for all terms in analyses of in-hospital and 30-day mortality).

Final analyses within the 5 most common categories of procedures classified by major diagnostic category (Table 4) found that the adjusted 30-day mortality rate was significantly higher (P = .03) for respiratory procedures and higher (P = .04) for digestive system procedures but not significantly higher for circulatory system, nervous, and musculoskeletal system procedures. These findings were similar for in-hospital mortality (data not shown; available on request from authors).

This study reports 2 main findings. First, in a large cohort of veterans, the presence of existing psychiatric comorbidity was associated with a modestly increased risk of in-hospital and 30-day mortality in surgical ICU admissions. Second, the degree of such associations is influenced by the specific types of surgical procedure condition and psychiatric comorbidity. The risk was highest among patients with depression and/or anxiety but was not significantly higher for veterans with preexisting PTSD, bipolar disorders, or schizophrenia.

It is important to consider our results in the context of the current literature. Several reports have examined associations between psychiatric comorbidity and surgical patient outcomes; however, it is difficult to in-
fer valid conclusions because of the heterogeneity of the studies regarding the temporal relationship of psychiatric comorbidity identified (eg, psychiatric illness identified before or after surgical admission), type of psychiatric comorbidity studied, and types of outcomes considered.

First, it is known that patients undergoing surgery are at risk for developing psychiatric comorbidity after surgery. For example, Liberzon et al\(^34\) found an incidence of postsurgical psychiatric comorbidity as high as 32% for patients after vascular operations, whereas Rincon et al\(^35\) demonstrated a 29% incidence of psychiatric comorbidity in a mixed population of medical and surgical ICU admissions. Other studies have found that such patients subsequently identified with psychiatric comorbidity have longer lengths of stay,\(^27,28\) higher incidences of adverse outcomes,\(^29,30\) and worse reported health-related quality of life after the surgery.\(^36-38\)

Second, of the few studies examining the effects of psychiatric comorbidity identified at the time of admission, analyses are limited to patients with schizophrenia, and only 3 such studies\(^20,30,31\) examined associations with mortality. For example, using a Maryland statewide administrative database, Daumit et al\(^20\) examined a cohort of medical and surgical admissions in 2001 and 2002 and found that patients with a secondary diagnosis of schizophrenia had higher rates of iatrogenic infections, postoperative respiratory failure, postoperative deep venous thrombosis, and postoperative sepsis. Patients with schizophrenia and respiratory failure or sepsis had at least twice the risk of ICU admission and death. Next, Cooke et al\(^30\) used the VHA Patient Treatment File to identify 55 patients with diagnoses of schizophrenia or schizoaffective disorder and appendicitis from 1995 through 1999. The authors then reviewed the medical records and noted that patients with schizophrenia and respiratory failure or sepsis had at least twice the risk of ICU admission and death.

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<tr>
<th>Table 3. Adjusted Odds of In-Hospital and 30-Day Mortality for Patients With Psychiatric Comorbidity Relative to Those Without the Selected Condition</th>
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<tbody>
<tr>
<td><strong>No. (%) of Patients</strong></td>
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<tr>
<td>Any psychiatric comorbidity</td>
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<tr>
<td>In-hospital mortality</td>
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<td>30-Day mortality</td>
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<td>Individual psychiatric conditions</td>
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<tr>
<td>Depression</td>
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<td>30-Day mortality</td>
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<td>Anxiety</td>
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<td>30-Day mortality</td>
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<td>Posttraumatic stress disorder</td>
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<td>In-hospital mortality</td>
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<td>30-Day mortality</td>
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<td>Bipolar disorder</td>
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<td>In-hospital mortality</td>
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<td>30-Day mortality</td>
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<td>Psychosis</td>
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<td>In-hospital mortality</td>
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<th>Table 4. Unadjusted and Adjusted Odds of 30-Day Mortality for Patients With Existing Psychiatric Comorbidity as Determined by Prior Outpatient Encounters</th>
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<td><strong>MDC</strong></td>
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<td>Circulatory</td>
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<td>Digestive</td>
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<td>Nervous</td>
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<td>Respiratory</td>
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<td>Musculoskeletal</td>
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<td>All other</td>
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Abbreviation: MDC, major diagnostic category.

\(^a\)This category contained a sample of fewer than 25 patients.
nal surgery, Matsuki et al\textsuperscript{31} found that patients with schizophrenia (n=12) had substantially higher mortality rates than control individuals.

Finally, studies designed to examine the effect of existing psychiatric comorbidity on surgical outcomes are limited. For example, in a study of pediatric trauma patients, Gaines et al\textsuperscript{32} found that children with a preexisting psychiatric illness had increased ICU and overall hospital-related lengths of stay and were more likely to be discharged to a location other than home. Next, in a further series of studies, Kudoh et al\textsuperscript{12-19} examined patients undergoing abdominal and orthopedic surgery and compared a number of outcomes (eg, pain responses to analgesic agents, postoperative psychosis or confusion after anesthesia, and rates of postoperative depression after anesthesia) in cohorts with or without depression or schizophrenia. None of these studies examined mortality as an outcome.

Thus, few studies have examined associations between a wide range of psychiatric conditions and mortality. This work may be subject to another important potential source of selection bias introduced by the method of identifying psychiatric comorbidity. Because the individual studies varied in their approach to identifying psychiatric comorbidity (eg, secondary diagnosis codes from the index hospitalization, prior psychiatric admissions, or prior outpatient claims), rates of identifying psychiatric comorbidity varied, which is consistent with studies among nonsurgical populations.\textsuperscript{1,2,3,5} Moreover, associations between psychiatric comorbidity and adverse patient outcomes may be influenced by the approach used to identify such comorbidity. For example, in previous analyses of patients hospitalized with congestive heart failure or pneumonia, we demonstrated that patients with psychiatric comorbidity, identified by inpatient secondary diagnosis codes, counterintuitively had lower predicted mortality and lower risk-adjusted mortality rates compared with patients without such comorbidity.\textsuperscript{7} However, when patients with psychiatric comorbidity were identified by prior outpatient visits, mortality rates were similar.

This study contributes to the existing literature in a number of ways. Most importantly, the study is one of the largest and most comprehensive analyses to date to find a positive association between existing psychiatric comorbidity and postsurgical mortality. Of additional importance, the study examined relationships between a broad range of existing psychiatric comorbidities and surgical conditions. Consistent with data examining nonsurgical hospitalized patients with acute coronary syndromes,\textsuperscript{6,11,22,33,39} we are the first, to our knowledge, to report positive associations between surgical-related mortality and anxiety and/or depression. Several potential mechanisms exist to explain these findings.

First, studies\textsuperscript{40-42} indicate that patients with depression frequently do not adhere to medical recommendations for underlying medical conditions. It is therefore plausible that such undertreated conditions may affect postoperative care and outcomes. Second, patients with existing psychiatric comorbidity may be more likely to undergo surgery by a lower-quality surgeon or hospital.\textsuperscript{43} Third, preexisting psychiatric comorbidity may serve as an indicator for greater severity of surgical risk. For example, such comorbidity may be mediated by unmeasured behaviors associated with increased postsurgical risk (eg, poor wound care, substance use, or failure to adhere to postsurgical recommendations).

Fourth, patients with psychiatric comorbidity may present in a later stage of illness requiring surgical intervention, thus increasing the chances of an adverse outcome. Finally, it is possible that operations may be delayed because of a lack of effective communication between the patient and surgeon or because of delays resulting from optimization of the psychiatric illness by the consulting psychiatrist.

One finding inconsistent with prior literature was the absence of an increased risk of postsurgical mortality for patients with PTSD, bipolar disorders, or schizophrenia. Absence of a positive relationship for patients with these serious mental illnesses may reflect recent efforts by the VHA to improve recognition and treatment for veterans with these disorders, or, alternatively, it may reflect a greater familiarity on the part of VHA surgeons or improved collaborative efforts between psychiatry and surgical care teams produced through the VHA infrastructure. Furthermore, the VHA has recently increased resource allotments for mental health services, in response to reports in the lay press\textsuperscript{44} about the mental health needs of veterans returning from recent combat.

Another important contribution of the current study is the identification of potential differences in the effect of psychiatric comorbidity surgical conditions, as grouped by major diagnostic categories. The odds of death ranged from 36.0% lower for musculoskeletal operations to 44.0% higher for nervous system operations.

It is important to acknowledge several potential limitations. First, our findings are based on a largely older male veteran population and may not be generalizable to non-VHA populations. Second, claims data may underrepresent the true prevalence of psychiatric comorbidity; as such, illnesses are likely to be underrecognized and underdiagnosed.\textsuperscript{45} Third, the spectrum of potential risk adjustment variables that can be captured by administrative files is limited, relative to data that may be captured by prospective clinical registries or medical records review. Thus, our estimates of the effects of psychiatric comorbidity may be subject to confounding by unmeasured severity.

Nevertheless, our risk-adjustment models included laboratory data. Prior studies\textsuperscript{46} indicate that models based on administrative data and laboratory data may yield similar risk predictions as models that included medical record data that had to be manually abstracted.

Despite these limitations, we believe the current study has important clinical, research, and policy implications. The findings highlight a modest increase in the risk of postsurgical death that may be associated with preexisting psychiatric comorbidity on a surgical-related hospitalization. Although the higher risk may be owing to other unmeasured factors, in the absence of identifying such factors, the findings suggest that greater clinical vigilance may be required in providing surgical care for patients with a range of psychiatric diagnoses. In particular, this may be true for patients with anxiety and
depression. Nonetheless, further research is needed to understand the factors underlying these associations and whether the increased risk is owing to differences in unmeasured severity or to differences in the effectiveness of care. Until further research is completed, we recommend that surgeons caring for patients with a history of anxiety or depression seek early involvement of multidisciplinary teams to help identify problematic areas in perioperative care processes, particularly regarding issues of surgeon-patient communication and adherence to postsurgical recommendations.

Finally, the current study demonstrates the value of linking inpatient and outpatient databases to identify the effect of chronic conditions on surgical outcomes. As shown previously, the use of prior outpatient claims represents an approach that identifies the presence of psychiatric comorbidity similar to prospective trials among hospitalized patients and, therefore, is likely to be more sensitive for identifying chronic conditions than relying on secondary diagnoses from inpatient claims. Given the increasing use of administrative data to examine a wide variety of patient outcomes and to publicly report postsurgical hospital outcomes, using linked inpatient and outpatient data may strengthen the validity of inferences regarding surgical quality.

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Author Contributions: All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Abrams and Rosenthal. Acquisition of data: Vaughan-Sarrazin and Rosenthal. Analysis and interpretation of data: Abrams and Rosenthal. Drafting of the manuscript: Abrams and Vaughan-Sarrazin. Critical revision of the manuscript for important intellectual content: Abrams, Vaughan-Sarrazin, and Rosenthal. Statistical analysis: Abrams and Vaughan-Sarrazin. Obtained funding: Rosenthal. Study supervision: Rosenthal.

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