ORIGINAL ARTICLE

Sex Differences in Mortality of ICU Patients According to Diagnosis-related Sex Balance

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Abstract

Rationale: Women have worse outcomes than men in several conditions more common in men, including cardiac surgery and burns.

Objectives: To describe the relationship between sex balance within each diagnostic group of ICU admissions, defined as the percentage of patients who were women, and hospital mortality of women compared with men with that same diagnosis.

Methods: We studied ICU patients in the Australian and New Zealand Intensive Care Society's Adult Patient Database (2011–2020). We performed mixed effects logistic regression for hospital mortality adjusted for sex, illness severity, ICU lead time, admission year, and hospital site. We compared sex balance with the adjusted hospital mortality of women compared with men for each diagnosis using weighted linear regression.

Measurements and Main Results: There were 1,450,782 admissions (42.1% women), with no difference in the adjusted hospital mortality of women compared with men overall (odds ratio, 0.99; 99% confidence interval [CI], 0.97 to 1). As the percentage of women within each diagnosis increased, the adjusted mortality of women compared with men with that same diagnosis decreased (regression coefficient, −0.015; 99% CI; −0.020 to −0.011; $P < 0.001$), and the illness severity of women compared with men at ICU admission decreased (regression coefficient, −0.0026; 99% CI, −0.0035 to −0.0018; $P < 0.001$).

Conclusions: Sex balance in diagnostic groups was inversely associated with both the adjusted mortality and illness severity of women compared with men. In diagnoses with relatively few women, women were more likely than men to die. In diagnoses with fewer men, men were more likely than women to die.

Keywords: sex factors; mortality; illness severity; women; men

Women are more likely than men to die after some critical illnesses, including cardiac arrest, cardiac surgery, and burns (1–5). However, this is not a consistent pattern across all critical illnesses. Considering the ICU population overall, women and men appear to have equivalent adjusted hospital or 30-day mortality (6–10). Moreover, women have lower mortality than men in some critical illnesses, including exacerbation of chronic obstructive pulmonary disease, coronavirus disease (COVID-19) pneumonia, and spinal surgery (11–15). This variation in the relative outcomes of women and men after different critical illnesses remains unexplained.

Some critical illnesses with higher mortality in women than in men also occur less commonly in women than in men. For example, only 25% of cardiac surgery patients and 20% of patients with burns are

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At a Glance Commentary

Scientific Knowledge on the Subject: More men than women are admitted to ICUs worldwide. The sex balance, or percentage of ICU patients who are women, varies widely between admission diagnoses.

What This Study Adds to the Field: Patients admitted to ICUs with a diagnosis relatively uncommon for their sex have higher illness severity and are more likely to die than patients of the opposite sex. In diagnoses with fewer women, the women are relatively more likely than men to die, and in diagnoses with fewer men, the men are relatively more likely than women to die.

women (3–5). This raises the possibility of a relationship between sex balance within a diagnostic group and the mortality of women compared with men with that diagnosis.

As previously presented in the form of an abstract (16), we hypothesized that among ICU patients, women have relatively better outcomes than men in diagnoses with a higher percentage of patients who are women, and men have relatively better outcomes in diagnoses with a higher percentage of patients who are men. Our primary objective was to describe the relationship between the sex balance within each diagnostic group of ICU admissions, defined as the percentage of patients who were women, and the adjusted hospital mortality of women compared with men with that same diagnosis. Our secondary objective was to describe the relationship between sex balance and the relative illness severity of women compared with men at ICU admission, by diagnostic group.

Methods

Ethics Approval

Ethics approval for this study was granted by the Alfred Health Human Research Ethics Committee (project number 200/21).

Study Design

We conducted a retrospective cross-sectional study of adult patients admitted to ICUs in Australia and New Zealand, as recorded in the Australian and New Zealand Intensive Care Society Adult Patient Database (ANZICS APD), one of five clinical quality registry datasets run by the ANZICS Centre for Outcome and Resources Evaluation. The APD records admissions from 90% of ICUs in Australia and New Zealand, including all tertiary hospital ICUs and most metropolitan, regional, and private ICUs (17). Each hospital has one ICU that admits both medical and surgical patients under the care of intensive care specialists; hospitals that perform cardiac surgery admit postoperative cardiac surgery patients to the hospital's general ICU (17, 18). The APD uses a standardized secure digital data collection tool with automated data validation rules at all sites and a standardized data dictionary. Regular training and accuracy checks are provided for data collectors (17). We undertook this study in keeping with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines for cohort observational studies (19).

Study Population

We included patients aged 17 years and older admitted to an ICU and reported to the APD between 2011 and 2020. We excluded repeat ICU admissions from within the same hospital visit, including those transferred to another ICU, and those with missing diagnosis, outcome, or sex classification. We also excluded patients classified as "intersex/indeterminate" because this nonbinary sex classification was added to the APD in 2017 and accounts for less than 0.1% of ICU admissions each year (20, 21). Given our focus on the sex balance within diagnostic groups, we excluded sex-specific diagnoses, defined as diagnoses with less than 1% or greater than 99% women.

Exposure and Outcomes

The exposure of interest in this study was sex, defined in the APD data dictionary as the biological distinction between female and male (20). Sex data were obtained from hospital admission details and therefore may be self-reported, reported by family members, or determined by hospital staff. There is no gender classification in the APD.

The primary objective of this study was to describe the association between sex balance, defined as the percentage of patients in a diagnostic group who were women, and sex differences in outcome, defined as the adjusted hospital mortality of women compared with men, by ICU admission diagnosis. The ICU admission diagnoses are based on the Acute Physiology and Chronic Health Evaluation III (APACHE III) diagnostic definitions; they are mutually exclusive and reflect the clinical diagnosis during the patient's first 24 hours of ICU admission (nonoperative diagnoses) or the operation performed immediately before ICU admission (postoperative admissions; *see* Tables E1 and E2 in the online supplement) (20). We assessed illness severity using the APACHE III score, which does not adjust for patient sex.

Statistical Analysis

We reported counts with percentages and means with standard deviations for normally distributed data and medians with interquartile ranges for nonnormally distributed data. We used the chi-square test, Wilcoxon rank-sum test, or *t* test for comparisons as appropriate. To increase the robustness of our findings, we reported 99% confidence intervals (CIs) and took $P < 0.01$ to indicate statistical significance. We performed complete case analysis, making no assumptions about missing data. We used STATA 17 for statistical analysis (StataCorp).

We performed mixed-effects logistic regression analysis for hospital mortality, adjusting for sex, APACHE III score, diagnosis, hours of hospitalization before ICU admission (henceforth ICU lead time), year of admission, and hospital site, with site treated as a random effect. We repeated this mixed-effects logistic regression for each of the 111 diagnoses (diagnosis removed from model), reporting the odds ratios (ORs) with 99% CIs for adjusted hospital mortality of women compared with men for each diagnosis. Therefore, ORs <1 indicate women were less likely than men to die and vice versa. To test the association between sex differences in mortality and sex balance, we performed a frequency-weighted linear regression of the adjusted hospital mortality of women compared with men for each diagnosis (OR) against the sex balance (percentage of female patients) within that diagnostic group. Regression results are reported as parametric estimates (99% CI) with a corresponding r^2 statistic and a P value to reflect if the slope differs significantly from 0.

We compared the illness severity of women and men using the ratio of female to male mean APACHE III scores. To test the association between sex balance and sex differences in illness severity, we performed weighted linear regression of female to male mean APACHE III scores against sex balance for each diagnosis.

To test the robustness of our findings, we repeated the analysis with the study population divided into groups of hospitals instead of diagnostic groups. Hospitals were ranked into 48 quantiles according to sex balance in admissions. We calculated hospital mortality for each hospital group adjusted for sex, diagnosis, illness severity, ICU lead time, and admission year but not hospital site. We then performed weighted linear regression of adjusted hospital mortality against sex balance for each hospital group. Further sensitivity analyses are described in the online supplement E1.

Results

Study Population and Sex Differences in Mortality

There were 1,614,045 admissions entered into the ANZICS Centre for Outcome and Resources Evaluation APD between 2011 and 2020, of which 1,450,782 were eligible for this study (Figure E1). Complete illness severity data were available for 1,447,135 patients, who were included in the regression models (99.7% of study population; complete patient numbers for all datapoints are available in Table E3).

Overall, 42.1% of the study population were women. On average, women were younger than men and had lower illness severity scores than men (Table 1). Women had lower unadjusted hospital mortality than men (8.1% vs. 8.6%; $P < 0.001$). After adjustment for APACHE III score, diagnosis, ICU lead time, year of admission, and hospital site, however, there was no difference in hospital mortality between women and men overall (OR, 0.99; 99% CI, 0.97 to 1.00; $P = 0.05$) (Table 2).

There were significant sex differences in adjusted hospital mortality within five of the nine major diagnostic categories of ICU admissions. Women had lower adjusted hospital mortality than men in three categories: respiratory; sepsis; and the combined metabolic, hematological, and renal disorders category (Table 2). Women had higher adjusted mortality than men in the cardiac surgery category and other cardiovascular diagnoses category. The most marked sex difference in mortality was observed in the cardiac surgery category, with women significantly more likely than men to die. There was no sex difference in mortality in four categories: neurological; trauma; musculoskeletal, soft tissues, and skin diagnoses; and gastrointestinal diagnoses.

Relationship between Sex Balance and Sex Differences in Mortality

The percentage of patients who were women within each diagnostic group was inversely associated with the adjusted hospital mortality of women relative to men (weighted linear regression coefficient, −0.015; 99% CI, −0.020 to −0.011; $P < 0.001$; $r^2 = 38\%$) (Figure 1). In diagnostic groups in which a lower percentage of the patients were women, the women were relatively more likely to die than the men. Conversely, in diagnostic groups with a higher percentage of female patients, the women were relatively less likely to die than the men. Diagnostic groups containing less than the average percentage female patients (less than 42.1% women) tended to have higher adjusted hospital mortality for women than for men (OR, >1) and vice versa.

Relationship between Sex Balance and Sex Difference in Illness Severity

There was an inverse association between the relative illness severity of women compared with men with a diagnosis and the sex balance in that diagnostic group (weighted linear regression coefficient, −0.0026; 99% CI, −0.0035 to −0.0018; $P < 0.001$; $r^2 = 38\%$) (Figure 2). In diagnostic groups in which a lower percentage of the patients were women, the women had higher illness severity than men at ICU admission and vice versa. A sensitivity analysis examining each component of APACHE III score separately found that the association between illness severity and sex balance was driven by the physiological and age components rather than chronic health conditions (Figure E2).

Sensitivity Analyses

The inverse relationship between mortality and sex balance persisted when the study population was divided by hospitals rather than admission diagnosis (Figure 3). However, there was no significant association between mortality and sex balance when the study population was divided according to age (Figure E3). A sensitivity analysis that excluded all patients with limitations of medical therapy in place at the time of ICU admission confirmed a significant relationship between sex differences in mortality and sex balance within diagnostic groups (Figure E4). Finally, there was a small but significant association between sex difference in ICU lead time and sex balance within diagnostic groups: Patients presenting with illnesses less common for their sex spent relatively longer in the hospital before ICU admission (Figure E5).

Table 1. Characteristics of Women and Men Admitted to ICU

Characteristics	All Patients ($N = 1,450,782$)*	Women ($n = 610,215$) (42.1%)	Men ($n = 840,567$) (57.9%)	P Value for Sex Difference
Age, yr, mean (SD)	62.3 (17.5)	61.8 (18.3)	62.7 (16.9)	<0.001
APACHE III score, mean (SD)	52.1 (24.9)	51.3 (24.8)	52.7 (24.9)	<0.001
Pre-ICU time, h, median [IQR]	9.7 [4.5–28.2]	9.25 [4.5–27.1]	10 [4.6–28.9]	<0.001
Length of stay, d, median [IQR]	1.8 [0.9–25.5]	1.7 [0.9–3.1]	1.8 [0.9–3.3]	<0.001
Admission type				
Elective, *n* (%)	610,729 (42.4)	242,910 (40.1)	367,819 (44.1)	<0.001
Nonelective, *n* (%)	829,334 (57.6)	362,852 (59.9)	466,482 (55.9)	<0.001
LOMT, *n* (%)	88,824 (6.3)	41,760 (7.0)	47,064 (5.8)	<0.001

Definition of abbreviations: APACHE = Acute Physiology and Chronic Health Evaluation; ICU = intensive care unit; IQR = interquartile range; LOMT = limitation of medical treatment at the time of admission to ICU.
*Complete data available for >99% of patients; patient numbers for each variable are provided in Table E3.

Table 2. Sex Differences in Illness Severity and Hospital Mortality, by Diagnostic Category

Diagnostic Category	Patients			Illness Severity, Female/Male APACHE III* (99% CI)	Unadjusted Hospital Mortality		Adjusted Hospital Mortality of Women Compared with Men,† Odds Ratio (99% CI)
	Total	Women [n (%)]	Men [n (%)]		Women [n (%)]	Men [n (%)]	
Cardiovascular (excludes cardiac surgery)	186,770	69,282 (37.1)	117,488 (62.9)	0.97 (0.96–0.97)	11,094 (16)	19,277 (16.4)	1.07 (1.02–1.12)
Cardiac surgery	174,425	43,659 (25)	130,766 (75)	1.04 (1.04–1.05)	965 (2.21)	1,612 (1.23)	1.63 (1.45–1.82)
Respiratory	218,252	97,905 (44.9)	120,347 (55.1)	0.98 (0.97–0.99)	9,090 (9.3)	12,700 (10.6)	0.92 (0.88–0.96)
Gastrointestinal	243,174	112,890 (46.4)	130,284 (53.6)	0.96 (0.95–0.96)	7,255 (6.4)	9,344 (7.2)	1.00 (0.95–1.05)
Neurological	184,702	88,754 (48.1)	95,948 (51.9)	0.97 (0.96–0.98)	7,794 (8.8)	9,219 (9.6)	1.00 (0.95–1.05)
Sepsis	105,071	47,316 (45)	57,755 (55)	0.95 (0.94–0.96)	7,369 (15.6)	10,187 (17.6)	0.94 (0.89–0.98)
Trauma	69,381	19,707 (28.4)	49,674 (71.6)	1.09 (1.07–1.11)	1,890 (9.6)	4,463 (8.9)	0.91 (0.83–1.00)
Metabolic, renal hematology	169,059	80,617 (47.7)	88,442 (52.3)	0.96 (0.96–0.97)	2,814 (3.5	3,696 (4.2)	0.87 (0.81–0.94)
Musculoskeletal, soft tissue, skin	99,948	50,085 (50.1)	49,863 (49.9)	1.00 (0.99–1.01)	1,205 (2.4)	1,388 (2.8)	0.89 (0.79–1.00)
Total	1,450,782	610,215 (42.1)	840,567 (57.9)	0.97 (0.97–0.97)	49,476 (8.1)	71,866 (8.6)	0.99 (0.97–1.00)

Definition of abbreviations: APACHE = Acute Physiology and Chronic Health Evaluation; CI = confidence interval; ICU = intensive care unit.
*Ratio of female-to-male mean APACHE III scores.
†Adjusted for APACHE III score, ICU lead time, admission year, and hospital site, in addition to sex.

Discussion

Key Findings

In this study of nearly 1.5 million ICU patients in Australia and New Zealand, women had lower unadjusted hospital mortality and equivalent adjusted hospital mortality compared with men overall. However, there were sex differences in adjusted hospital mortality in five of nine major diagnostic categories of ICU admissions.

We found an inverse relationship between the percentage of patients admitted with a given diagnosis who were women and the adjusted hospital mortality of women compared with men with that diagnosis. This sex-based minority effect was bidirectional: Women were more likely to die if admitted with a diagnosis relatively less common in women (e.g., cardiac surgery), and men were relatively more likely to die if admitted with a diagnosis less common in men (e.g., metabolic disorders). The minority effect persisted across hospitals: Patients admitted to ICUs with relatively few patients of their own sex were more likely to die than patients in the majority sex group for that ICU.

There was also an inverse relationship between sex balance and the relative illness severity of women compared with men with the same diagnosis. In diagnostic groups with relatively few women (i.e., diagnostic groups in which the percentage of patients who were women was less than the mean of 42.1%), women were admitted to an ICU at a higher illness severity than men and vice versa.

Relationship to Previous Studies

To the best of our knowledge, no previous study has addressed the issue of sex balance and its association with outcome. A meta-analysis of sex differences in outcomes of ICU patients found no difference in the hospital mortality of women and men overall, although there was substantial heterogeneity associated with this result (6). Similarly, our study found no sex difference in the adjusted hospital mortality of the overall study population. We found significant differences in the outcomes of women compared with men within most diagnostic categories, suggesting that the heterogeneity in findings of previous studies could be due partly to variations in case mix.

In contrast to most previous studies, the women in our study population were

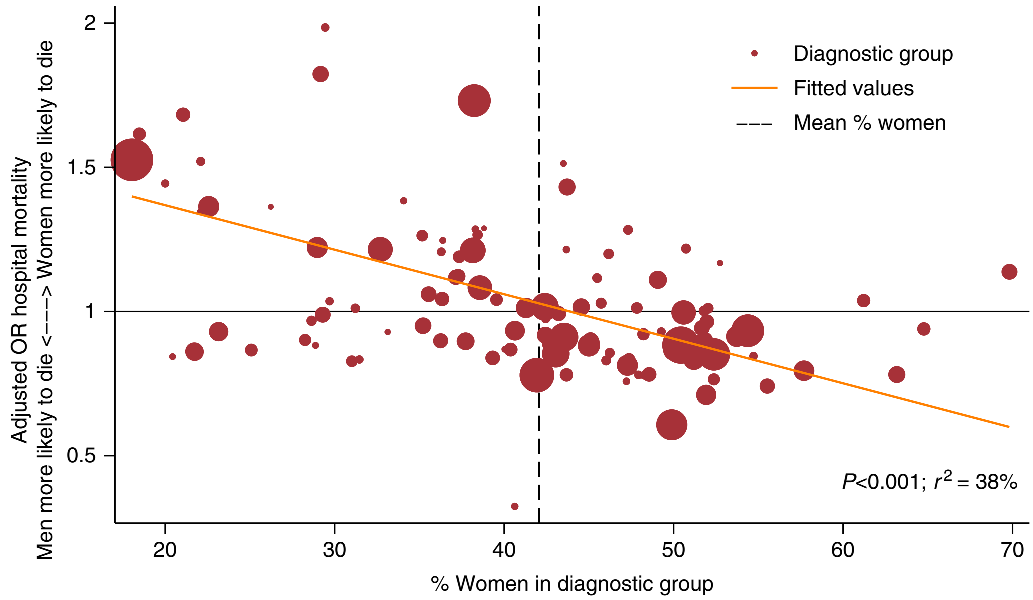

Figure 1. Adjusted hospital mortality of women compared with men versus the percentage of patients who were women, by diagnostic group. The weighted regression (fitted values) shows that the adjusted mortality of women compared with men was inversely associated with the percentage of women in the diagnostic groups. As the percentage of female patients within a diagnostic group increased by 10% (e.g., from 30% to 40%), the odds ratio (OR) for hospital mortality of women compared with men decreased by 0.15, from approximately 1.2 to 1.05 (regression coefficient, −0.015; 99% confidence interval, −0.020 to −0.011; $P < 0.001$).

younger and had lower illness severity scores than the men (2, 10, 11, 22–24). This suggests an important difference between the Australian and New Zealand ICU population and those of previous studies of sex differences in ICU patients from Europe, North America, and Taiwan.

Concordant with previous studies, we found that women had higher mortality than men after cardiac surgery (3, 11) and that the cardiac surgery cohort had the most pronounced sex difference in mortality of all the major diagnostic categories of ICU admission.

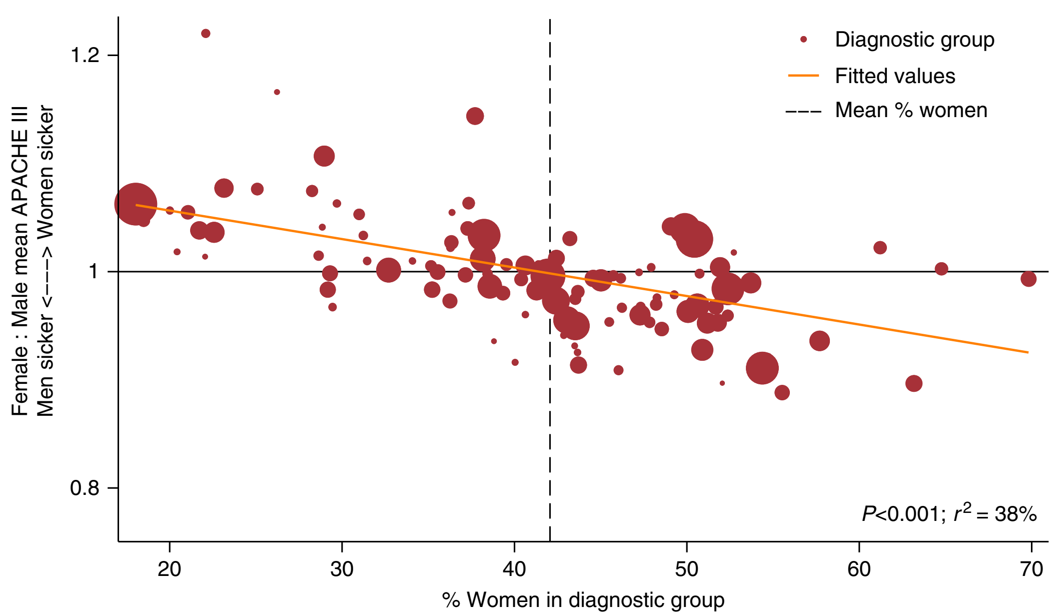

Figure 2. Illness severity of women compared with men versus the percentage of patients who were women, by diagnostic group. The weighted regression (fitted values) shows that the illness severity of women compared with men was inversely associated with the percentage of patients who were women in the diagnostic group. An increased percentage of patients who were women within the diagnostic group was associated with lower illness severity of women compared with men at ICU admission (linear regression coefficient, −0.0026; 99% confidence interval, −0.0035 to −0.0018; $P < 0.001$; $r^2 = 38\%$). APACHE III = Acute Physiology and Chronic Health Evaluation III.

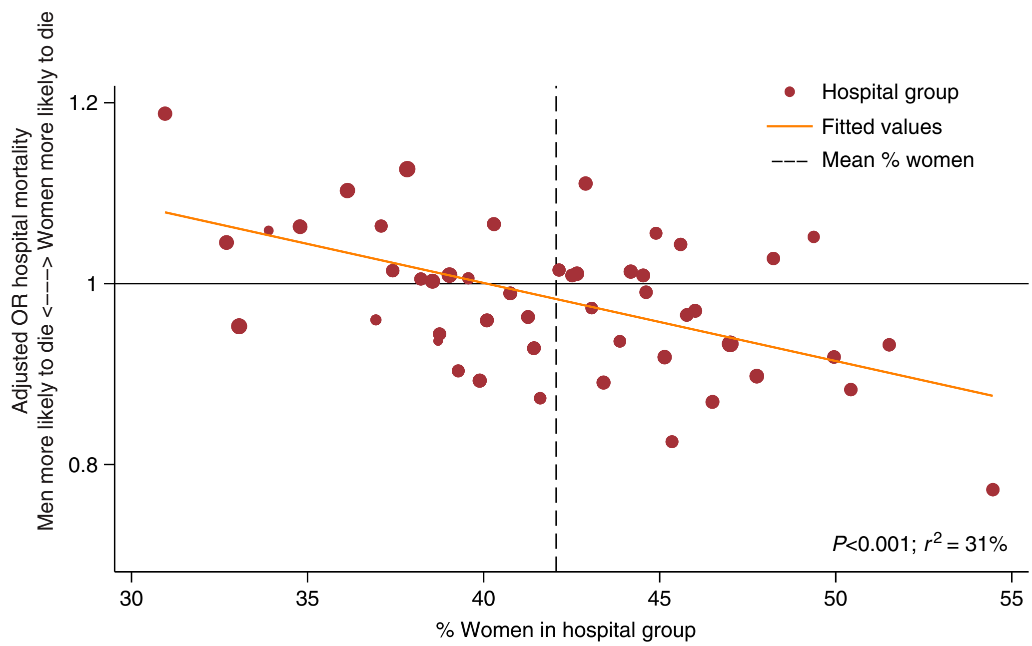

Figure 3. Adjusted hospital mortality of women compared with men versus sex balance, by hospital group. Hospitals were grouped into 48 quantiles based on the percentage of female patients admitted during the study period. Hospital mortality was adjusted for Acute Physiology and Chronic Health Evaluation III score, diagnosis, ICU lead time, and admission year, in addition to sex. As the percentage of female patients increased, the odds ratio (OR) for adjusted hospital mortality of women compared with men decreased (linear regression coefficient, −0.0086; 99% confidence interval, −0.0137 to −0.0035; $P < 0.001$; $r^2 = 31\%$).

Implications of Study Findings

Our key finding that sex balance is associated with the relative outcomes and illness severity of women and men within diagnostic groups has important implications. First, it suggests a type of sex-based volume–outcome relationship. Such volume–outcome relationships are well recognized in critical care (25, 26).

A sex-based volume–outcome effect could be mediated by clinician cognitive bias. Patients may receive more prompt diagnosis and treatment if they present with an illness expected for their sex, a form of ascertainment bias (27). This is supported by our finding that patients were admitted to ICUs after a shorter time in the hospital and at a lower illness severity if their illness was common in their sex. Availability bias, where the clinician's familiarity or recent experience of treating similar patients affects their diagnosis and treatment, may also contribute to the observed association between sex balance and outcomes (28). Greenwood and colleagues found that female patients with acute myocardial infarction had lower mortality if their male physician had recently treated female patients with acute myocardial infarction, supporting the theory that a clinician's familiarity with treating male or female patients in a given clinical situation affects the treatment they provide (29). There is also evidence that the sex balance of the treating team affects sex-based outcomes. This includes both the sex concordance of the physician–patient pair and the sex balance within a clinical team (29, 30). Therefore, future studies should examine the impact of the sex balance among ICU clinicians on the observed sex differences in patient outcomes.

Second, our findings suggest that the exposure of being male or female across the lifespan may affect both the incidence and outcomes of various critical illnesses. Biological differences in sex hormones and cytokine response, combined with different patterns of risk-taking behavior between women and men, could contribute to the observed sex differences (31, 32). However, the association between sex balance and mortality persisted across groups of hospitals after adjusting for admission diagnosis, suggesting that the relationship is driven by system-level rather than simply disease-level factors. Moreover, there was no significant relationship between sex balance and chronic diseases in women and men, which somewhat speaks against the impact of long-term risk-taking behaviors such as smoking or alcohol consumption.

From a clinical perspective, our findings suggest that clinicians should pay heed to patients presenting with illnesses uncommon in their sex. This could be incorporated into clinical warning systems for diseases with a marked female preponderance (e.g., metabolic disorders) or marked male preponderance (e.g., cardiac surgery). From a research perspective, our findings underscore the importance of obtaining sex-disaggregated data in critical care clinical trials and examining sex as a variable in observational research.

Strengths and Limitations

Our study has several strengths. To the best of our knowledge, this is the first to investigate the relationship between sex balance and sex differences in outcomes. We further interrogated the significance of sex balance by examining its relationship with illness severity and performing sensitivity analyses using hospital groups and age cohorts instead of diagnostic cohorts.

We used data obtained from a well-established clinical registry with high-quality governance, capturing the vast majority of ICU admissions across Australia and New Zealand (16). Where previous studies focused on sex differences in either the ICU population overall or selected critical illnesses (2, 7, 11), our very large study comprehensively described sex differences in illness severity and outcomes across diagnoses leading to ICU admission.

The relatively low mortality rate in our study population suggests that our findings are not due to poor clinical performance overall. Furthermore, the equivalent adjusted outcomes of women and men overall speaks against overt sex discrimination affecting our results.

We acknowledge several limitations. We assessed only patients admitted to the ICU rather than all potential ICU patients admitted to a hospital. Because we did not compare the sex balance and outcomes of the ICU and hospital populations, we cannot comment on equity of access to the ICU. In comparing the mortality of women and men after ICU admission, we are comparing the outcomes of a complex process including treatment received before ICU admission. It is possible that both the presumptive diagnosis and the decision for ICU admission were impacted by bias, in turn affecting the observed relationship between sex, diagnosis, and mortality.

Because of the very limited data available on transgender or nonbinary ICU patients, we adopted a binary definition of sex. Therefore, we cannot comment on the outcomes of nonbinary ICU patients compared with women or men. Finally, although our study describes a potentially important relationship between sex balance and sex differences in outcomes, we cannot confirm the mechanism underlying this relationship.

Conclusions

For ICU patients, the hospital mortality of women compared with men is inversely related to the percentage of women admitted within the same diagnostic category: Women are more likely to die in diagnostic groups with relatively few women, and men are more likely to die in diagnostic groups with fewer men. A similar relationship exists between sex balance and the relative illness severity of women and men: In diagnostic categories with more women, women are admitted at relatively lower illness severity than men. Awareness of this minority effect may allow clinicians to modify their management of patients presenting with illnesses uncommon in their sex. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

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References

1. Lei H, Hu J, Liu L, Xu D. Sex differences in survival after out-of-hospital cardiac arrest: a meta-analysis. *Crit Care* 2020;24:613.
2. Todorov A, Kaufmann F, Arslani K, Haider A, Bengs S, Goliasch G, *et al.*; Swiss Society of Intensive Care Medicine. Gender differences in the provision of intensive care: a Bayesian approach. *Intensive Care Med* 2021;47:577–587.
3. Johnston A, Mesana TG, Lee DS, Eddeen AB, Sun LY. Sex differences in long-term survival after major cardiac surgery: a population-based cohort study. *J Am Heart Assoc* 2019;8:e013260.
4. Karimi K, Faraklas I, Lewis G, Ha D, Walker B, Zhai Y, *et al.* Increased mortality in women: sex differences in burn outcomes. *Burns Trauma* 2017;5:18.
5. Moore EC, Pilcher D, Bailey M, Cleland H. Women are more than twice as likely to die from burns as men in Australia and New Zealand: an unexpected finding of the Burns Evaluation And Mortality (BEAM) Study. *J Crit Care* 2014;29:594–598.
6. Modra L, Higgins A, Vithanage R, Abeygunawardana V, Bailey M, Bellomo R. Sex differences in illness severity and mortality among adult intensive care patients: a systematic review and meta-analysis. *J Crit Care* 2021; 65:116–123.
7. Samuelsson C, Sjöberg F, Karlström G, Nolin T, Walther SM. Gender differences in outcome and use of resources do exist in Swedish intensive care, but to no advantage for women of premenopausal age. *Crit Care* 2015;19:129.
8. Hessey E, Montgomery C, Zuege DJ, Rolfson D, Stelfox HT, Fiest KM, *et al.* Sex-specific prevalence and outcomes of frailty in critically ill patients. *J Intensive Care* 2020;8:75.
9. Hollinger A, Gayat E, Féliot E, Paugam-Burtz C, Fournier MC, Duranteau J, *et al.*; FROG ICU study investigators. Gender and survival of critically ill patients: results from the FROG-ICU study. *Ann Intensive Care* 2019;9:43.
10. Valentin A, Jordan B, Lang T, Hiesmayr M, Metnitz PG. Gender-related differences in intensive care: a multiple-center cohort study of therapeutic interventions and outcome in critically ill patients. *Crit Care Med* 2003;31:1901–1907.
11. Mahmood K, Eldeirawi K, Wahidi MM. Association of gender with outcomes in critically ill patients. *Crit Care* 2012;16:R92.
12. Nguyen NT, Chinn J, De Ferrante M, Kirby KA, Hohmann SF, Amin A. Male gender is a predictor of higher mortality in hospitalized adults with COVID-19. *PLoS One* 2021;16:e0254066.
13. Lisspers K, Larsson K, Janson C, Ställberg B, Tsiligianni I, Gutzwiller FS, *et al.* Gender differences among Swedish COPD patients: results from the ARCTIC, a real-world retrospective cohort study. *NPJ Prim Care Respir Med* 2019;29:45.
14. Poorman GW, Moon JY, Wang C, Horn SR, Beaubrun BM, Bono OJ, *et al.* Rates of mortality in lumbar spine surgery and factors associated with its occurrence over a 10-year period: a study of 803,949 patients in the Nationwide Inpatient Sample. *Int J Spine Surg* 2018;12:617–623.
15. Schoenfeld AJ, Reamer EN, Wynkoop EI, Choi H, Bono CM. Does patient sex affect the rate of mortality and complications after spine surgery? A systematic review. *Clin Orthop Relat Res* 2015;473:2479–2486.
16. Modra L. Sex differences in mortality of ICU patients in Australia and New Zealand. Paper presented at the Australia and New Zealand Intensive Care Society and Australian College of Critical Care Nurses Annual Scientific Meeting, April 2022, Sydney, Australia.
17. Australian and New Zealand Intensive Care Society, Centre for Outcomes and Resource Evaluation. Centre for Resource and Outcomes Evaluation 2020 report; 2021 [accessed 2022 Mar 9]. Available from: https://www.anzics.com.au/wp-content/uploads/2021/09/2020-ANZICS-CORE-Report.pdf.
18. College of Intensive Care Medicine of Australia and New Zealand. Minimum standards for intensive care units; 2016 [accessed 2022 Jun 20]. Available from: https://www.cicm.org.au/CICM_Media/CICMSite/Files/Professional/IC-1-Minimum-Standards-for-Intensive-Care-Units.pdf.
19. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet* 2007; 370:1453–1457.
20. Australian and New Zealand Intensive Care Society, Centre for Outcomes and Resource Evaluation. Adult patient database data dictionary, Version 6.0; 2022 [accessed 2022 Mar 9]. Available from: https://www.anzics.com.au/wp-content/uploads/2021/03/ANZICS-APD-Data-Dictionary.pdf.
21. Modra LJ, Pilcher D, Bailey M, Bellomo R. Sex differences in intensive care unit admissions in Australia and New Zealand. *Crit Care Resusc* 2021;23:86–93.
22. Reinikainen M, Niskanen M, Uusaro A, Ruokonen E. Impact of gender on treatment and outcome of ICU patients. *Acta Anaesthesiol Scand* 2005;49:984–990.
23. Shen HN, Lu CL, Yang HH. Women receive more trials of noninvasive ventilation for acute respiratory failure than men: a nationwide population-based study. *Crit Care* 2011;15:R174.
24. Zettersten E, Jäderling G, Bell M, Larsson E. Sex and gender aspects on intensive care. A cohort study. *J Crit Care* 2020;55:22–27.

25. Nguyen YL, Wallace DJ, Yordanov Y, Trinquart L, Blomkvist J, Angus DC, *et al.* The volume-outcome relationship in critical care: a systematic review and meta-analysis. *Chest* 2015;148:79–92.
26. Barbaro RP, Odetola FO, Kidwell KM, Paden ML, Bartlett RH, Davis MM, *et al.* Association of hospital-level volume of extracorporeal membrane oxygenation cases and mortality. Analysis of the extracorporeal life support organization registry. *Am J Respir Crit Care Med* 2015;191: 894–901.
27. Catalogue of Biases Collaboration; Spencer EA, Brassey J. Ascertainment bias. In: Catalogue of bias. Oxford, UK: University of Oxford; 2017 [accessed 2022 Jun 20]. Available from: https://catalogofbias.org/biases/ascertainment-bias/.
28. Hayes MM, Chatterjee S, Schwartzstein RM. Critical thinking in critical care: five strategies to improve teaching and learning in the intensive care unit. *Ann Am Thorac Soc* 2017;14:569–575.
29. Greenwood BN, Carnahan S, Huang L. Patient-physician gender concordance and increased mortality among female heart attack patients. *Proc Natl Acad Sci USA* 2018;115:8569–8574.
30. Centola D, Guilbeault D, Sarkar U, Khoong E, Zhang J. The reduction of race and gender bias in clinical treatment recommendations using clinician peer networks in an experimental setting. *Nat Commun* 2021; 12:6585.
31. Vogel B, Acevedo M, Appelman Y, Bairey Merz CN, Chieffo A, Figtree GA, *et al.* The Lancet Women and Cardiovascular Disease Commission: reducing the global burden by 2030. *Lancet* 2021;397: 2385–2438.
32. Guidry CA, Swenson BR, Davies SW, Dossett LA, Popovsky KA, Bonatti H, *et al.* Sex- and diagnosis-dependent differences in mortality and admission cytokine levels among patients admitted for intensive care. *Crit Care Med* 2014;42:1110–1120.