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Gender differences in the provision of intensive care: a Bayesian approach

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Abstract

Purpose: It is currently unclear whether management and outcomes of critically ill patients differ between men and women. We sought to assess the influence of age, sex and diagnoses on the probability of intensive care provision in critically ill cardio- and neurovascular patients in a large nationwide cohort in Switzerland.

Methods: Retrospective analysis of 450,948 adult patients with neuro- and cardiovascular disease admitted to all hospitals in Switzerland between 01/2012 and 12/2016 using Bayesian modeling.

Results: For all diagnoses and populations, median ages at admission were consistently higher for women than for men [75 (64;82) years in women vs. 68 (58;77) years in men, $p < 0.001$]. Overall, women had a lower likelihood to be admitted to an intensive care unit (ICU) than men, despite being more severely ill [odds ratio (OR) 0.78 (0.76–0.79)]. ICU admission probability was lowest in women aged > 65 years (OR women:men 0.94 (0.89–0.99), $p < 0.001$). Women < 45 years had a similar ICU admission probability as men in the same age category [OR women:men 1.03 (0.94–1.13)], in spite of more severe illness. The odds to die were significantly higher in women than in men per unit increase in Simplified Acute Physiology Score (SAPS) II (OR 1.008 [1.004–1.012]).

Conclusion: In the care of the critically ill, our study suggests that women are less likely to receive ICU treatment regardless of disease severity. Underuse of ICU care was most prominent in younger women < 45 years. Although our study has several limitations that are imposed by the limited data available from the registries, our findings suggest that current ICU triage algorithms could benefit from careful reassessment. Further, and ideally prospective, studies are needed to confirm our findings.

Keywords: Gender bias, Critical illness, Cardiovascular disease, Women, Survival

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Introduction

Cardiovascular disease (CVD) remains the most common cause of morbidity and mortality in both women and men in the Western World [1]. Since the 1980s, age-adjusted mortality for CVD has continuously declined, however to a lesser extent in women than in men [2]. Despite growing evidence regarding sex and gender differences in CVD, mechanisms behind these differences remain largely unexplored [3]. Further, significant cardiovascular health inequalities between women and men persist in the diagnostic accuracy of tests, timely and evidence-based treatment, secondary prevention, and outcomes [3–6]. Importantly, younger women with CVD have a particularly unfavorable prognosis and a plethora of unanswered questions remains in this demographic group [7–10].

The impact of gender on provision and outcomes of critical care treatment has been described in several smaller cohorts. Overall, women remain underrepresented amongst intensive care unit (ICU) patients, in particular amongst higher age groups [11–14], are less likely to receive life-supporting treatments, and have overall shorter ICU stays than men [15–17]. This contrasts with the fact that CVD prevalence is higher in older women than in older men with women having a higher burden of pre-existing disabilities [3, 18, 19]. With the anticipated surge in the ageing population, the prevalence of these conditions is projected to increase even further and will be set against a limited number of ICU beds and staff. As simultaneously medical technology advances, there is an urgent need to understand barriers for the provision of ICU care to ensure optimal and unbiased use of resources. Thus, we sought to assess how sex and age influence ICU admission in cardio- and neurovascular patients in a large nationwide cohort in Switzerland.

Methods

Study population

The designated primary outcome measure of this study was admission to ICU. Secondary outcome measures included advanced treatments and ICU mortality. Patients aged < 20 years, ICU readmissions within the same hospital stay, and planned ICU admissions were excluded from the analysis. Data on ICU admissions were obtained from the Swiss ICU-Registry. The Swiss ICU-Registry (MDSi—Minimal Dataset for ICUs) is owned and operated by the Swiss Society of Intensive Care Medicine (SSICM). Details of the MDSi dataset have previously been described [20]. Briefly, the database contains prospectively collected data from 86 certified Swiss ICUs including information on origin and type of admission, diagnostic group and intervention, severity

Take-home message

In our analysis of 450′948 neuro- and cardiovascular patients, women, and in particular young women, had a lower likelihood to receive ICU care than men, despite being more severely ill. Although our study is limited by the number of available variables, our data suggest that health care inequalities between women and men might still exist, even in one of the highest ranked health care systems worldwide. Careful reassessment of triage algorithms and local protocols might help to ensure optimal and equitable use of critical care resources, thereby improving outcomes.

of acute illness, daily process variables and discharge details comprising ICU mortality. The MDSi dataset does not contain data from intermediate care units. Data are transferred anonymously to the MDSi from each contributing ICU.

The MDSi dataset provides data on ICU patients (main diagnosis, death, sex, age) to the Swiss Federal Office of Statistics (*Schweizer Bundesamt für Statistik* [BfS]). For our analysis, data on ICU admissions were obtained from the MDSi database, while data on general hospital admissions were provided by the BfS. From both datasets, patients who were admitted to either ICU or normal ward between 01/2012 (begin of detailed prospective data collection by the Swiss ICU-Registry) and 12/2016 (data validation completed) with one of the following cardiovascular diagnoses were extracted: acute coronary syndrome including cardiac arrest, pulmonary embolism, acute heart failure, rhythm disturbances or stroke. We extracted demographic data, admission diagnoses codes, type of admission, the Simplified Acute Physiology Score (SAPS) II [21], the nine equivalents of nursing manpower use score (NEMS) [22], ICU length-of-stay (LOS), and ICU mortality. In both datasets, no information on the patients' pre-admission status (comorbidities or chronic diseases) is provided. Completeness (no missing data) and high quality of the dataset were ensured using only validated data acquired between 01/2012 and 12/2016. The study was approved by the Ethics committee of Northwestern Switzerland (EKNZ UBE-15/47) as well as by the scientific committee of the SSICM.

Definitions

Unplanned ICU admissions were defined as unstable patients transferred from the emergency department, normal wards, the operating theater, or other hospitals with the need for extended medical care and monitoring. Type of admission was defined as either admission from home or from another hospital. Interventions upon admission were included when performed within 48 h prior or after admission. LOS was defined as the time from ICU admission to discharge or death, and LOS was expressed in fractions of days. The overall NEMS was

normalized to LOS. ICU mortality was defined as the rate of all-cause mortality during the ICU hospitalization.

Statistical analysis

Statistical analysis was performed using R version 3.6.1 with the packages rstan, rstanarm and survival [23]. Simple group comparisons were performed using t-test, non-parametric rank sum test or chi-square test as appropriate. Bayesian models were used to estimate the hospital admission counts as a function of age and the probability of ICU admission (primary objective) [24, 25]. Frequentist analyses were performed to model the likelihood of ICU mortality (secondary objective) and to assess gender differences in advanced treatments (secondary objective) [26, 27]. Linear regression models of SAPS II and NEMS and binomial logistic regression models of death comprised the sex-dependent covariates age and diagnosis. Detailed information on statistical modeling is provided in the Supplementary Information File.

Results

Patient characteristics

Admission

450,948 patients admitted to either the ICU ($n = 77,803$, 17.3%) or general ward ($n = 373,145$, 82.7%) with the diagnoses of pulmonary embolism ($n = 24,077$, 5.3%), heart failure (89,326, 19.8%), rhythm disturbance ($n = 72,975$, 16.2%), acute coronary syndrome including cardiac arrest patients ($n = 183,762$, 40.8%), and stroke ($n = 80,808$, 17.9%) between 01/2012 and 12/2016 were included in our analysis (Table 1). Women were less often admitted to the ICU, independent of diagnoses (pulmonary embolism 10.6 vs. 12.3%, heart failure 10.0 vs. 14.5%, rhythm disturbance 11.2 vs. 13.0%, acute coronary syndrome including cardiac arrest 21.7 vs. 22.3%, stroke 16.5 vs. 19.3%, Table 1), independent of age category (Supplementary Table S1). Conversely, more women than men were admitted to the general wards (pulmonary embolism 89.4 vs. 87.7%, heart failure 90.0 vs. 85.5%, rhythm disturbance 88.8 vs. 87.0%, acute coronary syndrome 78.3 vs. 77.7%, stroke 83.5 vs. 80.7%, Table 1). Men who were transferred from another hospital were more often admitted to the ICU than women (13.5 vs. 16.1% in men, $p < 0.001$, Table 1), while direct ICU admissions were more frequent in women (74.6 vs. 74.0% in men, $p < 0.001$, Table 1).

Age at admission

In ICU patients, median age was higher in women as compared to men (75 [interquartile range [IQR] 64;82] years in women vs. 68 [IQR 58;77] years in men, $p < 0.001$) Accordingly, overall peak ages at admission (ICUs and general wards) were significantly higher in women as compared to men, independent of diagnosis (Fig. 1, Supplementary Table S2).

Disease severity

In ICU patients, median SAPS II was higher in women as compared to men [29 (IQR 23;40) in women and 27 (IQR 20;38) in men, $p < 0.001$]. Accordingly, multivariate linear regression models showed higher estimates for SAPS II in women admitted to the ICUs as compared to men [8.47 (6.71–10.23) in women and 4.06 (2.74–5.39) in men, ratio women:men 4.40 (2.20–6.61), $p < 0.001$]. When stratified by age, younger women < 45 years had consistently higher baseline estimates for SAPS II as compared to men; while, an opposite trend was observed at the age > 65 years (Supplementary Fig. S1). Hence, sex differences in median SAPS II were most pronounced in younger individuals, with younger women presenting with higher SAPS II than younger men (Supplementary Fig. S1). When stratified by diagnoses, baseline estimates of SAPS II were significantly higher in women across all diagnoses (Supplementary Table S3).

Probability of ICU admission (primary outcome)

Overall, women had a lower likelihood to be admitted to the ICU than men [odds ratio (OR) 0.78 (0.76–0.79), Table 2]. Multivariate Bayesian regression analysis adjusted for admission diagnosis, age categories (< 45 years, > 65 years) and proximity to peak age revealed that the odds for ICU admission were significantly lower in women as compared to men for heart failure [women 0.17 (0.16–0.18); men 0.24 (0.23–0.25); women:men OR 0.73 (0.69–0.77)] and stroke [women 0.29 (0.28–0.31); men 0.32 (0.31–0.33); women:men OR 0.92 (0.87–0.98), Table 2]. In contrast, women presenting with an acute coronary syndrome including cardiac arrest had a higher probability than men to be admitted to the ICU [women odds 0.40 (0.39–0.42); men odds 0.37 (0.36–0.39); women:men OR 1.08 (1.03–1.14), Table 2]. When the overall study population was stratified by age categories, women < 45 years of age showed a trend towards a lower admission probability as compared to men (Fig. 2), yet the odds ratio women:men did not reach significance in the adjusted Bayesian model [admission probabilities women:men < 45 years OR 1.03 (0.94–1.13), Table 2]. Women > 65 years had a lower probability to be admitted to the ICU than men [women:men OR 0.94 (0.89–0.99), Fig. 2 and Table 2].

Table 1 Patient characteristics and treatments stratified by sex and diagnoses

	All patients n=450,948			Pulmonary embolism n=24,077			Heart failure n=89,326			Rhythm disturbances n=72,975			Acute coronary syndrome including cardiac arrest n=183,762			Stroke n=80,808		
	Women	Men	p-value	Women	Men	p-value	Women	Men	p-value	Women	Men	p-value	Women	Men	p-value	Women	Men	p-value
Total, n	178,637	272,311		12,418	11,659		43,449	45,877		32,065	40,910		53,680	130,082		37,025	43,783	
Wards, n (%)	151,653 (84.9%)	221,492 (81.3%)		11,103 (89.4%)	10,222 (87.7%)		39,112 (90%)	39,219 (85.5%)		8,467 (88.8%)	35,603 (87.0%)		42,052 (78.3%)	101,106 (77.7%)		30,919 (83.5%)	35,342 (80.7%)	
ICU admissions, n (%)	26,984 (15.1%)	50,819 (18.7%)	<0.001	1,315 (10.6%)	1,437 (12.3%)	<0.001	4,337 (10%)	6,658 (14.5%)	<0.001	3,598 (11.2%)	5,307 (13.0%)	<0.001	11,628 (21.7%)	28,976 (22.3%)	0.004	6,106 (16.5%)	8,441 (19.3%)	<0.001
Transfer from other hospital, n (%)	3,631 (13.46%)	8,188 (16.11%)	<0.001	123 (9.35%)	150 (10.44%)	<0.001	526 (12.13%)	880 (13.22%)	<0.001	315 (8.75%)	460 (8.67%)	<0.001	2,110 (18.15%)	5,889 (20.32%)	<0.001	557 (9.12%)	809 (9.58%)	<0.001
Direct admission, n (%)	20,140 (74.64%)	37,625 (74.04%)	<0.001	1,029 (78.25%)	1,150 (80.03%)	<0.001	3,113 (71.78%)	4,877 (73.25%)	<0.001	2,921 (81.18%)	4,348 (81.93%)	<0.001	8,592 (73.89%)	21,083 (72.76%)	<0.001	4,485 (73.45%)	6,167 (73.06%)	<0.001
Median age (IQR)	75 (64–82)	68 (58–77)	<0.001	72 (60–80)	67 (56–75)	<0.001	78 (70–84)	74 (65–81)	<0.001	77 (67–83)	71 (62–80)	<0.001	72 (62–80)	65 (55–75)	<0.001	76 (65–83)	70 (60–79)	<0.001
Disease severity																		
Median SAPS II (IQR)	29 (23–40)	27 (20–38)	<0.001	29 (22–38)	26 (20–35)	<0.001	37 (29–49)	38 (29–50)	0.047	30 (24–38)	29 (22–37)	<0.001	28 (22–39)	25 (20–36)	<0.001	26 (22–35)	25 (20–34)	<0.001
Advanced treatments																		
PCI, n (%)	5,498 (20.38%)	16,405 (32.28%)	<0.001	15 (1.14%)	12 (0.84%)	<0.001	269 (6.02%)	479 (7.19%)	<0.001	85 (2.36%)	203 (3.83%)	<0.001	5,085 (43.73%)	15,637 (53.97%)	<0.001	44 (0.72%)	74 (0.88%)	<0.001
CABG, n (%)	269 (1.0%)	962 (1.89%)	<0.001	1 (0.08%)	3 (0.21%)	<0.001	21 (0.48%)	53 (0.8%)	<0.001	6 (0.17%)	19 (0.36%)	<0.001	241 (2.07%)	882 (3.04%)	<0.001	0 (0%)	5 (0.06%)	<0.001
NEMS normalized to LOS (IQR)	72.41 (57.80–94.57)	71.68 (56.67–94.29)	0.129	70.19 (60–85.83)	69.90 (60–85.94)	0.353	82.81 (68.57–102.86)	84.21 (69.87–104.38)	0.635	73.74 (58.94–100.77)	72.90 (57.23–103.45)	0.499	72.21 (56.64–96.00)	70.99 (55.56–94.46)	0.011	64.86 (52.64–82.60)	63.33 (52.04–80.51)	0.228
Non-invasive breathing aid, n (%)	19,834 (73.5%)	36,457 (71.74%)	<0.001	1,132 (86.08%)	1,291 (89.84%)	0.003	3,801 (87.64%)	5,740 (86.21%)	0.033	2,886 (80.21%)	4,210 (79.33%)	0.323	8,224 (70.73%)	20,123 (69.45%)	0.012	3,791 (62.09%)	5,093 (60.34%)	0.034
Mechanical ventilation, n (%)	6,075 (22.51%)	11,894 (23.4%)	0.005	276 (20.99%)	271 (18.86%)	0.177	2,068 (47.68%)	3,368 (50.59%)	0.003	216 (6.0%)	463 (8.72%)	<0.001	2,625 (22.57%)	6,492 (22.4%)	0.72	890 (14.58%)	1,300 (15.4%)	0.177
Intravenous medication, n (%)	23,853 (88.4%)	44,810 (88.18%)	0.368	1,203 (91.48%)	1,333 (92.76%)	0.240	4,229 (97.51%)	6,495 (97.55%)	0.939	3,217 (89.41%)	4,712 (88.79%)	0.375	10,008 (86.07%)	25,035 (86.4%)	0.389	5,196 (85.1%)	7,235 (85.71%)	0.310

Table 1 (continued)

	All patients n=450,948			Pulmonary embolism n=24,077			Heart failure n=89,326			Rhythm disturbances n=72,975			Acute coronary syndrome including cardiac arrest n=183,762			Stroke n=80,808		
	Women	Men	p-value	Women	Men	p-value	Women	Men	p-value	Women	Men	p-value	Women	Men	p-value	Women	Men	p-value
One vasoactive, n (%)	8,400 (31.13%)	16,687 (32.84%)	<0.001	301 (22.89%)	270 (18.79%)	0.009	2,256 (52.02%)	3,848 (57.8%)	<0.001	763 (21.21%)	1,160 (21.86%)	0.479	3,637 (31.28%)	9,311 (32.13%)	0.097	1,443 (23.63%)	2,098 (24.85%)	0.094
Multiple vasoactives, n (%)	3,177 (11.77%)	6,442 (12.68%)	<0.001	156 (11.86%)	140 (9.74%)	0.083	1,163 (26.82%)	2,204 (33.1%)	<0.001	169 (4.7%)	251 (4.73%)	0.984	1,343 (11.55%)	3,316 (11.44%)	0.776	346 (5.67%)	531 (6.29%)	0.127
RRT, n (%)	544 (2.02%)	1,360 (2.68%)	<0.001	26 (1.98%)	28 (1.95%)	1.000	239 (5.51%)	547 (8.22%)	<0.001	20 (0.56%)	61 (1.15%)	0.005	247 (2.12%)	675 (2.33%)	0.223	12 (0.2%)	49 (0.58%)	0.001
ICU mortality																		
Death, n (%)	1,819 (6.7%)	3,092 (6.1%)	<0.001	114 (8.67%)	69 (4.8%)	<0.001	425 (9.8%)	695 (10.44%)	0.293	36 (1%)	56 (1.06%)	0.886	1,064 (9.2%)	2,025 (7%)	<0.001	180 (2.95%)	247 (2.93%)	0.979

Data are presented as median and interquartile range or number and percentage of patients. *ICU* intensive care unit, *IQR* interquartile range, *SAPS II* Simplified Acute Physiology Score II; *PCI* percutaneous coronary intervention; *CABG* coronary artery bypass grafting, *NEMS* Nine Equivalents of Nursing Manpower Use Score, *LOS* length-of-stay, *RRT* renal replacement therapy
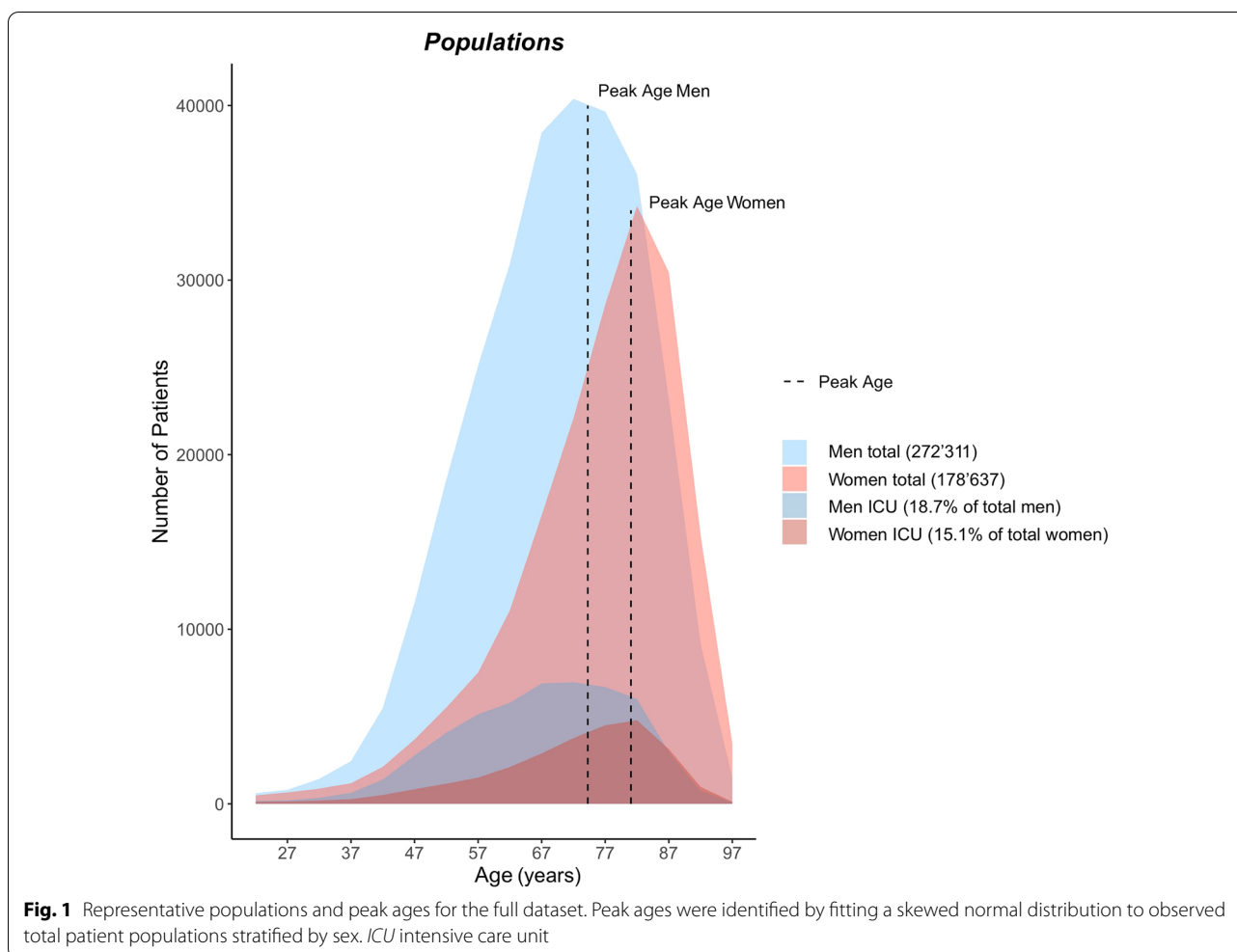
Fig. 1 Representative populations and peak ages for the full dataset. Peak ages were identified by fitting a skewed normal distribution to observed total patient populations stratified by sex. *ICU* intensive care unit

Table 2 Multivariate model of odds for ICU admission stratified by sex

	Odds ratio, women	Odds ratio, men	Odds ratio, women:men
Overall baseline	0.18 (0.18–0.18)	0.23 (0.23–0.23)	0.78 (0.76–0.79)
Pulmonary embolism	0.17 (0.16–0.18)	0.18 (0.17–0.19)	0.93 (0.85–1.02)
Heart failure	0.17 (0.16–0.18)	0.24 (0.23–0.25)	0.73 (0.69–0.77)
Rhythm disturbances	0.18 (0.17–0.19)	0.20 (0.19–0.20)	0.94 (0.88–1.00)
Acute coronary syndrome including cardiac arrest	0.40 (0.39–0.42)	0.37 (0.36–0.39)	1.08 (1.03–1.14)
Stroke	0.29 (0.28–0.31)	0.32 (0.31–0.33)	0.92 (0.87–0.98)
Age < 45 years	1.29 (1.20–1.39)	1.25 (1.18–1.31)	1.03 (0.94–1.13)
Age > 65 years	0.79 (0.75–0.82)	0.84 (0.82–0.86)	0.94 (0.89–0.99)

Bayesian multivariate binomial model adjusted for admission diagnosis, age categories (< 45 years, > 65 years) and proximity to peak age. Given are median odds and 95%-credible intervals. *ICU* intensive care unit

Secondary outcome measures
Advanced treatments

No significant sex differences were observed for NEMS in the overall population (Table 1) and in age-stratified subgroups (Supplementary Table S1). When individual components of the NEMS were analyzed, men had higher rates of mechanical ventilation (23.40 vs. 22.51% in women, $p = 0.005$, Table 1), while women

Fig. 2 Calculated total probability of admission for men and women for each age category. Age categories in proximity to peak age show the lowest overall probability of admission for both sexes. Bold lines represent median probabilities. Probability of ICU admission plotted for each age group (5 year intervals). *ICU* intensive care unit
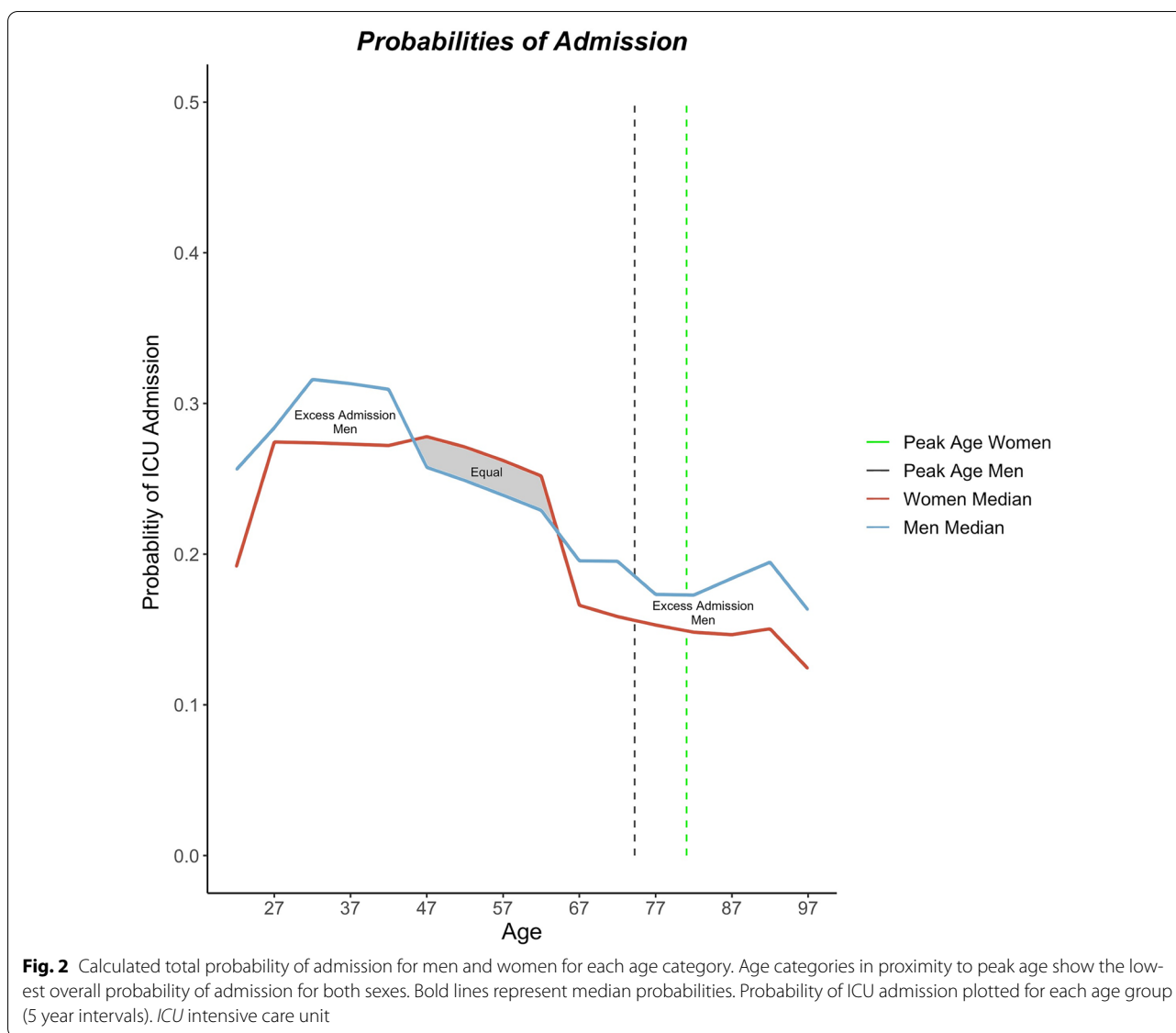
more often received non-invasive respiratory support (73.50 vs. 71.74% in men, $p < 0.001$, Table 1). Men had a greater use of vasoactive substances (12.68 vs. 11.77% in women, $p < 0.001$ for multiple vasoactives, Table 1) and a higher rate of renal replacement therapy (RRT, 2.68 vs. 2.02%, $p < 0.001$, Table 1). When stratified by age, women < 45 years had higher rates of mechanical ventilation (25.25 vs. 21.02% in men, $p = 0.004$), received more often multiple vasoactives (14.71 vs. 11.41% in men, $p = 0.004$) and RRT (4.25 vs. 2.47% in men, $p = 0.003$) than men (Supplementary Table S1). An opposite trend was observed in women > 65 years with regard to these treatments ($p < 0.001$, Supplementary Table S1).

Amongst patients with an acute coronary syndrome, 21,845 patients underwent percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG). Significantly more men than women underwent PCI (53.97 vs. 43.73%, $p < 0.001$, Table 1) or CABG (2.07 vs. 3.04%, $p < 0.001$, Table 1). This was also true when the study sample was stratified by age categories, with gender differences being most pronounced in the younger age group < 45 years (PCI: 13.56 vs. 33.38% in men, $p < 0.001$, Supplementary Table 1).

ICU mortality

Frequentist statistics revealed that ICU mortality was 6.7% in women and 6.1% in men ($p < 0.001$, Table 1). Women < 45 years and women aged 45–65 years died more often during ICU stay than men in the same age category (< 45 years: 7.03 vs. 5.30%, $p = 0.039$ and

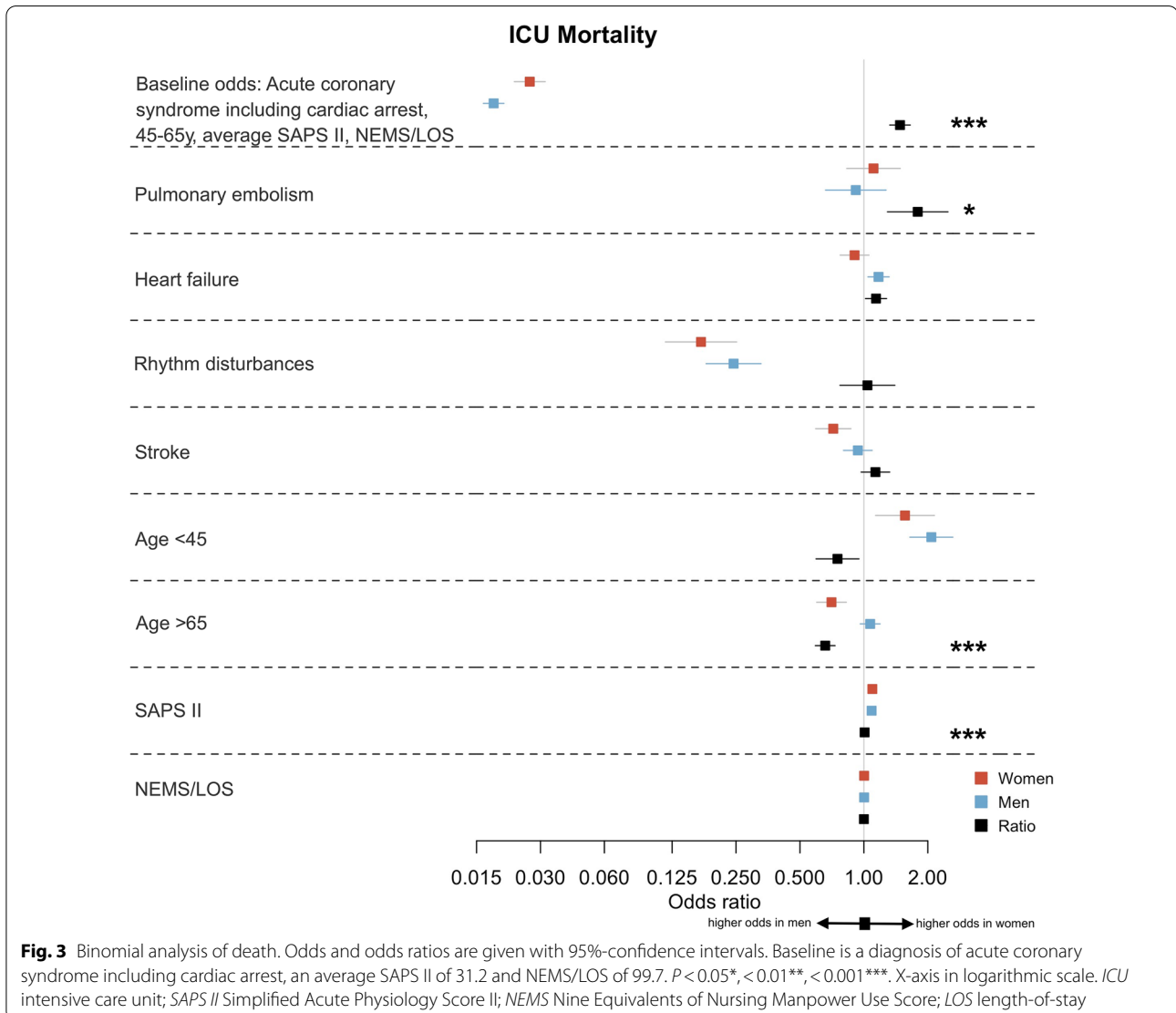45–65 years: 6.23 vs. 4.04%, $p < 0.001$, Supplementary Table S1). In contrast, in individuals > 65 years, ICU mortality was lower in women as compared to men in the same age category (6.86 vs. 7.35%; $p = 0.039$). Binomial logistic regression of the probability of all-cause death during ICU stay using unscaled covariates (diagnoses, age < 45 years, age > 65 years, SAPS II, NEMS / LOS) showed a significantly higher mortality in women with an acute coronary syndrome [OR 1.479 (1.21–1.81), $p < 0.001$, Fig. 3, Supplementary Table S4] or pulmonary embolism [OR 1.793 (1.11–2.90), $p < 0.05$, Fig. 3, Supplementary Table S4], as compared to men, while mortality for heart failure, rhythm disturbance, and stroke did not differ significantly between sexes (Fig. 3, Supplementary Table S4). In both sexes, a higher SAPS II was associated with a higher ICU mortality [women 1.096 (1.09–1.10),

$p < 0.001$ and men 1.088 (1.085–1.090), $p < 0.001$, Fig. 3, Supplementary Table S4], but the association between increased SAPS II and the risk of death was significantly stronger in women as compared to men [OR 1.008 (1.004–1.012), $p < 0.001$, Fig. 3, Supplementary Table S4].

Discussion

Our nationwide analysis in 450,948 patients with cardio- and neurovascular diseases shows that women in the upper and lower extremes of age are the demographic groups most affected by inequalities in ICU care.

Recent studies report an increasing incidence and mortality rate of CVD in younger women [7–10]. Mechanisms and robust data explaining the excess risk for cardiovascular mortality in younger women are

Fig. 3 Binomial analysis of death. Odds and odds ratios are given with 95%-confidence intervals. Baseline is a diagnosis of acute coronary syndrome including cardiac arrest, an average SAPS II of 31.2 and NEMS/LOS of 99.7. $P < 0.05^*, < 0.01^{**}, < 0.001^{***}$. X-axis in logarithmic scale. *ICU* intensive care unit; *SAPS II* Simplified Acute Physiology Score II; *NEMS* Nine Equivalents of Nursing Manpower Use Score; *LOS* length-of-stay

currently lacking, but data from the VIRGO study indicate that younger women have a worse overall health status than younger men [28]. In line with these data, young women < 45 years were more severely ill than men of similar age in our study. More severe illness usually requires a higher level of medical care. However, despite their more severe illness, younger women in our study were not admitted more frequently to the ICU than younger men. Instead, the probability to receive ICU care was similar in younger women and men. Unfortunately, current data are insufficient to clarify the extent to which such inequalities originate from sex differences in pathophysiology (e.g., presentation of symptoms), risk stratification (diagnostic bias), less aggressive treatment preferences by younger women or underuse of resources.

Age > 65 years was associated with a significantly lower probability of ICU admission in women as compared to men. The reason for this gender disparity remains elusive. Although social networks, family support as well as triage decisions are known to be important predictors for ICU admissions, recent studies have demonstrated that these variables were not associated with the male predominance amongst the elderly ICU population [11, 13, 14]. Recent data on treatment limitations derived from the same database show that women were more likely to have a documented patient decree upon ICU admission [29]. Accordingly, limitation decisions were more frequent in women, despite their less severe illness. This observation is consistent with previous studies reporting that female sex was an independent predictor of treatment limitation decisions in patients with sepsis [30, 31]. Accordingly, women or their surrogates had less aggressive treatment preferences in previous studies [32, 33]. Thus, the higher frequency of advanced directives in elderly women might impact the decision process of ICU admission, resulting in a selection bias. In addition, there is extreme variability in how health care providers influence end-of-life decisions [34]. Hence, there is urgent need to evaluate whether there is an unconscious bias in how critically ill elderly women and men are assessed and whether their wishes are (mis)perceived.

Our findings are consistent with previous studies derived from smaller and more heterogenous populations demonstrating a male predominance in ICU hospital admissions [11–15, 17]. We now extend the existing literature by showing that women hospitalized for neuro- and cardiovascular diseases were significantly older than men across all conditions. The largest sex difference in age was observed in patients presenting with an acute coronary syndrome, with a larger age gap between men and women being seen in the ICU population as compared to the general ward population. Accordingly,

women presenting with an acute coronary syndrome had higher estimates of SAPS II and encountered an excess ICU mortality as compared to men in our study. However, it is notable that women with acute coronary syndrome were the only female subgroup in our study that had a higher likelihood to be admitted to the ICU than their male counterparts. The latter might be indicative of the growing attention that has been paid to health disparities in women presenting with acute coronary syndrome [8, 35]. Nevertheless, consistent with published literature, we also observed that women with an acute coronary syndrome underwent less often life-saving invasive procedures including percutaneous coronary interventions or coronary artery bypass grafting. The fact that women with CVD receive less evidence-based treatment than men was first described in 1991 and was named the'Yentl Syndrome' [36]. Our data indicate that health care inequalities between men and women persist in contemporary practice and emphasize the need to identify barriers for the underuse of advanced treatment options in critically ill women. Indeed, while there is increasing awareness for sex and gender differences in the cardiovascular field, gender disparities in intensive care medicine are still a widely neglected topic.

Multivariate linear regression models showed higher estimates for SAPS II in women admitted to the ICUs as compared to men, independent of diagnoses. In addition, the association between increased SAPS II and the risk of death was significantly stronger in women as compared to men indicating that more severe illness in women had a greater impact on mortality than in men. Although the influence of sex on the SAPS II score's ability to predict outcome was not specifically tested in our study, our data suggest that the SAPS II performs different in women and men. A similar observation has previously been reported for the sequential organ failure assessment (SOFA) score [37]. The fact that these prediction tools perform different in men and women is not surprising, given that none of these scores includes sex as a variable. In cardiovascular patients, the outcome predictive value of ICU scores related to sex was only explored in one recent study. In this report, the performance of currently used ICU-based risk stratification systems in predicting in-hospital mortality was limited in both women and men, especially in those subgroups of disease with the highest mortality [38]. Given the overall higher ICU mortality observed in women in our cohort, our limited knowledge regarding the influence of sex and sex-specific variables on the predictive value of ICU-based risk prediction tools is particularly remarkable. Future studies will have to assess whether sex changes how the other variables in SAPS II account for total risk estimation.

Some limitations to this study should be pointed out. First, our study is retrospective and observational, and does not provide information on underling causal mechanisms. Second, data on in- and out-of-hospital mortality were not available in our dataset. Hence, the question whether gender imbalances in ICU admission have altered these endpoints cannot be answered by our study. Third, information on patient demographics and health status prior to admission was limited in our study sample. Hence, we cannot rule out potential confounding by variables (e.g., distribution of pre-existing comorbidities and chronic diseases in different age categories, patient frailty or socio-economic variables) not accounted for in our statistical models. Fourth, SAPS II was only available as the overall score, precluding a more informative analysis as compared to the use of SAPS II subitems. Fifths, given that information on mechanical ventilation, hemodialysis and vasoactive support is included in the NEMS, the latter was used as an estimate of disease severity, although it was originally developed as a predictor for the burden of nursing care. Sixth, our dataset was dichotomized in patients being admitted to the ICU or normal ward. Patients being admitted to intermediate care units were not included in the ICU dataset which might limit the generalizability of our findings. Nevertheless, ICU mortality observed in our study is comparable with previously reported data [39] thereby indicating that our dataset is representative of a typical and contemporary ICU population. Seventh, data for cardiac arrest and acute coronary syndrome were aggregated in our study sample leading to a slightly higher overall mortality in this subgroup of patients as compared to previous studies [40].

Intensive care is expensive and demand for ICU resources often exceeds supply. Our data suggest that women, in particular young women, have to present with more severe illness to receive equal treatment as men. Thus, intensivists and emergency physicians making triage decisions should carefully reassess whether critically ill young women are at risk to fail receiving the care they need. Addressing gender biases in triage algorithms and local protocols will help to ensure equal application of intensive therapy.

While our study is limited by the number of available variables from the registries, our findings may serve as a catalyst for further research on sex disparities in the provision of ICU care. Future studies will have to identify biological and social factors influencing the decision to withhold or withdraw intensive care in women. Prospective studies delivering more detailed information on pre-admission health status are needed to confirm our findings. Finally, further education is needed to raise awareness for gender inequalities in intensive care in both healthcare professionals and patients.

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Data availability

Data are available from the University Hospital Basel Institutional Data Access for researchers who meet the criteria for access to confidential data.

Declarations

Conflicts of interest
CG has received speakers' fees from Sanofi Genzyme, travel support from Siemens Healthineers, and research support from the Novartis Foundation, Switzerland, and Bayer Pharmaceuticals. The Department of Nuclear Medicine, University Hospital Zurich, holds a research contract with GE Healthcare.

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