ICU

MANAGEMENT & PRACTICE

INTENSIVE CARE - EMERGENCY MEDICINE - ANAESTHESIOLOGY

VOLUME 21 - ISSUE 4 - 2021

Gender in the ICU

04

9 771377 756005

FRESENIUS
MEDICAL CARE

Xenios‘ virtual ICU

Join us at ISICEM 2021

August 31st – September 3rd 2021

- Experience our **virtual ICU**
- Take a short guided tour and learn more about our **ECLS products and therapies** directly on a VV ECMO patient case

Register at ISICEM congress website!

End of 2016, Xenios became a part of Fresenius Medical Care, the world’s leading provider of products and services for people with chronic kidney failure.
Head office: Fresenius Medical Care Deutschland GmbH · 61346 Bad Homburg v. d. H. · Germany · Phone: +49 (0) 6172-609-0
www.freseniusmedicalcare.com

Gender in the ICU

Gender inequity in critical care medicine remains a pressing issue as the representation of women and minorities continues to be lowest in this specialty. Women continue to be underrepresented in leadership roles and senior positions. Whether it is overall compensation, lucrative opportunities, recipients of research funding, lead authors and editors, or presence at medical conferences, men continue to outnumber women.

Despite significant debate and focus on gender equity and diversity, a significant gender gap still exists in the field of critical care medicine. It is time to change societal ideas about the roles of men and women, and opportunities for women and people of colour must be enhanced so that they too can succeed in this specialty. Issues like workplace harassment and discrimination from both colleagues and patients must be addressed, and preventive and supportive strategies that promote and facilitate diversity in the workplace must be implemented.

At the same time, it is also important to consider gender-related outcome differences among critically ill patients. Most clinical trials in critical care focus on the overall long-term outcome of critically ill patients as a whole but ignore outcome differences that may be associated with gender. There is evidence to show that males tend to consume more ICU resources and have longer ICU stays compared to women. Mortality and survival among men and women also tend to be significantly different because of gender-related factors. There is thus a need to consider gender as an important variable when evaluating ICU admission, patient assessment, ICU referral, diagnosis, treatment and follow-up.

In this issue, our contributors discuss **Gender in the ICU.** Francesca Rubulotta and Antonio Artigas look at gender, bias and equality through the lens of the COVID-19 crisis and highlight the importance of developing best practices for the post-pandemic future. Raphael Bruno, Bernhard Wernly, Bertrand Guidet, Antonio Artigas, Hans Flaatten and Christian Jung talk about gender differences in elderly critically ill patients and emphasise using gender-specific management strategies to reduce gender-specific outcomes.

Sheila Myatra and Francesca Rubulotta discuss the devastating impact of the COVID-19 pandemic on women and communities of colour and the need for diversity among healthcare workers and public health leaders. Sharon Einav and Anne-Sophie Bouthors highlight the impact of gender on the severity of illness, impact and outcomes of coronavirus disease and, in particular, the treatment of pregnant women with COVID-19.

Alexandre Lopez, Ines Lakbar, and Marc Leone discuss how sex is an important determinant in the trajectory of patients developing critical illness and why it should be considered an important variable for personalised care in the ICU. Shahla Siddiqui provides an overview of gender inequity in critical care medicine, barriers to women's progress and possible solutions.

In our Matrix section, Yeow Chan offers a personal observation and reflection on how to handle a chronic ventilator user and offers suggestions to smoothen the sojourn of the next chronic ventilator user through an ICU while Shahla Siddiqui, Margaret Hayes, and Todd Sarge present an ethical analysis of the pros and cons of having family members present at the death of a COVID-19 positive ICU patient and framework that can be used in future surges.

As always, if you would like to get in touch, please email JLVincent@icu-management.org.

Jean-Louis Vincent

Jean-Louis Vincent
Editor-in-Chief
ICU Management & Practice
Professor
Department of Intensive Care
Erasme Hospital
Université libre de Bruxelles
Brussels, Belgium

JLVincent@icu-management.org

ICU_Management

IN EVERY ISSUE

COVER STORY


ISICEM
we care
intensively
40th
ISICEM
INTERNATIONAL
SYMPOSIUM
ON INTENSIVE CARE
& EMERGENCY MEDICINE
AUG 31-SEPT 3, 2021
SQUARE - BRUSSELS
CONVENTION CENTER
FIND US : ISICEM
YouTube
ISICEM.ORG
Hôpital
Erasme
ULB

MATRIX

MANAGEMENT

DIGICONF

ISICEM 2021 Lunch Satellite Symposium

Post-Cardiac Surgery: **Management of POAF and Vasoplegic Shock**

DATE AND TIME: Tuesday, August 31, 2021 at 12:30 – 13:30 CET

ROOM: Studio Room

MODERATOR: Prof. Philip J. Devereaux *(CAN)*

PROGRAM:

Catecholamine refractory hypotension in vasoplegic shock
(20 mins) – Prof. Johann Knotzer *(AT)*

Landiolol for POAF management after cardiac surgery
(20 mins) – Prof. Fabio Guarracino *(IT)*

Landiolol for the prevention of POAF: a systematic review and meta-analysis
(10 mins) – Dr. Teresa Cafaro *(CAN)*

Q&A (10 mins)

Follow via

LIVE STREAM

SEV_02_072021_INT

www.aoporphan.com

AOP ORPHAN
FOCUS ON RARE DISEASES

Diversity and Equality During COVID-19: The World Series

Looking at gender, bias and equality through the lens of the COVID-19 crisis and its potential for broad and lasting effects and addressing how this unprecedented situation can be a chance for interaction, learning and the development of best practices, such as developing work structures that could be continued in our post-pandemic future.

Francesca Rubulotta
Honorary Clinical Lecturer and Consultant in Anaesthesia and Intensive Care Medicine
Imperial College
London, UK

frubulotta@hotmail.com

@frubulotta

Antonio Artigas
Intensive Care Medicine Department CIBER Enfermedades
Respiratorias Corporación Sanitaria
Universitaria Parc Tauli Autonomous University of Barcelona
Sabadell, Spain

aartigas@tauli.cat

Epidemiological findings, outcome data, and socio-economical global concerns, among other factors, compel us to write this world series on diversity and equality during the COVID-19 pandemic. The number of male patients infected with and dying from COVID-19 during the first wave was perceived to be higher compared to women. Yet this data is not universally confirmed and there may have been further differences during the first and the second wave of the pandemic (Wernly et al. 2020; Jung et al. 2021; Ibarz et al. 2020). As a matter of fact, a study of patients >70 years of age admitted during the first wave of COVID-19 to 138 ICUs from 28 countries included 1346 patients (28% females). Mean age was 75 years and overall survival was 59% for women. Frailty was present in 41% of all patients and this was associated with a higher mortality. Frailty in females was present in 39% (Wernly et al. 2020; Jung et al. 2021; Ibarz et al. 2020). In the very old critically ill patient group (the "VIP") sex study (no COVID-19 and >80 years admitted to ICU) male sex was associated with adverse 30-day mortality but not with ICU mortality (Jung et al. 2021; Ibarz et al. 2020).

Authors of this world series sought answers from the VIP collaboration to understand the impact of frailty in the ICU population short-term outcome. The statement that men suffered a worse outcome then women might be simply a matter of perception. It should therefore not be relied upon as fact when deciding on resource allocation, triage, life expectancy, or prognostication. This issue will address the contradicting data and the preliminary evidence to highlight whether COVID-19 affected genders differently when it comes to infection risks and infection outcomes.

Data reported in the United Kingdom (U.K.) showed that while black and minority ethnic people make up only 14% of the U.K.'s population, they account for 35% of all coronavirus patients admitted to the intensive care unit (ICU). The U.K. government has commenced an inquiry to assess the triggers behind this disproportionate impact of coronavirus on minorities. Similarly, Black Lives Matter (BLM) has raised several concerns regarding the care and outcomes of COVID-19 patients in the US (Wernly et al. 2020; Klein et al. 2020). The most obvious reason for a potential difference in the mortality rate is the gender and ethnicity related risk (Klein et al. 2020; Lokken et al. 2021).

Similarly, there are several concerns related to pregnancy and vertical transmission to neonates. Among these concerns are the fact that there is a lacuna when it comes to the effect of medications given to treat COVID -19 during pregnancy. This lack of adequate clinical data extends to the use of vaccines during pregnancy or among those planning for pregnancy. As a matter of fact, vaccination has not been advised for pregnant women or for women planning to get pregnant within two months of vaccination. Of course, this lack of definitive knowledge has a major impact on the life of young women or young couples.

There have been arguments put forward that the COVID-19 economical global crisis has affected women and men differently. This hypothesis has been validated by the fact that more women were made redundant compared to men in 2020. ICU staff, with additional caring responsibilities, such as educating children and caring for the elderly or for sick or vulnerable relatives, suffered the most in general.

The world faces an economic crisis that is likely to impact research funding opportunities for a long time. For one example, there is already concern about reduced income for universities. For another, there is a high risk that research and development in the private sector will be severely constrained. Since many women are already disadvantaged when it comes to career development and funding opportunities, this poses

the question: will women and other disadvantaged groups be disproportionately affected by these cuts? Experience shows that when resources are limited, powerful groups are likely to strengthen their position, which could increase bias. Indeed, a participant described how during a recent grant application process the applicant asked if the submission deadline could be extended due to increased childcare responsibilities. The grant administrators refused to allow the extension arguing that the proposal did not require travel or lab access and would therefore not be affected by the pandemic. Other funding bodies have been more understanding of the wider impacts of COVID-19 and have extended submission deadlines for all applicants.

This special issue will therefore look at gender, bias and equality through the lens of the COVID-19 crisis and its potential for broad and lasting effects. How is the pandemic's peak, sickness, quarantine and economic shutdowns affecting our perceptions of equality? How are they challenging our preconceptions of what are reasonable expectations for frontline workers - especially those with caring responsibilities?

The Gender in the ICU issue will address how this unprecedented situation can be a chance for interaction, learning and the development of best practices, such as developing work structures that could be continued in our post-pandemic future.

> **"the COVID-19 pandemic provides us with a unique, even if unwelcome, opportunity to press the "reset button", which will either reduce or exacerbat the inequality amongst disadvantaged groups"**

Authors have noted significant issues for the future of intensive care medicine (ICM) due to the drop in the number of medical students selecting ICM or any frontline discipline for their future career. This has recently been discussed among international women in intensive and critical care foundation (iWIN) and results are available following the link www.iwinideal.com.

History teaches that pandemics are a time to regroup and reflect. The COVID-19 pandemic provides us with a unique, even if unwelcome, opportunity to press the "reset button", which will either reduce or exacerbate the inequality amongst disadvantaged groups, in particular for low-income individuals.

Once the pandemic is over, what will be the new normal? Adaptations developed during the current pandemic hold the potential to help overcome or reinforce disadvantages that are rooted in bias. Ways to address all these issues are illustrated in the articles featured in this issue.

Conflict of Interest

None. ■

References

Ibarz M, Boumendill A, Haas LEM et al. (2020) Sepsis at ICU admission does not decrease 30 days survival in very old patients: a post-hoc analysis of the VIP1 multinational cohort study. Annals Intensive Care, 10(1):56.

Jung C, Flaatten H, Fjølner J et al on behalf of the COVIP study group (2021) The impact of frailty on survival in elderly intensive care patients with COVID-19– the COVIP study. Critical Care 25, 149.

Klein SL, Dhakal S, Ursin RL, Deshpande S, Sandberg K, Mauvais-Jarvis F (2020) Biological sex impacts COVID-19 outcomes. PLoS Pathog, 16(6):e1008570.

Lokken EM, Huebner EM, Taylor GG et al. (2021) COVID-19 in Pregnancy Collaborative. Disease severity, pregnancy outcomes, and maternal deaths among pregnant patients with severe acute respiratory syndrome coronavirus 2 infection in Washington State. Am J Obstet Gynecol., 225(1):77.e1-77.e14.

Wernly B, Bruno RR, Kelm M et al. (2020) Sex-specific outcome disparities in very old patients admitted to intensive care medicine: a propensity matched analysis. Scientific reports, 10, 18671.

Raphael Romano Bruno
Department of Cardiology, Pulmonology and Angiology
University Hospital
Düsseldorf, Germany

raphael.bruno@med.uni-duesseldorf.de

Bernhard Wernly
Department of Cardiology
Paracelsus Medical University Salzburg
Austria

bernhard@wernly.net
BernhardWernly

Bertrand Guidet
Assistance Publique Hôpitaux de Paris
Hôpital Saint-Antoine service de réanimation médicale
Paris, France

bertrand.guidet@aphp.fr

Male Sex - An Independent Risk Factor for Mortality in Very Old Intensive Care Patients With Respiratory Failure

Among 1,841 very old ICU patients with respiratory failure, although women had higher age and frailty, males had higher 30-day mortality assessed one month after ICU admission. Particularly in light of the ongoing pandemic, male patients appear to be at significantly higher risk for worse outcomes than females.

Introduction

Demographic change does not stop at the intensive care unit (ICU). Among all ages, the very old ICU patients (VIP) are a fast-expanding subgroup (Flaatten et al. 2017a). For Europe, approximately 24.4 million people older than 85 years in 2040 are expected. But this development is not limited to Europe; it has been assumed that worldwide the percentage of patients older than 60 years will rise from approximately 12% in 2013 to 21% in 2050 (Leblanc et al. 2017). This demographic shift already has an impact on the admission rates of VIP in ICU in the past decade (Ihra et al. 2012). This observation has potential major impact on hospital, ethical issues, and the health economy. VIPs are generally patients at risk; large prospective trials found a 30-day-mortality of 42% (de Lange et al. 2019). Within this special group of VIPs, gender differences in treatment outcomes have been reported for many medical conditions (Schiele et al. 2011). However, in this particularly vulnerable high-risk population of ICU patients, the available evidence is heterogeneous (Schoeneberg et al. 2013; Park et al. 2018). Male and female ICU patients differ in baseline characteristics, predisposition to disease, and these differences may influence outcomes (Tibullo and Esquinas 2019; Cillóniz et al. 2019). In very old septic VIPs male sex was an independent negative predictor of prognosis (Cillóniz et al. 2019; Martin et al. 2003). In contrast, female sex was identified as a risk factor for discontinuation or refusal of further ICU treatment (Block et al. 2019), although elderly women have a significantly higher survival after ICU stay than men (Hollinger et al. 2019). A recently published retrospective analysis of 17,146 ICU patients with sepsis found no clinically relevant sex-specific mortality differences (Wernly et al. 2020a). However, in another study of 7,555 very old intensive care patients, male sex was an independent risk factor for an adverse 30-day-mortality but not ICU-mortality (Wernley et al. 2020b).

Currently, it is unclear whether these observations also apply to patients with respiratory failure. This subgroup analysis uses data from two recent large, multinational studies of VIPs to compare male and female patients with regards to crude unadjusted and adjusted baseline characteristics and outcomes (Guidet et al. 2019; Flaatten et al. 2017b; D'Agonstino 2007; Guidet et al. 2020).

Methods

VIP1 and VIP2 were prospective, multicentre studies (ID: NTC03134807, NCT03370692) that recruited very old intensive care patients. VIPs were defined as patients admitted to an ICU and being 80 years or older. The recruitment process differed slightly between the two studies: For VIP1, each participating ICU could include either consecutive patients for three months or the first 20 consecutive patients fulfilling the inclusion criteria (all patients 80 years of age or older). Thus, data were collected between October 2016 and February 2017. For VIP2, VIPs were included from May 2018 to May 2019. In both studies, all experimental protocols were approved by the local institutional and/or licensing committees. Informed consent was obtained from all subjects if not omitted by the ethics vote. This post-hoc analysis of these two prospective trials examines all patients who

Hans Flaatten
Department of Clinical Medicine
University of Bergen
Department of Anaesthesia and Intensive Care
Haukeland University Hospital
Bergen, Norway

hans.flaatten@uib.no

Antonio Artigas
Department of Intensive Care Medicine
CIBER Enfermedades Respiratorias,
Corporacion Sanitaria Universitaria Parc Tauli
Autonomous University of Barcelona
Sabadell, Spain

aartigas@tauli.cat

Christian Jung
Division of Cardiology, Pulmonology, and
Vascular Medicine
University Duesseldorf
Dusseldorf, Germany

christian.jung@med.uni-duesseldorf.de

CjungMD

were admitted for respiratory failure. The primary endpoint of this study was 30-day-mortality. Frailty was assessed by CFS as described previously (Rockwood et al. 2005; Jorm and Jacomb 1989; Katz 1983). Continuous data points are expressed as median ± interquartile range depending on the distribution. Differences between independent groups were calculated using the Mann-Whitney U-test. Categorical data are expressed as numbers (percentage). Chi-square test was applied to calculate differences. Univariable and multivariable logistic regression analysis was performed to assess associations with mortality. Odds ratios (OR) and adjusted odds ratios (aOR) with respective 95% confidence intervals (CI) were calculated. All tests were two-sided, and a p-value of <0.05 was considered statistically significant. Stata 16 was used for all statistical analyses.

Results

A subgroup of 1,841 patients with respiratory failure (938 male, 903 female) was included. Patient characteristics are summarised in **Table 1.** In the cohort, the proportion of nonagenarians was significantly greater among women. The mean age was also significantly lower (83±5 years for males versus 84±4 for females, p<0.001). When frailty was used as a binary marker (CFS > 4), significantly more women than men (43.1% in males versus 51.6% in females, respectively, p>0.001) could be classified as frail. Accordingly, the mean CFS was higher in females (4±3 for males, and 5±3 in males, respectively, <0.001). There was no difference in the use of invasive ventilation (47.3% in males versus 46.1% in females, respectively, p=0.602), and vasoactive drugs (44.7% versus 41.2%, p=0.124). Only very few patients needed renal replacement therapy without any difference between both groups (7.7% in males and 7.5% in females, respectively, p=0.887). We found no difference between men and women in the limitation of life sustaining therapy.

	MALE	FEMALE	p
Invasive Ventilation (yes, n (%))	468 (47.3)	436 (46.1)	0.602
Vasoactive Drugs (yes, n (%))	442 (44.7)	390 (41.2)	0.124
Renal replacement therapy (yes, n (%))	76 (7.7)	71 (7.5)	0.887
Frailty (yes, n (%))	426 (43.1)	487 (51.6)	<0.001
Nonagenarians (yes, n (%))	58 (5.9)	100 (10.6)	<0.001
Any limitation of life sustaining therapy, n (%))	345 (35.1)	357 (37.8)	0.209
Age [years]	83 (5)	84 (4)	<0.001
CFS	4 (3)	5 (3)	<0.001
SOFA	6 (5)	6 (5)	0.0076

Table 1. Baseline characteristics in the cohort, male versus female patients
CFS – Clinical Frailty Scale; SOFA - Sepsis-related organ failure assessment.

SV Series

Upgrade

Ventilator

All for Pro

Mindray introduces a major upgrade to our popular SV Series turbine-based ventilator family. The upgrade features the release of the new SV300 Pro ventilator, which allows smooth transitional use on all levels of patient acuity and in multiple care settings with its intra-hospital transport friendly designs.

The SV Series ventilator family include four models, SV800, SV600, SV300 Pro, SV300, which bring Mindray's state-of-the-art functions and technologies to confront difficult clinical challenges in respiratory care.

Preventive

Prevent cross-infection and ventilator-associated pneumonia.

Protective

Help achieve individualized **lung protective** strategy.

Perceptive

See more and do more by smartly detecting and adapting to the ever-changing conditions of the patient.

Meet the SV Series Ventilators

https://www.mindray.com/en/productlist/Ventilators.html#SV_Series?

mindray

30-day-mortality was significantly higher in males (43% vs. 35%; OR 1.16 95% CI 1.06-1.26; p<0.001) in univariate analysis (**Figure 1**). The association between male sex and increased mortality remained after multivariable adjustment for age, SOFA, and frailty (aOR 1.18 95% CI 1.07-1.29; p=0.001).

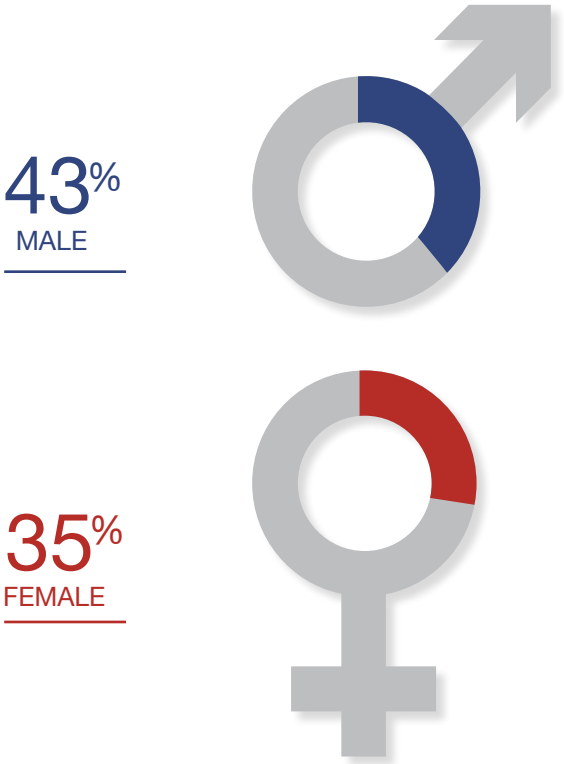


Figure 1. Comparison of 30-day-mortality (male and female patients)

Discussion

Male sex is an independent risk factor for mortality in very old intensive care patients with respiratory failure. Our previously published results also show different results depending on the subgroup and collective analysed (Wernly et al. 2020a; Wernly et al. 2020b). Thus, based on current scientific evidence, it might be speculated that the gender influence on mortality manifests itself primarily in elderly men with respiratory failure. It should be noted that not all types of respiratory failure have an infectious aetiology. This analysis shows that elderly male patients with respiratory insufficiency have a significantly worse prognosis than women, regardless of aetiology.

In general, data on gender differences in ICU patients are controversial. In the total cohort, we found male sex to be an independent risk factor for an adverse 30-day-mortality in very old intensive care patients (Wernly et al. 2020b). Our current results are in line with Cillóniz et al. (2019) who analysed 1,238 very old intensive care patients with community-acquired pneumonia. Men were significantly more likely to develop septic courses in this cohort, and male sex was an independent predictor of this in this context. However, in a large retrospective analysis of septic adult ICU patients of all ages, no gender difference was demonstrated (Wernly et al. 2020a). Accordingly, no gender difference was observed in a large cohort study on 25,998 patients without age-restriction for illness-adjusted mortality (Valentin et al. 2003).

> **"there should be an awareness that there are gender differences - especially in elderly critically ill patients that affect outcome"**

It is well known from the literature that women and men are treated differently in the ICU. For example, Block et al. (2019) performed a registry study and used data from the Swedish Intensive Care Registry from 2014 to 2016. They analysed 97,095 patients and found that being female resulted in an increased risk for a treatment limitation of life sustaining therapy (OR 1.18; CI 1.13- 1.23). However, in the present sub-study from the VIP-trials in VIPs with respiratory failure, we could not observe this effect. If these gender differences do exist, the cause remains unclear and needs further exploration. Various explanatory models exist. For example, socioeconomic factors might influence outcomes (Ski et al. 2014). In addition, depending on the genesis of respiratory failure, there also appear to be significant pathophysiological-biochemical differences between the sexes which became especially apparent during the current SARS-CoV-2 pandemic.

It is known that when men are infected with viruses, they have increased susceptibility, different early pathogenesis, and a different balance in immune response and tissue consequences (Scully et al. 2020). It has been observed early that severity of the COVID-19 disease, outcome as well as antibody titers differed (Klein et al. 2020a). In SARS-CoV-2, there exist mechanistic differences between genders including in the expression and activity of angiotensin-converting enzyme 2 (ACE2) as well as in antiviral immunity (Klein et al. 2020b). In mice, it has been described that males are more susceptible to SARS-CoV compared to age-matched female mice. In these *in vivo* studies, male mice consecutively evidenced higher virus titers, resulting in more vascular leakage, alveolar oedema, and more inflammatory migration of monocytes, macrophages, and neutrophils. Interestingly, these gender-specific effects increased with advancing age, but decreased when female mice received ovariectomy or were treated with an oestrogen receptor antagonist (Channappanavar et al. 2017). In fact, several important mediators of the immune response such as monocytes, macrophages, and neutrophils express surface oestrogen receptors. The activation of these receptors leads to an enhanced production of interferon I and III, resulting in a reduced immune response, increased immune tolerance and antibody production (Mauvais-Jarvis et al. 2020; Suba 2020).

In the human disease course, this might explain why females with severe COVID-19 evidence lower inflammatory biomarkers compared to men (Mussini et al. 2021; Qin et al. 2020). Another centrally involved protein is transmembrane serine protease 2 (TMPRSS2). Together with other proteins, TMPRSS2 plays a crucial role in cell entry of coronaviruses. In fact, the

viral surface spike SARS-CoV-2 protein penetrates host cells. TMPRSS2 splits the viral spike protein, which increases viral attachment to cell membranes (Hoffman et al. 2020). Under physiologic conditions, TMPRSS2 is upregulated by androgenic hormones and is primarily expressed in prostate secretory epithelial cells (Afshari et al. 2020). At least for coronaviruses, these gender differences appear to have implications resulting in an increased viral uptake in men (Qiao et al. 2020). Another possible pathogenesis leading to a milder course of respiratory failure in women compared with men appears to be Mas-receptor. *In vitro*, oestrogen increases the Mas-receptor expression leading to an attenuated endothelial leakage. *In vivo*, ovariectomy resulted in a decreased Mas-receptor expression and increased pulmonary damage (Erfinanda et al. 2021). Some gender differences in the immunomodulation are additionally dependent on the ageing process [immunoageing] (Gebhard et al. 2020).

These observations may be relevant in the context of currently tested immunomodulatory therapeutic approaches in critically ill COVID-19 patients. In a recent multicentre study, COVID-19 increased the risk of ICU-acquired bloodstream infections. This was possibly attributed to the increased use of anakinra and tocilizumab. Thus, the use of these drugs might be deleterious in elderly COVID-19 patients (Buetti et al. 2021).

Hence, our findings of differences in outcome in elderly patients with respiratory failure was already present before the existence of the SARS-CoV-2 pandemic. This needs further exploration but especially attention during the treatment of ICU patients. However, these findings became even more up-to-date in COVID-19. Currently, a global prospective observational study in 346 ICUs in 43 countries is investigating the outcome of very elderly patients infected with COVID-19 (Jung et al. 2021). We expect this study to provide deeper insights into this topic (NCT04321265, www.vipstudy.org).

In sum of these findings, there should be an awareness that there are gender differences - especially in elderly critically ill patients that affect outcome.

Conclusion

In very old ICU patients with respiratory failure, females evidence higher age and frailty, but male sex is an independent predictor of one month mortality. Particularly considering the ongoing pandemic, gender-specific management both during and after an ICU stay might reduce gender-specific outcomes.

Conflict of Interest

The authors declare that they have no competing interests.

Financial Disclosure Statement

No (industry) sponsorship has been received for this investigator-initiated study. ■

References

Afshari A, Janfeshan S, Yaghobi R et al. (2020) Covid-19 pathogenesis in prostatic cancer and TMPRSS2-ERG regulatory genetic pathway. Infect Genet Evol, 88: 104669.

Block L, Petzold M, Syrous AN et al. (2019) Age, SAPS 3 and female sex are associated with decisions to withdraw or withhold intensive care. Acta Anaesthesiol Scand, 63: 1210-1215.

Buetti N, Ruckly S, de Montmollin E et al. (2021) COVID-19 increased the risk of ICU-acquired bloodstream infections: a case-cohort study from the multicentric OUTCOMEREA network. Intensive Care Med.

Channappanavar R, Fett C, Mack M et al. (2017) Sex-Based Differences in Susceptibility to Severe Acute Respiratory Syndrome Coronavirus Infection. J Immunol, 198: 4046-4053.

Cillóniz C, Dominedo C, Ielpo A et al. (2019) Risk and Prognostic Factors in Very Old Patients with Sepsis Secondary to Community-Acquired Pneumonia. J Clin Med, 8: 961.

D' Agostino RB Jr. (2007) Propensity scores in cardiovascular research. Circulation, 115: 2340-2343.

de Lange DW, Brinkman S, Flaatten H et al. (2019) Cumulative Prognostic Score Predicting Mortality in Patients Older Than 80 Years Admitted to the ICU. J Am Geriatr Soc, 67: 1263-1267.

Erfinanda L, Ravindran K, Kohse F et al. (2021 Oestrogen-mediated upregulation of the Mas receptor contributes to sex differences in acute lung injury and lung vascular barrier regulation. Eur Respir J, 57.

Flaatten H, de Lange DW, Artigas A et al. (2017a) The status of intensive care medicine research and a future agenda for very old patients in the ICU. Intensive Care Med, 43: 1319-1328.

Flaatten H, De Lange DW, Morandi A et al. (2017b) The impact of frailty on ICU and 30-day mortality and the level of care in very elderly patients (>/= 80 years). Intensive Care Med, 43: 1820-1828.

Gebhard C, Regitz-Zagrosek V et al. (2020) Impact of sex and gender on COVID-19 outcomes in Europe. Biol Sex Differ, 11: 29.

Guidet B, de Lange DW, Boumendil A et al. (2020) The contribution of frailty, cognition, activity of daily life and comorbidities on outcome in acutely admitted patients over 80 years in European ICUs: the VIP2 study. Intensive Care Med, 46: 57-69.

Hoffmann M, Kleine-Weber H, Schroeder S et al. (2020) SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. Cell, 181: 271-280 e278.

Hollinger A, Gayat E, Feliot E et al. (2019) Gender and survival of critically ill patients: results from the FROG-ICU study. Ann Intensive Care, 9: 43.

Ihra GC, Lehberger J, Hochrieser H et al. (2012) Development of demographics and outcome of very old critically ill patients admitted to intensive care units. Intensive Care Med, 38: 620-626.

Jorm AF, Jacomb PA (1989) The Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE): socio-demographic correlates, reliability, validity and some norms. Psychol Med, 19: 1015-1022.

Jung C, Bruno RR, Wernly B et al. (2021) Inhibitors of the renin-angiotensin-aldosterone system and COVID-19 in critically ill elderly patients. Eur Heart J Cardiovasc Pharmacother, 7: 76-77.

Katz S (1983) Assessing self-maintenance: activities of daily living, mobility, and instrumental activities of daily living. J Am Geriatr Soc, 31: 721-727.

Klein SL, Pekosz A, Park HS et al. (2020a) Sex, age, and hospitalization drive antibody responses in a COVID-19 convalescent plasma donor population. J Clin Invest, 130: 6141-6150.

Klein SL, Dhakal S, Ursin RL et al. (2020b) Biological sex impacts COVID-19 outcomes. PLoS Pathog, 16: e1008570.

Leblanc G, Boumendil A, Guidet B (2017) Ten things to know about critically ill elderly patients. Intensive Care Med, 43: 217-219.

Martin GS, Mannino DM, Eaton S et al. (2003) The epidemiology of sepsis in the United States from 1979 through 2000. N Engl J Med, 348: 1546-1554.

Mauvais-Jarvis F, Klein SL, Levin ER (2020) Estradiol, Progesterone, Immunomodulation, and COVID-19 Outcomes. Endocrinology, 161.

Mussini C, Cozzi-Lepri A, Menozzi M et al. (2021) Better prognosis in females with severe COVID-19 pneumonia: possible role of inflammation as potential mediator. Clin Microbiol Infect, S1198-1743X(1120)30765-30765.

For full references, please email editorial@icu-management.org or visit https://iii.hm/1b4a

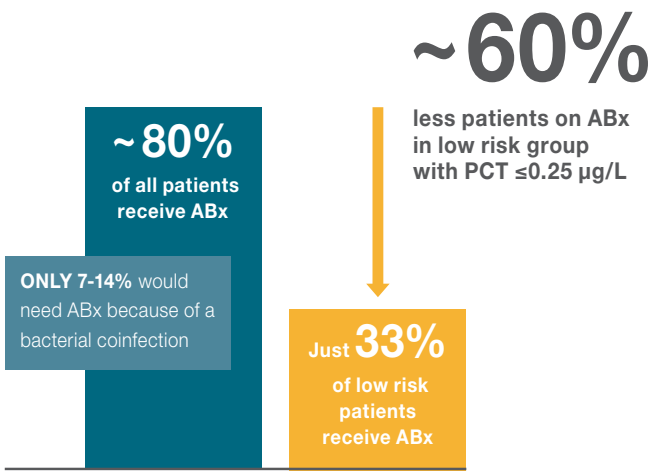
thermo scientific

Avoid unnecessary antibiotic usage in COVID-19 patients

Find out more at **thermoscientific.com/procalcitonin**

Not all products are CE marked or have 510(k) clearance for sale in the U.S. Availability of products in each country depends on local regulatory marketing authorization status.

ThermoFisher SCIENTIFIC



Antibiotic treatment of COVID-19 patients[1]

Procalcitonin (PCT) algorithm facilitates safe reduction of antibiotic exposure

Decision on antibiotic treatment of COVID-19 patients based on application of **Thermo Scientific™ B·R·A·H·M·S PCT™ LRTI cut-off 0.25 µg/L** together with clinical assessment of low risk for bacterial coinfection resulted in

- Lower number of AB-treated patients
- Reduced antibiotic exposure
- No negative impact on the outcome[1]

Reference: 1. Williams EJ et al., preprint doi: https://doi.org/10.1101/2020.06.29.20136572 posted July 2, 2020.

Working in the Pandemic and Preserving Diversity

Sheila Nainan Myatra
Professor
Department of Anaesthesiology, Critical Care and Pain
Tata Memorial Hospital
Homi Bhabha National Institute
Mumbai, India

sheila150@hotmail.com
@SheilaMyatra

Francesca Rubulotta
Associate Professor
Department of Anaesthesia Faculty of Medicine
McGill University
Chief of the Critical Care Program
McGill University Health Centre
Quebec, Canada

Honorary Senior Lecturer
Imperial College London

Intensive Care Unit
Charing Cross Hospital
London, UK

frubulotta@hotmail.com
@frubulotta

The devastating impact of the COVID-19 pandemic on women and communities of colour and the need for diversity among healthcare workers and public health leaders.

Introduction

Diversity is the condition of having many different elements. These may include people with different opinions, backgrounds (degrees and social experience), religious beliefs, political beliefs, sexual orientations, heritage, and life experience. The definition of diversity is broad and it is really difficult to outline in practical term what is diverse in a specific context. As a matter of fact, diversity might change based on the context and location. Diversity is very important in the clinical setting to support both patients and healthcare professionals. Diversity facilitates better communication (Laveist and Nura 2002), improves patient satisfaction with care (Walker et al. 2012), provides good practice in underserved areas, and care for minority, poor, and uninsured patients.

In academic settings, work produced by diverse research teams may be of higher quality and more impactful than that by less diverse teams (Valentine and Collins 2015; Cooper et al. 2003). Doctors and nurses from different origins and beliefs have diverse perspectives, better understanding of minorities, increased creativity and productivity which all together improves the clinical decision-making process (Walker et al. 2012; Valentine and Collins 2015; Cooper et al. 2003).

Despite longstanding efforts, diversifying the biomedical research workforce remains an elusive goal, and large sectors of the population remain underrepresented. Certain racial/ethnic groups are represented only minimally in biomedical research: of the nation's scientific research faculty positions, 4% are African American, 4% are Hispanic, 0.2% are Native American, and 0.1% are Hawaiian/Pacific Islander (nsf.gov/statistics/2015/nsf15311/tables/pdf/tab9-30.pdf). There has been little increase in representation of these groups over the last decades, despite them collectively being the most rapidly growing portion of the population, predicted collectively to comprise the majority of the population of the U.S. by 2050.

A number of factors have been shown to contribute to the lack of diversity in science, technology, engineering, and mathematics (STEM) careers in general and in biomedical research. In particular among them are limited infrastructure and research experiences (National Academy of Sciences, National Academy of Engineering, and Institute of Medicine 2011; McGee and Krulwich 2012).

The COVID-19 pandemic has negatively impacted this aspect, leading to even less diversity in the workplace (Wernly et al. 2020; Klein et al. 2020; Lokken et al. 2020; CoBaTriCE Collaboration 2009; CoBaTriCE Collaboration 2011; Lane-Fall et al. 2017; Rubulotta et al. 2020). ICU staff, with additional caring responsibilities, such as educating children and caring for the elderly or for sick or vulnerable relatives, suffered the most during these years. Since many women are already disadvantaged when it comes to career development and funding opportunities, COVID-19 challenges pose the question: will women and other disadvantaged groups be disproportionately, affected by the pandemic?

The United Kingdom (U.K.) ethnic minority people make up only 14% of the U.K.'s population, but they account for 35% of all coronavirus patients admitted to the intensive care unit (ICU). The U.K. government has commenced an inquiry to assess the triggers behind this disproportionate impact of coronavirus on minorities. Similarly, Black Lives Matter (BLM) has raised several concerns regarding the care and outcomes of COVID-19 patients in the U.S. (Wernly et al. 2020; Klein et al. 2020). The most obvious reason for a potential difference in the mortality rate is the gender and ethnicity related risk (Klein et al. 2020; Lokken et al. 2020).

Why Should We Preserve Diversity?

Patient-centred communication is key for rating the quality of care according to a recent survey including 252 adults (142 African-American patients and 110 white patients) receiving care from 31 physicians (Cooper et al. 2003). African-American patients who visit physicians of the same race rate their medical visits as more satisfying and participatory compared to those who see physicians of other races. Increasing ethnic diversity among physicians may be the most direct strategy to improve health care experiences for patients of ethnic minority groups (Cooper et al. 2003).

The National Health System (NHS) in the U.K. has published a report in 2018 suggesting that diversity is the new prescription for the NHS (Fanshawe 2018). This volume "is designed to open up a new approach to diversity that makes it central to an NHS trust because it delivers a dividend to patients and staff – in terms of health, and clinical and personal success - in line with the NHS

Constitution: the NHS *"is there to improve our health and wellbeing, supporting us to keep mentally and physically well, to get better when we are ill and, when we cannot fully recover, to stay as well as we can to the end of our lives"* (Fanshawe 2018).

Diversity in the ICU gives a different perspective, better understanding, increased creativity, productivity and this translates into better patient care. Administrators, critical care societies and individuals should work toward promoting and facilitating diversity. This is even more needed following the COVID-19 challenges. According to nursing literature, being exposed to cultural diversity including living in multicultural countries, speaking a second language and visiting other countries may influence the development of key competencies and soft skills. Therefore, programmes which facilitate multicultural clinical practice are strongly recommended. Soft skills generated by working in a multicultural environment are required also for doctors. Traditional medical education has been criticised for its failure to ensure that all graduates are adequately prepared for independent work at the bedside (CoBaTriCE Collaboration 2009). Learning and assessing soft skills is challenging. However major effort has been made to address human factor variables, enhance communication/collaboration in clinical practice through improvements in leadership, management, situational awareness and decision-making. Communication, professionalism, as well as negotiation and team working are all needed skills (CoBaTriCE Collaboration 2009; CoBaTriCE Collaboration 2011). Finally, reflective learning and patient or family-oriented feedback are becoming crucial in medical education and these are particularly important in a stressful environment such as the ICU.

Since 2020, ICU physicians are increas-ingly faced with providing care to a multicultural society complicated by the COVID-19 pandemic. Ensuring safe and quality healthcare for all patients requires physicians to understand how each patient's sociocultural background affects his or her health beliefs and behaviour. In the light of the pandemic, physicians and healthcare systems will need to respond to factors that put racial and ethnic minority groups at a greater risk of getting sick and dying. The conditions where people work and live affect underlying health conditions and also make it more difficult to access needed medical care and tests. This can be complicated by literacy and language barriers along with socioeconomic barriers, such as lack of insurance, lack of access to transportation, and even immigration status. Dr Denis Nash, an epidemiologist and the executive director of the City University of New York Institute for Implementation Science in Population Health (ISPH) said *"we live in a country where your wealth and your socioeconomic status is a big determinant for how healthy you are, how long you will live and whether you live with a higher burden of disease while you're alive"*.

The BMA recommended junior doctors to campaign for better work-life balance (Rubulotta et al. 2020). This was before the pandemic and it has created concerns for starting residency in jobs requiring long shifts such as intensive care medicine. In particular, published data comparing annual trends in the representation of women and racial/ethnic groups across critical care fellowship types between 2004 and 2014 show underrepresentation of women and racial/ethnic minorities in critical care programmes (Lane-Fall et al. 2017). There are concerns about reduced income for universities and decreased number of women interested in critical care medicine as a discipline.

> **"published data comparing annual trends in the representation of women and racial/ethnic groups across critical care fellowship types show underrepresentation of women and racial/ethnic minorities in critical care programmes"**

Experience shows that when resources are limited, powerful groups are likely to strengthen their position, which could increase bias. There is a high risk that research and development in the private sector will be severely constrained. Data from several countries have shown that women are underrepresented in the field of intensive care medicine (Rubulotta et al. 2020). The reasons for the persistent gender imbalance in critical care medicine have been studied extensively over recent years (Vincent et al. 2021). In a survey of 283 American anaesthesiologists who were asked to make a collaborative decision, Helzer and colleagues found that when treatment advice was delivered by an inexperienced physician, participants reported relying significantly more on the advice of a man versus a woman. Of interest, although participants' reliance on advice from a woman physician was a function of her experience, reliance on advice from a man physician was not (Helzer et al. 2020).

More importantly, these biases are reinforced through repetitive exposure to stereotypical images seen in social and work groups and in the media, and by the frequent underrepresentation of women speakers at international meetings and in leadership positions. Diversity is crucial to improve these aspects and enhance better team working and problem solving. Parsons Leigh and colleagues described institutional (lack of flexibility and limited job prospects) and interpersonal (bias against women) factors as key drivers of the gender gap in critical care medicine (Leigh et al. 2019). Organisations can promote gender equity and enhance inclusion by developing effective, appropriate and sustainable gender mainstreaming strategies that can be implemented, monitored, compared and updated as required. The diversity report in the U.K. has shown that at the top of British businesses, of the 297 CEOs CFOs and Chairs of the FTSE 100 companies, there are, at the time of writing, more men called John, David and Andrew than women or minorities (Fanshawe 2018). In the House of Commons on 28th October 2015, the Shadow Business Secretary quoted the latest annual survey of 10,000 top business leaders by executive recruiter Green Park: *"it shows that the number of visible ethnic minority CEOs is falling, and the number of all-white Boards is increasing, at a time when 14% of our population is from a black or minority ethnic background"* (Fanshawe 2018). Institutional changes should be broad and include different fields of science, research, economy and so on.

How Should We Preserve Diversity?

Employers need to change their approach to recruitment and promotion. To achieve greater diversity leaders have to recognise that people make assessments driven by preferences. Awareness does not change behaviour because the only way to change it

is to design the processes differently. In the words of the most persuasive researcher on the subject, Professor Iris Bohnet of Harvard University, Co-Chair of the Behavioural Insights Group and Professor of Public Policy at the Kennedy School of Government, *"we need to create situations where our biased minds can make unbiased choices. If we want to appoint the best person for the job, we need to design processes where we can eliminate as much noise from our own biases and preferences as possible so we really can appoint the best"* (Fanshawe 2018). Iris Bohnet's latest book, What Works – Gender Equality by Design, starts with a famous example. In the 1970s, only 5% of musicians in U.S. orchestras were women and today they are 35%. To achieve this result, they put a curtain between the auditioning players and the people who were listening. That way those choosing could just listen to how the candidates played. When they then selected the best players, they were not all, as before, white and male, but much more mixed (Fanshawe 2018).

We all have preferences. Our intentions may not be to exclude, but the data tell us that this is exactly what is happening. We need to face up to it and make appropriate changes (Fanshawe 2018). Future research should focus on identifying gaps and best strategies to improve diversity in the ICU. We should identify psychological and social factors that mitigate individual and institutional barriers to workforce diversity (Rubulotta et al. 2020; Fanshawe 2018; Vincent et al. 2021). Trusts should develop a sustainable strategy to effectively disseminate and create more diversity within the nationwide scientific workforce.

> **"there is no possibility of ignoring the resources and energy that employing women and minorities could bring to the workforce structure"**

There is robust evidence suggesting in numerous industries that diversity is fundamental for maintaining a healthy and productive organisation. Women in particular have proven numerous times to bring innovation, equilibrium and balance in the working and production side. According to Prof Goffee and Jones from Harvard Business school *"the organization of your dreams… it's a company where individual differences are nurtured; information is not suppressed or spun; the company adds value to employees, rather than merely extracting it from them; the organization stands for something meaningful; the work itself is intrinsically rewarding; and there are no stupid rules"*. This is even more crucial after this pandemic. The workforce is limited, and emotionally and physically exhausted. There is no possibility of ignoring the resources and energy that employing women and minorities could bring to the workforce structure.

Conclusion

Diversity and code of conduct policies have been adopted by several critical care societies and the World Federation of Societies of Intensive and Critical Care Medicine. Widespread use of such policies will help eliminate inequity and enhance inclusion as well as develop needed soft skills. Acknowledging the existence of implicit and explicit biases is an essential first step. Several strategies need to be put in place by leaders, societies, industries and employers in general. The pandemic's devastating impact on communities of colour clarifies the need for diversity among healthcare workers and public health leaders. Intelligent measures such as having a diverse workforce and a commitment to progress in the quality of care, innovation and engagement of staff are vital.

Conflict of Interest

None. ■

References

CoBaTrICE Collaboration (2009) The educational environment for training in intensive care medicine: structures, processes, outcomes and challenges in the European region. Intensive Care Med, 35(9):1575-83.

CoBaTrICE Collaboration (2011) International standards from programmes of training in intensive care medicine in Europe Intensive Care Med, 37(3):385-93.

Cooper LA, Roter DL, Johnson RL et al. (2003) Patient-centered communication, ratings of care, and concordance of patient and physicians race. Ann Intern Med, 139: 907–915.

Fanshawe S (2018) Diversity is the new prescription for the NHS. Available from good-governance.org.uk. More information from diversitybydesign.co.uk.

Helzer EG, Myers CG, Fahim C et al. (2020) Gender bias in collaborative medical decision making: emergent evidence. Acad Med, 95:1524–1528.

Klein SL, Dhakal S, Rebecca L et al. (2020) Biological sex impacts COVID-19 outcomes. PLOS pathogens, 1008570.

Lane-Fall MB, Miano TA, Aysola J et al. (2017) Diversity in the emerging Critical Care Workforce: analysis of demographic trends in Critical Care Fellows from 2004 to 2014. Crit Care Med, 45(5): 822-27.

Laveist TA, Nuru A (2002) Is doctor-patient race concordance associated with greater satisfaction with care? J Health Soc Behav, 43:296–306.

Leigh JP, Grood C, Ahmed SB et al. (2019) Toward gender equity in critical care medicine: a qualitative study of perceived drivers, implications, and strategies. Crit Care Med, 47:e286–e291.

Lokken EM, Huebner EM, Taylor G et al. (2020) Disease Severity, pregnancy outcomes and maternal deaths among pregnant patients with SARS-CoV-2 infection in Washington State. American Journal of Obstetrics and Gynecology.

McGee R Jr, Saran S, Krulwich TA (2012) Diversity in the biomedical research workforce: Developing talent. Mt Sinai J Med, 79(3):397–411.

National Science Foundation (2013) Women, minorities, and persons with disabilities in science and engineering: Table 9 to 30. Available from nsf.gov/statistics/2015/nsf15311/tables/pdf/tab9-30.pdf

National Academy of Sciences, National Academy of Engineering, and Institute of Medicine. (2011). Expanding Underrepresented Minority Participation: America's Science and Technology Talent at the Crossroads. Washington, DC: The National Academies Press.

Rubulotta F, Mehta S, Leigh JP (2020) Intensive care medicine: reflections on the gender gap. ICU Management and Practice, 20(4):319-324.

Valantine HA, Collins FS (2015) National Institutes of health addresses the science of diversity. Proc Natl Acad Sci, 112:12240–12242.

Vincent JL, Juffermans NP, Burns K et al. (2021) Addressing gender imbalance in intensive care. Crit Care, 25, 147.

Walker KO, Moreno G, Grumbach K (2012) The association among specialty, race, ethnicity, and practice location among California physicians in diverse specialties. J Natl Med Assoc, 104:46–52.

Wernly B, Bruno RR, Kelm M. et al. (2020) Sex-specific outcome disparities in very old patients admitted to intensive care medicine: a propensity matched analysis. Sci Rep 10, 18671.

Make the most of your Servo-u

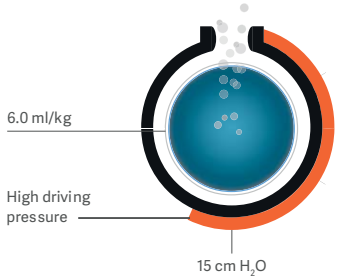
Servo-u is an investment both for now and for the future. The flexible, modular platform is always ready to adapt to your changing clinical needs, and our expert support is on hand every step of the way.

Servo-u is a platform that can grow with you and the ever changing needs of your patients. Our tools for personalized lung protection are all designed to help you continuously assess risk, monitor key variables, expedite intervention and improve patient-ventilator interaction.

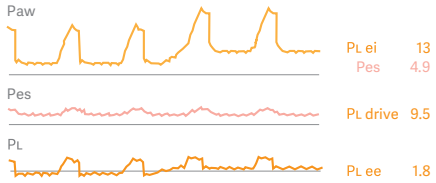
→ Click here for more information

www.getinge.com

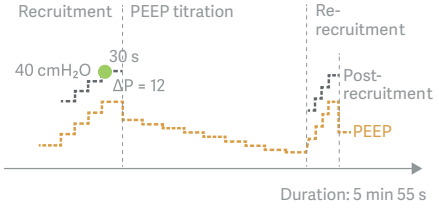
Servo Compass



Transpulmonary pressure monitoring



Auto SRM



GETINGE

Sharon Einav
General Intensive Care Unit
Shaare Zedek Medical Centre and Hebrew
University Faculty of Medicine
Jerusalem, Israel

einav_s@szmc.org.il

Anne-Sophie Bouthors
Anesthesia Intensive Care Unit
Jeanne de Flandre
Women Hospital
Academic Hospital
Lille, France

anne-sophie.bouthors@chru-lille.fr

Sex, Lies and COVID-19

An overview of the impact of gender on the severity of illness, impact and outcomes of COVID-19.

The human coronaviruses (HCoVs) include two alpha-CoVs (HCoV-229E and HCoV-NL63) and five beta-coronaviruses (HCoV-OC43, HCoV-HKU1, severe acute respiratory syndrome CoV [SARS-CoV], Middle East respiratory syndrome CoV [MERS-CoV], and most recently (β-CoV SARS-CoV-2). Early data relating to the severe acute respiratory Syndrome (SARS) epidemic (2002-2003) suggested that the case fatality rate of infected males is significantly higher than that of females (Karlsberg et al. 2004). However, as the SARS epidemic was contained, this finding was never pursued. More recent data regarding the Middle East Respiratory syndrome (MERS) coronavirus also suggests excess male mortality (Goggins 2004; Alghamdi et al. 2014). The current severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has been proposed to affect men and women differently.

Does It?

Between the first and second pandemic waves, the calculated global employment loss rates for women due to COVID-19 were estimated to be 1.8 times higher than those of men (5.7% vs. 3.1% respectively). Yet even when industry-mix effects were taken into consideration, survey data showed higher loss of employment among women than that expected. Before the pandemic, 46% of the United States workforce was comprised of women. The overall proportion of women among those losing their employment was expected to be 43% whereas unemployment data showed that women comprised 54% of those newly unemployed. Similarly, in India, 20% of the workforce before the pandemic were women. Their calculated proportion of employment loss was estimated at 17% while unemployment surveys showed they were actually 23%. The gendered nature of work across industries explains only one-fourth of the difference in employment loss rates for men and women. The lack of systemic progress to resolve societal barriers for women probably explains the rest (McKinsey Global Institute 2020). Gender-equality in society is strongly linked to gender equality in work. A typical example during the current pandemic is the availability of women versus men for work once the need for home nursery and schooling arose. So should women or men be staying at home?

In terms of disease infectivity, men were often overrepresented in early publications of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (Guan et al. 2020; Grasselli et al. 2020). This led to the misconception that men are more susceptible to infection with SARS-CoV-2 than women. More recent, sex-disaggregated data suggests there is probably no difference in disease infectivity. The Global Health 50/50 project reports almost equal global numbers of men and women having a confirmed diagnosis of infection with SARS-CoV-2 (i.e. based on laboratory testing) (https://globalhealth5050.org/the-sex-gender-and-covid-19-project/). This finding could easily be biased by differences in access to testing. Whether this is indeed the case remains unclear; reports from non-selective screening programmes are conflicted with some showing male predominance of varying proportions (Teherán et al. 2020; Stringhini et al. 2020) and some showing equal prevalence among men and women (Slot et al. 2020; Pollán et al. 2020).

With regards to disease severity and case-fatality rates, there have recently been several important findings. Although coronaviruses have been reported to cause respiratory, enteric, hepatic, and neurological diseases in various animal species, until recently beta-HcoVs were typically associated with self-limiting upper respiratory infections in immune-competent human hosts and occasional pneumonias in immune-compromised or older hosts (Letko 2020; Woo et al. 2005). The coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), seems to be an exception to this rule and in the clinical manifestations of this disease lies a real difference between men and women.

Results from observational studies almost consistently show overrepresentation of males among COVID-19 patients with severe disease, among COVID-19 intensive care unit admissions and among those who die (Penna et al. 2020; Gebhard et al. 2020). Two meta-analyses of observational studies strengthened this impression, showing that when compared to women, the unadjusted proportions of men presenting with severe disease, admitted to an intensive care unit and dying are all higher. At the time of this writing, no well conducted, sex-stratified analyses have been conducted with regards to these observed differences. Both meta-analyses also noted that adjusted analyses could not be conducted due to lack of data (Lakbar et al. 2020; Ortolan

et al. 2020). However, specifically among SARS-CoV-2 stroke patients, the modified Rankin Score of patients surviving to hospital discharge has been noted to be worse in male versus female patients even after adjustment (Trifan et al. 2020).

Several explanations have been put forward for the worse disease severity in males. The viral surface spike (S-) protein of SARS-CoV-2 enters host cells by binding to the ACE2 receptor. The transmembrane protease, serine 2 (TMPRSS2) splits the S-protein, which increases viral attachment to cell membranes (Hoffmann et al. 2020). Both ACE2 and TMPRSS2 have been proposed as modulators of the susceptibility of men and women to SARS-CoV2 (Penna et al. 2020).

ACE2 receptors are prevalent in lung cells and may also be found in the endothelium of blood vessels in the myocardium and brain. However, the receptor for ACE2 is primarily expressed in the testis (i.e. spermatogonia; Leydig and Sertoli cells). ACE2-positive spermatogonia express more genes associated with viral reproduction and transmission (Wang and Xu 2020). Male mice are more susceptible to SARS-CoV than age-matched females; they have higher virus titers, more vascular leakage and alveolar oedema and accumulate more inflammatory monocyte macrophages and neutrophils in the lungs and ultimately die more. These differences between male and female mice increased with advancing age and decreased when females underwent ovariectomy or were treated with an oestrogen receptor antagonist (Channappanavar et al. 2017). A protective effect of oestrogen receptor signalling may also be plausible with regards to SARS-CoV-2 as cell mediators of the immune response (i.e. monocytes, macrophages, neutrophils) express surface oestrogen receptors. This receptor mediates the production of type I and III interferon, thereby creating a state of decreased innate immune inflammatory response and increased immune tolerance and antibody production (Mauvais-Jarvis et al. 2020; Suba 2020). Indeed women with severe COVID-19 have been shown to have a lesser rise in inflammatory biomarkers (Mussini et al. 2020; Qin et al. 2020).

TMPRSS2 protein is highly expressed in prostate secretory epithelial cells, and its expression is dependent on androgen signals (Afshari et al. 2020). TMPRSS2 has been proposed to be involved in genetic susceptibility to H1N1 and A (H7N9) influenzas (Cheng et al. 2015.) and probably also plays a role in male susceptibility to SARS-CoV2 (Qiao et al. 2020).

> **"sex-disaggregated data suggests there is probably no difference in disease infectivity between genders"**

So What Happens During Pregnancy?

A cytokine-tolerant environment between mother and fetus prevents activation of natural killer cells against fetal cells. This environment is created by T-helper type 2 cells which mediate hormonal suppression of inflammatory cytokine production and cellular activation (Littauer and Skountzou 2018). The rise in oestrogen that accompanies pregnancy increases the T-helper type 2 cell response (Kourtis et al. 2014). At the same time, T-helper cells also moderate the humoral immune response to large extracellular pathogens via interleukin secretion.

Compared to pregnant women with no infection, those with symptomatic or asymptomatic SARS-CoV2 infection seem to have an increased rate of complications not during pregnancy, but after delivery (Prabhu et al. 2020). This preliminary observation suggests that the overall post-partum reduction in hormonal levels is accompanied by a parallel decrease in protection against SARS-CoV-2.

At the time of this writing, only four papers have compared the laboratory findings of pregnant women with and without COVID-19 and these have shown normal rather than elevated white blood cell counts in pregnant women with the disease (Areia and Mota-Pinto 2020). COVID-19 disease also seems to manifest similarly in pregnant and recently pregnant women and in the general population, i.e. fever, chills, cough, dyspnoea, headache, lethargy, joint or muscle pain, sore throat, diarrhoea, nausea and vomiting (Knight et al. 2020). Yet anxiety regarding disease susceptibility seems rife. Once diagnosed with clinical disease, the age-matched hospitalisation rate of women with COVID-19 is almost five times higher among those who are pregnant than among those who are not [31.5% versus 5.8%] (Ellington et al. 2020).

Whether this concern is justified remains to be seen. Systematic review of the literature shows that 4% (95% CI 2%-7%) of pregnant and recently pregnant women attending or admitted to hospital for any reason and diagnosed as having suspected or confirmed COVID-19, were also admitted to an intensive care unit. Most of these women received invasive mechanical ventilation (3%, 95% CI 1%-5%) and almost one in eight also required extracorporeal mechanical oxygenation (ECMO) support (0.4%, 95% CI 0.1%-0.9%) (Allotey et al. 2020). Maternal deaths due to COVID-19 have also been described in developed (Knight et al. 2020; Ellington et al. 2020; Blitz et al. 2020) and developing (Hantoushzadeh et al. 2020; Takemoto et al. 2020) countries. Unfortunately pregnant women have been almost consistently excluded from COVID-19 trials (Einav et al. 2020). Therefore treatment for pregnant women with COVID-19 remains largely supportive. Steroids may be administered for either circulatory shock or the acute respiratory distress syndrome (ARDS). Anticoagulation is of particular importance as pregnancy is a hypercoagulable condition and there is no evidence for increased risk of bleeding even with full anticoagulation (Jacobson 2020; D'Souza et al. 2017). In advanced pregnancy with severe hypoxaemia, the advantages of caesarean delivery should be weighed against the potential risk of bleeding as support with EMCO may be required. In case ECMO is initiated after surgery, anticoagulation may be withheld for a limited period (Bideerman et al. 2017).

Whether the relation between SARS-CoV-2 infection and preterm birth and perinatal death is mediated by or coincidental to the higher rates of caesarean delivery and or pre-eclampsia remains to be elucidated (Di Mascio et al. 2020). At this time there is no clear evidence of placental infection or definitive vertical transmission

of SARS-CoV-2 (Edlow et al. 2020). However, fetal and neonatal outcomes may still potentially be affected by the indirect effects of prolonged maternal hypoxaemia and by placental transmission of inflammatory cytokines, particularly IL-6 which has been tied to neonatal neurodevelopment (Rudolph et al. 2018).

In conclusion, more women have become unemployed during the current pandemic. This trend is counterproductive as pathophysiological and epidemiological findings suggest that despite a similar susceptibility to SARS-CoV2 infection, women are less likely to suffer from severe COVID-19 disease. Pregnancy seems to be accompanied by an increased protective hormonal effect but regardless of disease severity there may be a higher likelihood of postnatal maternal complications. No vertical transmission of the disease to the fetus has been shown but severe maternal disease may expose the fetus to secondary adverse effects.

Take Home Messages

1. Between the first and second pandemic waves, the calculated global employment loss rates for women due to COVID-19 were estimated to be 1.8 times higher than those of men (5.7% vs. 3.1% respectively).
2. Sex-disaggregated data suggests there is probably no difference in disease infectivity between genders.
3. Compared to pregnant women with no infection, those with symptomatic or asymptomatic SARS-CoV-2 infection seem to have an increased rate of complications not during pregnancy, but after delivery.
4. No vertical transmission of the disease to the fetus has been shown but severe maternal disease may expose the fetus to secondary adverse effects.

Conflict of Interest

Sharon Einav is a member of the European Society of Intensive Care diversity task force. ■

References

Afshari A, Janfeshan S, Yaghobi R et al. (2020) COVID-19 pathogenesis in prostatic cancer and TMPRSS2-ERG regulatory genetic pathway. Infect Genet Evol, 88:104669.

Alghamdi IG, Hussain II, Almalki SS et al. (2014) The pattern of Middle East respiratory syndrome coronavirus in Saudi Arabia: a descriptive epidemiological analysis of data from the Saudi Ministry of Health. Int J Gen Med, 7:417-23.

Allotey J, Stallings E PregCOV-19 Living Systematic Review Consortium et al. (2020) Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. BMJ, 370:m3320.

Areia AL, Mota-Pinto A (2020) Can immunity during pregnancy influence SARS-CoV-2 infection? - A systematic review. J Reprod Immunol, 142:103215

Biderman P, Carmi U, Setton E et al. (2017) Maternal Salvage With Extracorporeal Life Support: Lessons Learned in a Single Center. Anesth Analg, 125(4):1275-1280.

Blitz MJ, Rochelson B, Minkoff H et al. (2020) Maternal mortality among women with coronavirus disease 2019 admitted to the intensive care unit. Am J Obstet Gynecol, 223(4):595-599.e5.

Channappanavar R, Fett C, Mack M et al. (2017) Sex-Based Differences in Susceptibility to Severe Acute Respiratory Syndrome Coronavirus Infection. J Immunol, 198(10):4046-4053.

Cheng Z, Zhou J, To KK et al. (2015) Identification of TMPRSS2 as a Susceptibility Gene for Severe 2009 Pandemic A(H1N1) Influenza and A(H7N9) Influenza. J Infect Dis, 212(8):1214-21.

COVID-19 and gender equality: Countering the regressive effects (2020) McKinsey & Company. Available from https://www.mckinsey.com/featured-insights/future-of-work/covid-19-and-gender-equality-countering-the-regressive-effects

Di Mascio D, Khalil A, Saccone G et al. (2020) Outcome of coronavirus spectrum infections (SARS, MERS, COVID-19) during pregnancy: a systematic review and meta-analysis. Am J Obstet Gynecol MFM, 2(2):100107.

D'Souza R, Ostro J, Shah PS et al. (2017) Anticoagulation for pregnant women with mechanical heart valves: a systematic review and meta-analysis. Eur Heart J, 38(19):1509-1516.

Edlow AG, Li JZ, Collier AY et al. (2020) Assessment of Maternal and Neonatal SARS-CoV-2 Viral Load, Transplacental Antibody Transfer, and Placental Pathology in Pregnancies During the COVID-19 Pandemic. JAMA Netw Open, 3(12):e2030455.

Einav S, Ippolito M, Cortegiani A (2020) Inclusion of pregnant women in clinical trials of COVID-19 therapies: what have we learned? Br J Anaesth, 125(3):e326-e328.

Ellington S, Strid P, Tong VT et al. (2020) Characteristics of Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status - United States, January 22-June 7, 2020. MMWR Morb Mortal Wkly Rep, 69(25):769-775.

Gebhard C, Regitz-Zagrosek V, Neuhauser HK et al. (2020) Impact of sex and gender on COVID-19 outcomes in Europe. Biol Sex Differ, 11(1):29.

Goggins W (2004) Re: "Do men have a higher case fatality rate of severe acute respiratory syndrome than women do?" Am J Epidemiol, 160(9):925-6.

Grasselli G, Zangrillo A, COVID-19 Lombardy ICU Network et al. (2020) Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. JAMA, 323(16):1574-1581.

Guan WJ, Ni ZY, Hu Y, China Medical Treatment Expert Group for COVID-19 et al. (2020) Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med, 382(18):1708-1720.

Hantoushzadeh S et al. (2020) Maternal death due to COVID-19. Am J Obstet Gynecol;223(1):109.e1-109.e16.

Hoffmann M, Kleine-Weber H, Schroeder S et al. (2020) SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. Cell, 181(2):271-280.e8.

Jacobson B, Rambiritch V, Paek D et al. (2020) Safety and Efficacy of Enoxaparin in Pregnancy: A Systematic Review and Meta-Analysis. Adv Ther, 37(1):27-40.

Karlberg J, Chong DS, Lai WY (2004) Do men have a higher case fatality rate of severe acute respiratory syndrome than women do? Am J Epidemiol, 159(3):229-31.

Knight M, Bunch K, UK Obstetric Surveillance System SARS-CoV-2 Infection in Pregnancy Collaborative Group et al. (2020) Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study. BMJ, 369:m2107.

Kourtis AP, Read JS, Jamieson DJ (2014) Pregnancy and infection. N Engl J Med, 370(23):2211-8.

Lakbar I, Luque-Paz D, Mege JL et al. (2020) COVID-19 gender susceptibility and outcomes: A systematic review. PLoS One, 15(11):e0241827.

Letko M, Marzi A, Munster V (2020) Functional assessment of cell entry and receptor usage for SARS-CoV-2 and other lineage B betacoronaviruses. Nat Microbiol, 5(4):562-569.

Littauer EQ, Skountzou I (2018) Hormonal Regulation of Physiology, Innate Immunity and Antibody Response to H1N1 Influenza Virus Infection During Pregnancy. Front Immunol, 9:2455.

For full references, please email editorial@icu-management.org or visit https://iii.hm/1b3e

STAT PROFILE Prime+®

Most Comprehensive Critical Care Analyzer for the ICU

Up to 23 tests including unique tests for:

iMg | Urea | Creat | ePV*

Maintenance-Free Cartridge Technology

Automated, True Liquid QC

Clot Block™ Protection

Test Menu:

pH, PCO_2, PO_2, Na, K, Cl, iCa, iMg, TCO_2, Glu, Lac, Urea (BUN), Creat, Hct, ePV, SO_2%, O_2Hb, COHb, MetHb, HHb, tHb, HbF,** tBil**

nova biomedical®

Nova Biomedical
novabiomedical.com
info@novabio.com

Scan to Learn More

*Estimated Plasma Volume
**Not available in the U.S.

Alexandre Lopez
Aix-Marseille University
Assistance Publique
Hôpitaux de Marseille
Department of Anesthesiology and Intensive Care Unit
Marseille, France

alexandre.lopez@ap-hm.fr

Ines Lakbar
Aix-Marseille University
Assistance Publique
Hôpitaux de Marseille
Department of Anesthesiology and Intensive Care Unit
Marseille, France

ines.lakbar@ap-hm.fr

Marc Leone
Aix-Marseille University
Assistance Publique
Hôpitaux de Marseille
Department of Anesthesiology and Intensive Care Unit
Marseille, France

marc.leone@ap-hm.fr

Sex in the Intensive Care

Sex interplays with the development of several diseases and syndromes, impacting differently the need for intensive care unit admission between men and women. All in all, men are more prone to develop critical illness than women, which explains their over-representation in the intensive care unit. On the other hand, treatments differ between men and women with more aggressive and tailored interventions in men than in women. In this article, we discuss these different issues for patients developing critical illnesses.

Introduction

Most diseases and syndromes are differently expressed in men and women. While women represent nearly 80% of cases of autoimmune disease, men are the most affected by cancer (Ortana et al. 2016; Cook et al. 2009). This sex dimorphism affects patients admitted to the intensive care unit (ICU). Indeed, males represent 60% of ICU patients (Samuelsson et al. 2015). The mechanisms underlying this unequal distribution are based on both sex as a biological entity determined by chromosomal, hormonal, and immunological differences, and gender as a social construct, resulting in disparities in co-morbidities and access to healthcare.

The incidence and severity of a given disease may vary according to the sex of patients, as recently observed during the Coronavirus-19 (COVID-19) pandemic, with men developing more severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pneumonia than women (Lakbar et al. 2020). The acknowledgment of sex dimorphism could therefore be considered as the first step in personalised management of ICU patients (Lakbar and Leone 2021). Here, we briefly overview the current literature on the topic to discuss sex differences in patients admitted to the ICU.

Definition

In 1955, the controversial sexologist John Money was the first to use the term "gender" to describe human characteristics and behaviours. This term opened a new field of scientific research. In the recent literature, sex refers to the set of morphological differences between males and females, including primary and secondary sexual characteristics, anatomical, biological and genetic specificities.

Epidemiology

Infectious diseases and sepsis

Sex dimorphism is reported in infectious diseases (Gay et al. 2021), which are among the most common diseases encountered in ICUs. Men are predominantly affected by both sepsis and septic shock.

A 24-hour point prevalence study collecting global data revealed that out of 15,202 patients, 54% had a suspected or known infection (Vincent et al. 2020). Men were more likely to develop infection than women with a mean annual relative risk (RR) of 1.28 (confidence interval 95%, (CI95) [1.24-1.32]) (Martin et al. 2003). Sex differences are reported for the release of inflammation mediators. In response to lipopolysaccharides (LPS), peripheral blood mononuclear cells from men produce more tumour necrosis factor (TNF) (Asai et al. 2001), and in patients with sepsis, men have higher serum TNF concentrations and lower interleukin (IL)-10 concentrations than women (Schröder et al. 1998). This hyper-responsiveness of male-derived cells to LPS was suggested as a potential mechanism whereby men are more susceptible to sepsis than women. In an experimental model of Coxiella burnetii infection, our group showed that only 14% of the modulated genes were sex-independent, and the remaining 86% were differentially expressed in males and females, underlying the interplay between sex and host response to infection (Textoris et al. 2010).

Over the last decade, large-scale studies reported a higher incidence of sepsis in men than women. The agents responsible for sepsis differ in men and women. Bacteraemia due to *Staphylococcus aureus* and *Pseudomonas aeruginosa* are more frequent in men than in women (Benfield et al. 2007; Al-Hasan et al. 2008). Conversely, 60% of *Escherichia coli* bacteraemia occur in women (Laupland et al. 2008).

In sepsis, the source of infection differs in men and women.

Respiratory tract is identified as source of infection in 36% of cases in men and 29% of cases in women (p<0.01), whereas the infection of genitourinary tract is predominant in women (35% vs. 27% for men, p<0.01) (Laupland et al. 2008). Anatomical differences partly explain these findings.

Non-infectious diseases and syndromes

Traumatic brain injury (TBI) is a public health concern. Epidemiological studies show that men have an increased relative risk to suffer a TBI compared with women in the general adult population of the United States until 75 years-old (Faul and Coronado 2015). Acute kidney injury (AKI) has a variable prevalence in ICU. In observational studies, sex affects directly the risk to develop AKI in the ICU patients. The risk was significantly higher in men than in women (OR 1.23; 95% CI [1.11-1.36]) (Neugarten and Golestaneh 2018). Among 25,998 patients (58% of men), the use of renal replacement therapy was significantly higher in men than in women (OR, 1.28; 95% CI [1.16-1.42] (Valentin et al. 2003). All in all, the female hormonal status probably protects against AKI. In a French nationwide cohort study, men represented 67.7% of patients developing acute respiratory distress syndrome (Papazian et al. 2021).

Surprisingly, while the incidence of these diseases or syndromes is sex-dependent, there was, in most conditions, no difference in mortality between both sexes. The FROG-ICU study was performed on 2,087 patients, including 726 women and 1261 men, in 19 hospitals in France and Belgium (Hollinger et al. 2019). A similar one-year mortality after ICU admission was found between men and women (34.9% vs. 37.9%, p=0.18). Same results were found regarding ICU mortality and 28-day mortality. This finding is not confirmed in specific syndromes like ARDS, an increased 90-day mortality of males being reported (OR 1.104 95% CI [1.014-1.200]) (Papazian et al. 2021). Besides biological data that explain the sex dimorphism in the incidence of critical illness according to sex, social behaviours are a cornerstone of these differences **(Figure 1).**

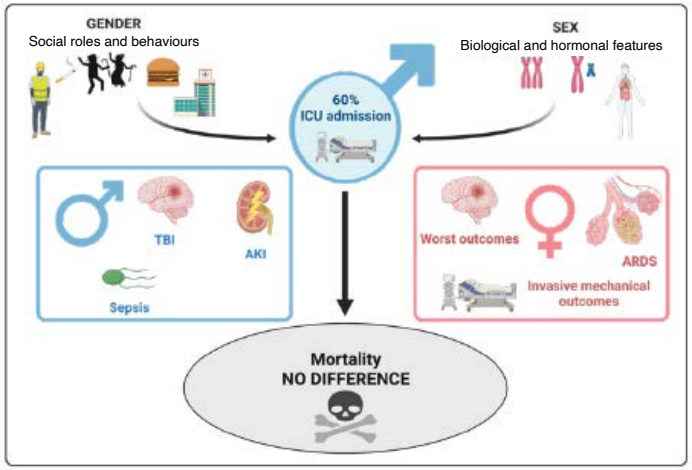


Figure 1. Sex differences in the ICU

Gender Behaviours

Differences in social behaviours, expressed as gender effect, may interfere with sex to highlight differences between men and women facing critical illness. As an example, differences in the prevalence of smoking between men and women could explain the increased risk of tobacco-associated respiratory diseases and infections in men than in women (Garrett et al. 2011).

Lifestyle is influenced by gender. In a population of 761 adolescents, young girls presented lower performance in physical exercise and physical and psychological wellbeing but higher vegetable consumption and greater satisfaction in educational context (Boraita et al. 2020). Such stereotypes could influence behaviours and affect susceptibility to infection.

Regarding access to healthcare, gender inequalities are persisting. The prevalence of perceived unmet healthcare is higher in women than in men. In 2019, the #LancetWomen movement was created to promote gender equality worldwide and highlight the inequality in science, medicine, and global health between men and women (Shannon et al. 2019). For patients with respiratory failure, a study showed that men had a higher probability of receiving mechanical ventilation (Schultz and Karagiannidis 2019). Inequity in the setting of ventilator parameters was also observed: being a woman is even a risk factor to receive an inappropriate and unsafe ventilation setting (Swart et al. 2021). Authors highlighted the need for a campaign "Save the life of Females in ICU".

Another concern is related to the design of randomised controlled trials. For safety concerns, they often exclude women of childbearing age. Hence, most drugs are essentially tested in men and are given to both men and women. In septic patients with tachycardia, a recent meta-analysis showed that beta-blocker use was associated with favourable outcomes (Hasegawa et al. 2021). However, in experimental murine models of sepsis, our group showed a sex-dimorphism of beta-receptors, suggesting that beta-blockers may be beneficial in septic males and deleterious in septic women (Mathieu et al. 2018; Tran et al. 2019). Thus, there is a need to refine our research criteria to test the drugs both in men and women.

Conclusion

Sex seems to be a major determinant in the trajectory of patients developing critical illness. Both biological and social factors play a role in this trajectory. Generally, male sex seems to be associated with an increased risk to develop severe forms of diseases mainly due to an inappropriate immune response. However, both the number and effects of interventions are unequally distributed between men and women, interplaying with outcomes. Considering sex as a critical variable should be recognised as one of the first steps of personalised medicine in the ICU.

Conflict of Interest

ML served as lecturer for MSD, Aspen and consultant for Amomed, Gilead. AL and IL do not have any conflict of interest. ■

References

Al-Hasan MN, Wilson JW, Lahr BD et al. (2008) Incidence of Pseudomonas aeruginosa bacteremia: A population-based study. Am J Med, 121(8):702-708.

For full references, please email editorial@icu-management.org or visit https://iii.hm/1bef

Shahla Siddiqui
Assistant Professor
Department of Anesthesia Critical Care and Pain Medicine
Beth Israel Deaconess
Medical Center
Harvard Medical School
Boston, USA

shahlasi@yahoo.com

Women in Critical Care

An overview of gender inequity in critical care medicine, why there is limited progress towards gender equity in this particular specialty, barriers to women's progress and possible solutions.

The United Nations Educational, Scientific and Cultural Organization have delineated the difference between two entities - equality and equity as "Gender equality, does not mean that women and men have to become the same, but that their rights, responsibilities, and opportunities will not depend on whether they were born male or female. Gender equity means fairness of treatment for men and women according to their respective needs. This may include equal treatment or treatment that is different, but which is considered equivalent in terms of **rights, benefits, obligations, and opportunities".**

Progress toward gender equality in the United States has slowed or stalled. Recent research on the gender differences in scientific careers shows that although almost 49% of high school graduates are women, only 11% occupy top academic positions as opposed to 89% of men showing the underrepresentation of women. Despite dramatic progress in moving toward gender equality between 1970 and 2018, in recent decades, change has declined. The slowdown on some indicators and stall on others suggests that further progress requires substantial institutional and cultural change. Progress may require increases in men's participation in household and care work, governmental provision of childcare, and adoption by employers of policies that reduce gender discrimination and help both men and women combine jobs with family care responsibilities.

Why Aren't We Making More Progress Towards Gender Equity?

Research shows that one reason may be that many leaders acknowledge that the bias exists in general but fail to recognise it in their daily workplace interactions. This "gender fatigue" means that people aren't motivated to make a change in their organisations. Through ethnographic studies and interviews across industries, the author identified several rationalisations leaders use to deny gender inequality. "First, they assume it happens elsewhere, at a competitor, for example, but not in their organisation. Second, they believe that gender inequality existed in the past but is no longer an issue. Third, they point to the initiatives to support women as evidence that inequality has been addressed. Last, when they do see incidents of discrimination, they reason that the situation had nothing to do with gender. *Until we stop denying inequality exists in our organisations, it will be impossible to make progress".*

While the number of women entering medical school now equals or surpasses the number of men, gender equity in medicine has not been achieved. Women continue to be underrepresented in leadership roles (e.g., deans, medical chairs) and senior faculty positions. In addition, women do not enter medical specialties as often as men, which can have important implications for the work environment, reimbursement, and the delivery of patient care. Compared with other medical specialties (e.g., anaesthesiology, dermatology, etc), critical care medicine (CCM) is a medical specialty with some of the lowest representation of women. While strategies to improve gender equity in critical care medicine exist in the published literature, efforts to comprehensively synthesise, prioritise and implement solutions have been limited.

CCM is not "gender-friendly" by design. This will have a major impact on the discipline given the increase in the number of female doctors. While there is an increase in females in critical care medicine, women continue to be underrepresented in roles such as full professors in academic critical care medicine (Mehta et al. 2018; Mehta et al. 2017; Parsons et al. 2019; Metaxa 2013), authors of scientific literature (Mehta et al. 2018; Metaxa 2013), speakers at international conferences (Mehta et al. 2018), editors in journals (Mehta et al. 2017; Parsons et al. 2019), members of scientific boards (Mehta et al. 2017; Metaxa 2013), entrepreneurs and CEO of start-ups (Kanze et al. 2017; Malmstrom et al. 2017), engineers and designers for medical devices (Kanze et al. 2017; Malmstrom et al. 2017), authors of guidelines (Metaxa 2013; Merman et al. 2018), and members task force panels (Mehta et al. 2018; Mehta et al. 2017; Parsons et al. 2019; Janssen et al. 2019). Participants unanimously described critical care medicine as a specialty practiced predominantly by men. Most women described experiences of being personally or professionally impacted by gender inequity in their group. Postulated drivers of the gender gap included institutional and interpersonal factors.

Barriers to Women's Progress

Female physicians continue to face myriad challenges in medicine ranging from implicit bias to gaps in payment and promotion to sexual harassment. Therefore, it is not surprising that although equal numbers of men and women now graduate from medical school, only a small fraction of female physicians become medical leaders. Currently, in the U.S., only 3% of healthcare CEOs are women, 6% are department chairs, 9% are division chiefs, and 3% are serving as chief medical officers. This is

despite women comprising 80% of the healthcare workforce and evidence that having women in upper management and on corporate boards is associated with improved financial performance and enhanced accountability.

The gender pay gap also varies from 34% to 50% among physicians. In a study by Chadwick et al. (2020), women's most important workplace concerns included work-life balance (64%), compensation (43%), combining parenthood and work (30%), gender equity (19%), career development (16%), relationships with colleagues and staff (16%), age discrimination (6%) and sexual harassment (1%).

Women are persistently underrepresented and the study of women's leadership is neglected or treated in a different way in leadership. "Women leaders' decision-making capacity and consequently their effectiveness as leaders, are judged based on conceptions about their motherly role, them being emotional and their physical attributes unrelated to their leader-ship capacity" (Sjoberg 2016). 'Gendered leadership' based on assumed group characteristics, spreads the weightage of "male and masculine characteristics, such as strength, power, autonomy, independence, and rationality, typically, while devaluing female and feminine characteristics, such as emotionality, passivity, dependence, marginalisation, and weakness". However, individual women (and men) experience 'gendering' and the processes by which gendering operate differently based on their diversity. Furthermore, men are associated with the public sphere (work politics and public life) and women are associated with the private sphere (motherhood, household, and the bedroom). These (mis)conceptions of gendered leadership associating good leadership with male characteristics and weak leadership with female characteristics are further reinforced through 'gender tropes' which signifies "gender norms and stereotypes which reinforce existing gendered leadership".

A Recent Survey on Women in CCM

A recent study by Siddiqui et al. (2021 - unpublished) reveals some important insights into the practice of critical care by anaesthesiologists, especially during the pandemic showing a high degree of stress and anxiety among anaesthesia trained intensivists. However, when these data were analysed by gender and age, it was found that women and younger respondents felt more anxiety symptoms. Also, there was strong evidence to suggest that women and younger physicians felt emphatical that bias and lack of diversity were present in CCM. This study provides new and telling information about the disparity of perception of anxiety, diversity, and bias within CCM by different demographics. This information can be used to address these issues of systemic bias and provide personalised avenues of burnout mitigation.

> **"critical care medicine is a specialty practiced predominantly by men .... women describe experiences of being personally or professionally impacted by gender inequity in their group"**

A Way Out

If programmes acknowledge gender fatigue and modify their behaviour, this opens the possibility of wider change within organisations. The goal is to create a culture where gender equality can be openly discussed without assigning blame or guilt, and instead, people at all levels of the organisation can be proactive about modifying their daily behaviours. According to Mehta et al. (2018), "critical care societies can establish diversity policies. Journals can publish the principles and methods of panel composition for professional document development. There should be publicly available metrics of women's representation on panels for definition documents, consensus statements, and practice guidelines. Gender parity policies can be incorporated into relevant bylaws within all areas of academic critical care. Training must be offered on diversity and unconscious bias for all critical care academics, particularly those in leadership positions". Until we stop denying inequality exists in our organisations and specialties, it will be impossible to make progress.

Conflict of Interest

None. ■

References

Chadwick AJ, Baruah R (2020) Gender disparity and implicit gender bias amongst doctors in intensive care medicine: A 'disease' we need to recognise and treat. J Intensive Care Soc, 21(1):12-17.

Janssen KT, Urbach HM, Ham KR et al. (2019) The gender gap in critical care task force participation. Lancet Respir Med, 7(7):566-567.

Kanze D, Huang L, Conley MA, Higgins ET (2017) Male and female entrepreneurs get asked different questions by VCs–and it affects how much funding they get. Harvard Business Review. Available from hbr.org/2017/06/male-and-female-entrepreneurs-get-asked-different-questions-by-vcs-and-it-affects-how-much-funding-they-get

Leigh JP, Grood C, Ahmed SB et al. (2019) Toward Gender Equity in Critical Care Medicine: A Qualitative Study of Perceived Drivers, Implications, and Strategies. Crit Care Med, 47(4):e286-e291.

Malmström B, Nohlert E, Ewald U, Widarsson M (2017) Simulation-based team training improved the self-assessed ability of physicians, nurses and midwives to perform neonatal resuscitation. Acta Paediatr, 106(8):1273-1279.

Mehta S, Burns KEA, Machado FR et al. (2017) Gender Parity in Critical Care Medicine. Am J Respir Crit Care Med, 196(4):425-429.

Mehta S, Rose L, Cook D et al. (2018) The Speaker Gender Gap at Critical Care Conferences. Crit Care Med, 46(6):991-996.

Merman E, Pincus D, Bell C et al. (2018) Differences in clinical practice guideline authorship by gender. Lancet, 392(10158):1626-1628.

Metaxa V (2013) Is this (still) a man's world? Crit Care, 17(1):112.

Parsons S, Kruijt A-W, Fox E (2019) Psychological Science Needs a Standard Practice of Reporting the Reliability of Cognitive-Behavioral Measurements. Advances in Methods and Practices in Psychological Science, 378-395.

Rubulotta F, Mehta S, Leigh JP (2020) Intensive Care Medicine: Reflections on the Gender Gap. ICU Management & Practice, 20(4):319-324.

Sjoberg L (2016) Women as Wartime Rapists: Beyond Sensation and Stereotyping. New York, NY: NZU Press.

Templeton K, Bernstein C, Sukhera J et al. (2019) Gender-based differences in burnout: Issues faced by women physicians. NAM Perspectives. Discussion Paper, National Academy of Medicine, Washington, DC.

DigiConf by ICU MANAGEMENT & PRACTICE

DigiConf

Gender in the ICU:
Differences, Patient Outcomes and Female Participation

14 September, 2021 @ 17:00 CET

REGISTER NOW >

Prof Jean-Louis Vincent

Professor | Department of Intensive Care | Erasme Hospital | Université libre de Bruxelles | Brussels, Belgium | Editor-in-Chief | ICU Management & Practice

Yeow Chan
Senior Consultant Department of Anaesthesiology, Intensive Care and Pain Medicine

Director
Home Ventilation and Respiratory Support Service (HVRSS)
Tan Tock Seng Hospital
Republic of Singapore

yeow_chan@ttsh.com.sg
ChanYeow1

"Help! My Patient Has Duchenne Muscular Dystrophy"

How should you handle a chronic ventilator user admitted to your ICU with acute critical illness?

A personal observation and reflection on how to handle a chronic ventilator user and suggestions to smoothen the sojourn of the next chronic ventilator user through an ICU, while ensuring maximal dignity and maintenance of function; minimising suffering and reducing the need for inappropriate withdrawal of life support.

"John is a nineteen year old, first year university student with Duchenne Muscular Dystrophy. He had undergone scoliosis surgery five years ago. For the past two years, he has been confined to the motorised wheelchair, and needs to use nocturnal non-invasive ventilation – S/T mode 16/5, RR 16/min.

He was crossing the road using his motorised wheelchair when he was hit by a slow moving van. He sustained the following injuries: Left humerus fracture; left 5th to 9th rib fractures with left lung contusion; left tibia-fibula fractures.

The Orthopaedics Consultant has decided that his injuries should be treated conservatively."

Such could be a typical introduction by your resident on a morning in the ICU. Or perhaps, more commonly, it could be that a similar chronic ventilator user is admitted for pneumonia, urinary tract infection, or acute appendicitis. They often end up in intensive care because of their pre-existing need for mechanical ventilation. How should we manage these individuals in a way that is adequate and humane? The following are some suggestions:

a. Many chronic ventilator users have managed to order their living arrangements optimally according to their personal limitations. Listen closely to the ventilator user or his/her family members about his/her usual baseline condition, and how he/she orders or organises his/her daily activities and needs.

b. Oral intubation in one stroke takes away both oral communication and swallowing, and sedation increases the risk of cognitive dysfunction. Minimise the use of sedation, making sure to incorporate daily awakening trials if deeper sedation is employed. Ideally the ventilator user is pain-free but not sedated (RASS 0 to -1), and augmentative and alternative means of communication (AAC) are reintroduced (if the ventilator user is already familiar with them) as soon as possible. A speech and language pathologist can help establish communication with AAC.

c. Aim to keep the duration of oral intubation as short as possible. In ventilator users with intact bulbar function, and with a current injury or illness not likely to impede breathing, aim to extubate the patient to non-invasive ventilation as soon as possible. The roadmap to a successful extubation was described in the 2010 article by Bach and co-workers. If this doesn't appear feasible, consider an early tracheostomy.

d. Not all users of non-invasive ventilation are familiar with the possibilities and limitations of a tracheostomy. Even many physicians think that a tracheostomised patient will never be able to speak verbally or swallow orally. The process of decannulating a chronic ventilator user is very different from that for a tracheostomised person with no respiratory muscle weakness. Getting the opinion of a chronic ventilation specialist would help you to make a better prognostic assessment so necessary for a meaningful discussion with the ventilator user.

e. Do not be surprised that the chronic ventilator user may request for "all resuscitative measures". A large proportion of ventilator users with disabilities are satisfied with their lives and want to continue living. Shed any "ableist" biases we may have. Recognise that there are inherent problems with using questionnaires like the SF-36 to assess disabled individuals. A disabled person may not be able to walk, but he/she may be perfectly happy going to the mall in the motorised wheelchair.

f. In the chronic ventilator user who requests for "no further resuscitation" incongruous with the severity of physical injury or illness, it is helpful to see if there are reversible socio-economic issues that are weighing on them. Often these issues cause fear and uncertainty, and arguably limit the freedom of the individual in making choices.

g. Should the chronic ventilator user receive a tracheostomy, once the ventilatory parameters are stabilised, partial or complete cuff deflation can be attempted for the purpose of vocalisation. This is better done using a portable, trach-compatible, life-support turbine ventilator (home ventilator) rather than an ICU ventilator, as the home ventilator has better leak compensating capabilities. Periods of cuff deflation for speech are as important, if not more important than periods of ventilator free breathing, and both should be incorporated into the routine of rehabilitation of such a patient.

h. Understand your portable ventilator. We assume that intensivists

would automatically be ventilation experts. Yes, and no. Ventilator manufacturers seem to set as their key performance indicator the ability to devise nomenclature that confounds clinicians. As an example, would I be able to succinctly explain the difference between pressure support mode and spontaneous/timed mode to my resident? Do we really know, or do we think we know?

i. Understand the impact of leak on ventilation. Leak is inconsequential in the orally intubated intensive care patient. If there is leak, the machine alarms, and the leak is sealed, one way or another. Leak is ubiquitous in chronic ventilation, whether in individuals on non-invasive ventilation or individuals on cuff-deflated/cuffless tracheostomy using leak speech. How much leak is acceptable? What is the impact of leak on cycling or triggering? Are there work-arounds with regards to leak (by changing modes or adjusting settings for example)? Are there things you can do to the interface to decrease leaks?

j. Understand the special requirements for airway clearance. What are the strategies that are essential for people with muscle weakness. Is there a difference in techniques for NIV vs tracheostomised patients. How about individuals with bronchiectasis?

k. Organise, train and motivate the team such that there is adequate care round the clock. The ventilator user constantly requires someone who knows how to operate the ventilator (portable ventilator, not ICU ventilator), troubleshoot the interface, perform airway clearance and perform rescue breathing. At home, this is done all year round by just a small number of (two to four) family members or carers. Could it be that in the ICU, we cannot replicate this level of care,even though we have many junior doctors, ICU bedside nurses and a variety of therapists? Do we need to rethink how to break down our silos?

> **“ oral intubation in one stroke takes away both oral communication and swallowing, and sedation increases the risk of cognitive dysfunction ”**

l. When allowing tracheostomy cuff deflation and leak speech, part of the inhaled air escapes through the upper airway (indeed this is how vocalisation occurs). As such passive humidification with a heat moisture exchanger may become ineffective. Active humidification with a heated humidifier and inhaled aerosolised saline therapy may be necessary to prevent encumbrance of the airway by dried, thick secretions.

m. Lengthening periods of ventilator free breathing should not impede the rehabilitation of strength and endurance of the chronic ventilator user, aiming to restore pre-illness, pre-injury function. The ventilator can be used during rehabilitative sessions to optimise cardiorespiratory function so that the focus can be on the musculoskeletal training.

n. The nasogastric tube can be an uncomfortable and cumbersome appendage. If a ventilator user is extubated to non-invasive ventilation, the nasogastric tube increases upper airway resistance and may also contribute to facial skin injuries. Changing a nasogastric tube by the bedside may be dangerous or impossible in someone dependent on continuous non-invasive ventilation. Even in a tracheostomised patient, the nasogastric tube may be cumbersome and uncomfortable. Whilst the risks of serious abdominal complications with gastrostomies is reported as up to 5%, this risk needs to be balanced against the above-mentioned issues. The gastrostomy can be inserted either endoscopically or radiologically. The radiologic approach is convenient and can be done with minimal sedation, and is the preferred approach in our institution for chronic NIV users with minimal respiratory reserve.

Upon stabilisation of the acute illness or injuries, it is very helpful to either transfer the patient to a chronic ventilation specialist team (indeed some legislations require this) or to seek the advice of such a specialist team at all phases in the rehabilitative journey of the chronic ventilator user.

These are my personal observations and reflections working both as an intensivist and a chronic ventilation physician. I hope the suggestions are relevant and helpful, and will smoothen the sojourn of the next chronic ventilator user through your ICU, allowing maximal dignity and maintenance of function; minimising suffering and reducing the need for inappropriate withdrawal of life support. Some useful articles for reading are listed in the references.

Conflict of Interest

None. ■

References

Bach JR, Goncalves MR, Hamdani I, Winck JC (2010) Extubation of patients with neuromuscular weakness: a new management paradigm. Chest, 137(5): 1033-9. doi: 10.1378/chest.09-2144.

Bruno M-A, Bernheim JL, Ledoux D et al. (2011) A survey on self-assessed well-being in a cohort of chronic locked-in syndrome patients: happy majority, miserable minority. BMJ Open, 1:e000039. doi:10.1136/bmjopen-2010-000039.

Chatwin M et al. (2018) Airway clearance techniques in neuromuscular disorders: A state of the art review. Respir Med, 136:98-110. doi: 10.1016/j.rmed.2018.01.012.

Gregoretti C et al. (2013) Choosing a ventilator for home mechanical ventilation. Breathe, 9: 394-409; doi: 10.1183/20734735.042312.

Hays RD et al. (2002) Use of the SF-36 and Other Health-Related Quality of Life Measures to Assess Persons With Disabilities. Arch Phys Med Rehabil, 83(2). doi: 10.1053/apmr.2002.36837.

McKim and Rocha (2008) Tracheostomy Weaning from Longer Term Ventilation (Book chapter). In book: Ventilatory Support for Chronic Respiratory Failure. Edition: 225. Chapter: 25. Publisher – Informa Healthcare. Editors: Ambrosino, N, Goldstein Roger.

Prigent H et al. (2010) Speech Effects of a speaking valve versus external PEEP in tracheostomized ventilator-dependent neuromuscular patients. Intensive Care Med, 36 (10):1681-7. Doi: 10.1007/s00134-010-1935-0.

Rabec C et al on behalf of the SomnoNIV group (2011) Ventilator modes and settings during non-invasive ventilation: effects on respiratory events and implications for their identification. Thorax, 66:170-178. doi:10.1135/thx.2010.142661.

Selim SJ et al. (2018) Initiation of Non-invasive Ventilation for Sleep Related Hypoventilation Disorders - Advanced Modes and Devices. CHEST Journal. Contemporary Reviews in Sleep Medicine, 153(1):251-265. doi:10.1016/j.chest.2017.06.036

LIVES 2021

34TH ANNUAL CONGRESS

3-6 OCTOBER

ESICM
EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

The Intensive Connection

Should Families Be Allowed To Visit Dying COVID-19 Patients in the ICU?

COVID-19 has drastically changed how end-of-life care is practiced in the intensive care unit. Safety concerns for society limits family visitation but is contrary to patient and family-oriented care. This article provides an ethical analysis of the pros and cons of having family members present at the death of a COVID-19 positive ICU patient and provides a framework that can be used in future surges.

Shahla Siddiqui
Assistant Professor
Department of Anesthesia, Critical Care and Pain Medicine
Beth Israel Deaconess
Medical Center
Harvard Medical School
Boston, USA

shahlasi@yahoo.com

Margaret M. Hayes
Attending Physician
Department of Medicine
Director of Critical Care
Beth Israel Deaconess
Medical Center
Harvard Medical School
Boston, USA

mhayes7@bidmc.harvard.edu

Todd Sarge
Attending Physician
Department of Anesthesia, Critical Care and Pain Medicine
Director of Critical Care
Beth Israel Deaconess Medical Center
Assistant Professor
Harvard Medical School
Boston, USA

sarge@bidmc.harvard.edu

The Ethical Dilemmas Involved in Restricting ICU Visitation at the End-of-Life

End-of-life care for ICU patients is highly variable in practice, even prior to the COVID-19 pandemic (Curtis et al. 2012; Kruser et al. 2019). A large proportion of patients who die in the hospital do so in the ICU, especially during the current COVID-19 pandemic due to severe organ dysfunction (Mularski 2006). However, with the rapid advent of the pandemic and the accompanying large scale ICU admissions and mortality, family visits were prohibited to ensure that relatives did not infect other family members, patients, or healthcare professionals. Family members could no longer be at the patient's bedside and the ICU team was unable to communicate and support family members. Involvement in decision-making was also compromised, and it was felt that this situation was harmful both for patients and family members (Robert et al. 2020).

Is it ethical to deprive families from being present at the bedside of a dying COVID-19 ICU patient? This article will argue that the considerations that point towards a more relaxed policy of family visitation simply outweigh those that point towards a stricter policy, when scrutinised in the context of what is at stake in the context of decision-making. The following sections are divided into the current strict visitation scenario, our own arguments against this policy, and finally proposed solutions.

Reasons for a Strict Policy of ICU Family Visitation at EOL

COVID-19 mortality is highest in those 85 years and older (10-27%) followed by those 65-84 years (3-11%) (Zhou et al. 2020). Many of these patients have died in the ICU without their loved ones close by. Hospitals and physicians have managed these difficult conversations via telephone or video chat, which remains erratic and sub-optimal, but the best that can be done under the present circumstances. Modern technology has allowed families to say goodbye to their loved ones through electronic devices, sometimes from all over the world (Etkind et al. 2020). This has become necessary due to i) a shortage of the personal protective equipment (PPE) required for interacting with a COVID-19 patient. Giving these to the family members may be considered a less optimal use of precious PPE that could be better used for frontline healthcare workers, ii) even with sufficient PPE, infection control issues play a big role in these decisions as the ICU staff may become exposed to family members who may be symptomatic or asymptomatic COVID patients, and who may not follow infection control instructions appropriately, and iii) another clinical and ethical premise is that allowing family members into COVID ICUs would expose them to the threat of hospital acquired COVID infection [primarily from their dying loved one] (Arabi et al. 2020). These choices can be justified by aiming to provide a safe environment for healthcare workers to practice and also to allocate resources fairly (Rodríguez-Prat

et al. 2016). The strict policy adopted by most COVID ICUs across the U.S. is generally framed in the argument that we could impart harm through broad visitation due to lapses in the strict infection control and the multi-faceted PPE use and complex management requirements of the COVID-19 pandemic containment (Goh et al. 2020).

The first concern relates to the use and availability of PPE to prevent infection of families visiting infected loved ones. There is a worldwide shortage of PPE, which is essential for protection of the healthcare workers. It is imperative during pandemics that healthcare workers have adequate protection to decrease personal harm and the spread of disease. This is especially true when limited availability of testing masks the true prevalence of COVID-19. It is therefore essential to preserve PPE. Using it for family members of ICU patients may be considered an unnecessary waste (Seibert et al. 2018). Secondly, the use of PPE to prevent infection relies on proper training and fit-testing (for N-95 masks) for the donning, doffing and PPE use to ensure adequacy of protection against infection. This would be a large burden to accomplish for all family members, especially those who are emotional and likely not thinking clearly, wishing to visit their loved ones to ensure the fit and use of PPE was done properly.

To mitigate the concern/risk that allowing family members in COVID ICUs would expose them to the threat of hospital acquired COVID-19 infection, some hospitals are buying iPads and other devices to allow virtual visits. There is no data that would support this premise, as strict visitation policies at times seem to be implemented on an ad hoc basis. Even if allowed to visit under special circumstances, the instances are inconsistent and therefore confusing to the public, and very often families are left to call patients when the patient is on his/her last breath and unable to interact at all. Very often this is a failure of following the policies in place, which advocate early virtual visits with the patient and in-person visits as the patient's death becomes more imminent.

The second concern is that the ICU staff will become exposed to infected family members who may be carriers of COVID-19 infection, and potentially lead to health care worker infections. A high proportion of healthcare workers (HCW) in Italy and a third of NHS healthcare workers in the U.K. have become COVID-19 positive. Over 9,000 U.S. healthcare workers contracted COVID-19, and 27 have died. A majority of those who tested positive (55%) think they were exposed while at work (Chu et al. 2020). Allowing family members to visit may bring in members of the public who may be COVID-19 carriers and pose a risk for staff and other patients. The Center for Disease Control (CDC) has issued guidance that visitors to healthcare facilities should be limited during the COVID-19 pandemic (Smith and Fraser 2020).

> **"the presence of family members at the bedside of a dying patient in the ICU is not only comforting for the patient, but is comforting for the families, and enhances the quality of the end-of-life care being delivered"**

Why We Should Allow Visits by Families at the EOL in the ICU

The ethics of end-of-life care rely on empathy and emotional responsiveness. Getting families through the difficult stage of acceptance of the prognosis, building rapport and trust and progressing through the stages of grief to let go peacefully takes time and multiple interactions between the teams and family members (Oczkowski et al. 2016). The presence of family members at the bedside of a dying patient in the ICU is not only comforting for the patient, even if they are minimally conscious, but is comforting for the families, and enhances the quality of the end-of-life care being delivered (Rawal et al. 2017). This experience can provide closure and acceptance in ways which any amount of communication alone may not offer (Hartog and Reinhart 2018). Families also feel some sense of participation and control when they are able to offer solace to the patient, even if the patient is unconscious (Osborn et al. 2012). This compassion for the family members comes from an active regard for another's welfare with sympathy, tenderness and emotional involvement. Good clinical care requires this insight, and a physician who acts according to clinical norms without aligned concern and sympathy for the suffering person and their families may seem non-compassionate. We owe something to the families without a direct duty of care in this unique context. This obligation arises from current constructs of justice and commitment which encapsulates patient-family-healthcare provider relationships (Holmvall et al. 2012). These difficult decisions are traditionally made face to face and with family members having access to the patient (Lautrette et al. 2007).

Studies have shown that the quality of death is significantly improved with the family present at the bedside (Nelson et al. 2010). Good end-of-life care is regarded as one where the family is present irrespective of the time of day. This presence is also of immense benefit for the families. Here justice also encapsulates the value of benefitting what is essentially a third party in the medical encounter. Families feel a sense of closure and control if they are allowed to participate in shared decision making at the end of their loved ones' life, which is the norm

in non-pandemic times. This sense of control can emanate from the decisions made regarding transitioning from a 'full code status' to 'comfort measures only' or 'do not resuscitate' status; or decisions regarding withdrawal of life sustaining therapies (Wong et al. 2019). Trust, which is inextricably bound to respect for human dignity, is an expectation that physicians will act for their patients as they would for their own families. This trust often requires visual and audible cues that families experience when they visit the loved one at the time that the patient is dying (Hutchison et al. 2016). However, the larger question is whether these advantages of family presence outweigh the danger of exposure for vulnerable families, other patients, and staff. Emotional distress of HCW when adequate EOL care is not delivered is not only a source of anxiety, but also burnout (Dodek et al. 2019). If families aren't allowed to be present at a patient's bedside as they die, optimal care is not being delivered, and may produce emotional turmoil among bedside staff. If this form of work-related stress builds to a level where a staff member's emotional wellbeing is seriously compromised, it is likely to have an impact on the quality of care of patients, as well as on unit morale and staff turnover. Given the pre-existing wide variability in EOL care for dying ICU patients, such a policy would provide uniformity and provide better patient and family-centred care (Davidson et al. 2007).

Proposed Solutions for Family Visitation

This discussion will present a practical strategy for proceeding with visitations of a certain kind, in light of the following arguments and in the context of additional evidence: i) this is necessary for delivering good clinical care; ii) it presents minimal risk to family members, iii) it does not present additional risk to other patients and staff if done with care; and iv) it is reasonable and justified, and an essential source of solace for family members of dying patients. A recent cohort study of 1,536 ICUs in the U.S., within a national quality improvement collaborative, showed that family presence at the end-of-life is a minimum standard of care (Kruser et al. 2019). For various notable reasons, this standard is maintained to promote patient and family-oriented care. The aim of this article is not to expound on the benefits of family presence at the EOL, but to argue that such a policy is not only ethically sound but a moral obligation of physicians and healthcare teams. The Center for Disease Control (CDC) has stipulated that "visits of family members should be scheduled and carefully controlled. Hospitals should also institute safety procedures; facilities must provide instruction on hand hygiene and use of PPE accord; visitors should not be present during aerosol generating procedures; visitors should be instructed to only visit the patient room and not go to other locations in the facility". With these restrictions, family visitation at their loved one's end-of-life, is permissible. These carefully orchestrated visits (with expert escorts, personal protective protection, and limits on numbers of family members) can prove to be extremely meaningful for families, patients as well as HCWs. In some reported cases, physicians and nurses perceived the visits as 'fulfilling and moving and gave them a sense of delivering dignified and compassionate end-of-life care for their patients (Bansal et al. 2020). Therefore, the argument can be made that individual hospital policies are aimed at protecting families from the threat of the infection from their loved ones or from other COVID-19 patients. Adopting such solutions, therefore, preserve respect for individual dignity and relationship at the end-of-life (Van Orden et al. 2020).

> **"having families present to say goodbye to their loved ones is simply the right thing to do, and it is the responsibility of the health care teams and organisations to make this possible"**

The risk of exposure to family members is reduced if they are provided with adequate PPE and proper instruction. The CDC recommends normal face coverings in the absence of aerosol generating procedures. This can avoid wastage of N95 masks which may be in short supply. If the EOL visit is carried out in a private room within the ICU (especially important for surge ICU space such as post-anaesthesia care units that are generally more open spaces that have been used for ICU space during the pandemic surge), the risk of this exposure is further reduced. Similarly, staff members are already adequately protected within COVID ICUs where policy dictates masks be worn in all areas of the hospital and hence, HCW are not at extra risk from families who may be COVID positive. In times of a pandemic, allowing families to be present at a dying patient's bedside is ethical, if done in a careful and thoughtful way. An underlying commitment to compassionate care for the patient also includes justice and consideration for the patient's family members.

The threat of another wave of SARS-CoV-2 infections or similar catastrophes is very real now. In such a scenario, institutions and hospitals must remain prepared with infection control policies in place. These should include family visitation in general and presence during EOL care in particular. If such a policy precluded family visitation, there would be much greater grief for countless people. Having families present to say goodbye to their loved ones is simply the right thing to do, and it is the responsibility of the health care teams and organisations to make this possible.

Conclusion

COVID-19 has shaken the delivery of healthcare across the world. The ethically sound clinical policies with respect to end-of-life care are seemingly in conflict with public safety and resource allocation. In these times, when death becomes commonplace, the deep core of humanity must underscore our actions and deeds. Welfare based on principles of compassion and virtue must be valued, whilst maintaining an emphasis on safety and care. This article makes an argument for allowing families to visit dying COVID-19 patients in the ICU by describing how this encapsulates humanity, fairness and compassion for them although they are not directly under our care.

Acknowledgements

We wish to thank the following experts for their opinions and advice on the article: Dr Michael Dunn, Lecturer in Health and Social Care Ethics, The Ethox Centre Research Fellow, Wellcome Centre for Ethics and the Humanities, Nuffield Department of Population Health, University of Oxford Big Data Institute, Li Ka Shing Centre for Health Information and Discovery; Dr Michael Gusmano, Professor of health policy, Rutgers University, and The Hastings Center, USA and David N. Sontag, Managing General Counsel, Beth Israel Lahey Health, Co-Chair Ethics Advisory Committee, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, USA.

Conflict of Interest

None of the authors have any competing interests or conflicts of interest. ■

References

Arabi YM, Fowler R, Hayden FG (2020) Critical care management of adults with community-acquired severe respiratory viral infection. Intensive Care Med, 46(2):315-328.

Bansal P, Bingemann TA, Greenhawt M et al. (2020) Clinician Wellness During the COVID-19 Pandemic: Extraordinary Times and Unusual Challenges for the Allergist/Immunologist. J Allergy Clin Immunol Pract, 8(6):1781-1790.e3.

Chu J, Yang N, Wei Y et al. (2020) Clinical characteristics of 54 medical staff with COVID-19: A retrospective study in a single center in Wuhan, China [published online ahead of print, 2020 Mar 29]. J Med Virol, 10.1002/jmv.25793.

Curtis JR, Engelberg RA, Bensink ME, Ramsey SD (2012) End-of-life care in the intensive care unit: can we simultaneously increase quality and reduce costs? Am J Respir Crit Care Med, 186(7):587-592.

Davidson JE, Powers K, Hedayat KM et al. (2007) American College of Critical Care Medicine Task Force 2004-2005, Society of Critical Care Medicine. Clinical practice guidelines for support of the family in the patient-centered intensive care unit: American College of Critical Care Medicine Task Force 2004-2005. Crit Care Med, 35(2):605-622.

Dodek PM, Norena M, Ayas N et al. (2019) Moral distress is associated with general workplace distress in intensive care unit personnel. J Crit Care, 50:122-125.

Etkind SN, Bone AE, Lovell N et al. (2020) The Role and Response of Palliative Care and Hospice Services in Epidemics and Pandemics: A Rapid Review to Inform Practice During the COVID-19 Pandemic. J Pain Symptom Manage, S0885-3924(20)30182-2.

Goh KJ, Wong J, Tien JC et al. (2020) Preparing your intensive care unit for the COVID-19 pandemic: practical considerations and strategies. Crit Care, 24(1):215.

Hartog CS, Reinhart K (2018) Staff and family response to end-of-life care in the ICU. Curr Opin Anaesthesiol, 31(2):195-200.

Holmvall C, Twohig P, Francis L et al. (2012) Applying justice and commitment constructs to patient-health care provider relationships. Can Fam Physician, 58(3):e159-e165.

Hutchison PJ, McLaughlin K, Corbridge T et al. (2016) Dimensions and Role-Specific Mediators of Surrogate Trust in the ICU. Crit Care Med, 44(12):2208-2214.

Kruser JM, Aaby DA, Stevenson DG et al. (2019) Assessment of Variability in End-of-Life Care Delivery in Intensive Care Units in the United States. JAMA Netw Open, 2(12):e1917344.

Lautrette A, Darmon M, Megarbane B et al. (2007) A communication strategy and brochure for relatives of patients dying in the ICU [published correction appears in N Engl J Med,12;357(2):203]. N Engl J Med, 356(5):469-478.

Mularski RA (2006) Defining and measuring quality palliative and end-of-life care in the intensive care unit. Crit Care Med, 34(11)(suppl):S309-S316.

Nelson JE, Puntillo KA, Pronovost PJ et al. (2010) In their own words: patients and families define high-quality palliative care in the intensive care unit. Crit Care Med, 38(3):808-818.

Oczkowski SJ, Chung HO, Hanvey L et al. (2016) Communication tools for end-of-life decision-making in the intensive care unit: a systematic review and meta-analysis. Crit Care, 20:97.

Osborn TR, Curtis JR, Nielsen EL et al. (2012) Identifying elements of ICU care that families report as important but unsatisfactory: decision-making, control, and ICU atmosphere. Chest, 142(5):1185-1192.

Rawal G, Yadav S, Kumar R (2017) Post-intensive Care syndrome: an overview. J Transl Intern Med, 5(2):90–2.

Robert R, Kentish-Barnes N, Boyer A et al. (2020) Ethical dilemmas due to the COVID-19 pandemic. Ann. Intensive Care, 10(84).

Rodríguez-Prat A, Monforte-Royo C, Porta-Sales J et al. (2016) Patient Perspectives of Dignity, Autonomy and Control at the End of Life: Systematic Review and Meta-Ethnography. PLoS One, 11(3):e0151435.

Seibert G, Ewers T, Barker AK et al. (2018) What do visitors know and how do they feel about contact precautions?. Am J Infect Control, 46(1):115-117.

Smith N, Fraser M (2020) Straining the System: Novel Coronavirus (COVID-19) and Preparedness for Concomitant Disasters. Am J Public Health, 110(5):648-649.

Van Orden KA, Bower E, Lutz J et al. (2020) Strategies to Promote Social Connections Among Older Adults During 'Social Distancing' Restrictions [published online ahead of print, 2020 May 18]. Am J Geriatr Psychiatry, 10.1016/j.jagp.2020.05.004.

Wong P, Liamputtong P, Koch S et al. (2019) Searching for meaning: A grounded theory of family resilience in adult ICU. J Clin Nurs, 28(5-6):781-791.

Zhou F, Yu T, Du R et al. (2020) Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The Lancet, 395(10229):1054-1062.

AGENDA

For a full listing of events visit https://iii.hm/icuevents2021

SEPTEMBER

1-5 17th World Congress of Anaesthesiologists WCA 2021
Virtual event
https://iii.hm/1biq

5-8 ERS International Congress 2021 - European Respiratory Society
Virtual event
https://iii.hm/1bir

8-10 European Society of Regional Anaesthesia (ESRA) Congress 2021
Virtual event
https://iii.hm/1bis

9-4 ESPEN 2021
Virtual event
https://iii.hm/1bit

13-14 British Association of Critical Care Nurses (BACCN) Conference
Virtual event
https://iii.hm/1biu

20-22 Pediatric Cardiac Intensive Care Society (PCICS) Annual International Meeting 2021
Virtual event
https://iii.hm/1biv

23-24 Association of Anaesthetists Annual Congress 2021
Hybrid event, Liverpool, UK
https://iii.hm/1biw

23-25 SFAR Annual Congress 2021
Paris, France
https://iii.hm/1bix

OCTOBER

3-6 ESICM 34th Annual Congress, LIVES 2021
Virtual event
https://iii.hm/1aat

7-9 10th Europaediatrics 2021
Hybrid event, Zagreb, Croatia
https://iii.hm/1aau

8-12 ANESTHESIOLOGY 2021 Annual Meeting
San Diego, USA
https://iii.hm/1aav

12-15 44th Annual Conference on Shock 2021
Portland, USA
https://iii.hm/1aaw

25-28 ACEP 2021 - American College of Emergency Physicians
Boston, USA
https://iii.hm/1aax

26-29 39th Vicenza Course on AKI & CRRT
Virtual event
https://iii.hm/1aay

27-31 EUSEM 2021
Lisbon, Portugal
https://iii.hm/1aaz

NOVEMBER

4-6 10th Annual Johns Hopkins Critical Care Rehabilitation Conference
Virtual event
https://iii.hm/1bj5

11-13 16th Annual Conference German Society for Interdisciplinary Emergency and Acute Medicine (DGINA)
Kassel, Germany
https://iii.hm/1bj6

ICU
MANAGEMENT & PRACTICE

ICU MANAGEMENT AND PRACTICE IS PUBLISHED BY
MindByte Communications Ltd
Kosta Ourani, 5 Petoussis Court, 5th floor, CY-3085 Limassol Cyprus
Email — office@icu-management.org
Website — icu-management.org

PRODUCTION, FULFILMENT AND DISTRIBUTION
Total distribution: 21,500
ISSN = 1377-7564

VERIFIED CIRCULATION
according to the standards of International Business Press Audits.

ICU Management & Practice is independently audited by Top Pro CY.

icu-management.org ICU_Management