Clinical Interventions in Aging

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REVIEW

Elderly Patients and Management in Intensive Care Units (ICU): Clinical Challenges

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Abstract: There is a growing population of older adults requiring admission to the intensive care unit (ICU). This population outpaces the ability of clinicians with geriatric training to assist in their management. Specific training and education for intensivists in the care of older patients is valuable to help understand and inform clinical care, as physiologic changes of aging affect each organ system. This review highlights some of these aging processes and discusses clinical implications in the vulnerable older population. Other considerations when caring for these older patients in the ICU include functional outcomes and morbidity, as opposed to merely a focus on mortality. An overall holistic approach incorporating physiology of aging, applying current evidence, and including the patient and their family in care should be used when caring for older adults in the ICU.

Keywords: geriatric syndrome, critical illness, organ dysfunction, shock, respiratory failure

Introduction

Older Americans (aged 65 and older) are expected to double in population from 46 million to over 98 million by 2060, with the proportion of this age group increasing from 15% to almost a quarter of the total population.[1] Intensive care unit (ICU) providers are already seeing the average age of admitted critically ill patients increasing.[2] The growing geriatric population necessitates the training of all health care providers to implement care that reflects the unique needs and conditions of this population. Targeting training in the care of older patients may prove significant as current reports demonstrate that established collaboration between geriatricians and other clinicians improves outcomes by catering care specifically to older adults, particularly in the perioperative and acute care populations.[3,4] Thus, geriatric specific knowledge and training among intensivists must be expanded to meet the complex needs of these older patients.[5] This review will describe ICU-specific concerns within the aging population by reviewing existing data, understanding the impact of aging on critical illness pathophysiology, and its impact on patient outcomes using current evidence and highlighting areas in need of future evaluation.

Geriatric Syndromes and Comorbidities

Older adults often experience several aging-related common clinical conditions outside of discrete disease processes that increase vulnerability to morbidity and poor outcomes. These conditions, termed "geriatric syndromes", include pressure ulcers, incontinence, falls, functional decline, and delirium.[6] While the prevalence of geriatric syndromes prior to ICU admission can be as high, up to 90% of older survivors of critical illness report one or more geriatric syndromes, which represents a 2.6-fold increase from baseline.[7] Presence of these syndromes may contribute to ongoing higher care or nursing care needs, decreased independence, and reduced quality of life after critical illness.[8]

Aging is associated with an increase in comorbidities and a higher risk of "multimorbidity" or the co-occurrence of two or more chronic conditions.[9,10] Common comorbidities in aging include hypertension, diabetes, chronic obstructive pulmonary disease, heart failure, cancer, and cognitive impairment.[10] Multimorbidity is associated with increased short- and long-term mortality among all ICU patients[11] and poses a significant risk for older populations.[12] The aging process and comorbidities

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in older adults increase the risk of developing frailty, a syndrome resulting from decline across multiple physiologic systems that decreases the body's reserve for managing stressful events and increases vulnerability to adverse outcomes.[13] Frail older adults experience higher hospital and long-term mortality than their non-frail counterparts.[14]

Geriatric syndromes lead to unique preoperative evaluation requirements in older surgical patients, with interventions aimed at improving perioperative outcomes in these high-risk patients. Geriatric specific risk factors that contribute to perioperative morbidity, unplanned postoperative ICU admission, and mortality include baseline cognitive impairment, cardiopulmonary disease, frailty, and poor functional status.[15,16] Identifying modifiable risk factors prior to surgery and intervention with multidisciplinary collaboration has been found to decrease postoperative complications.[17] Discussing these risks with patients, in addition to patient's goals, is an important component of informed surgical consent.[18]

Geriatric syndromes and multimorbidity add to the complexity of ICU care in older adults. As more older adults are admitted with and survive critical illness, the health care system will require increased resources and long-term support for this population. Further, intensivists and ICU staff must be trained and equipped to manage geriatric-specific considerations.

System-Specific Considerations in Older Adults

A summary of aging-specific considerations by organ system for older adults admitted to the ICU is shown in Figure 1.

Neurologic

The aging brain undergoes changes that make older adults more vulnerable to developing neurocognitive dysfunction. Imaging studies have shown notable losses in grey and white matter volume and integrity with aging.[19] Cerebral blood flow also declines, leading to impaired oxygen delivery, slowed metabolism, and altered activity and production of

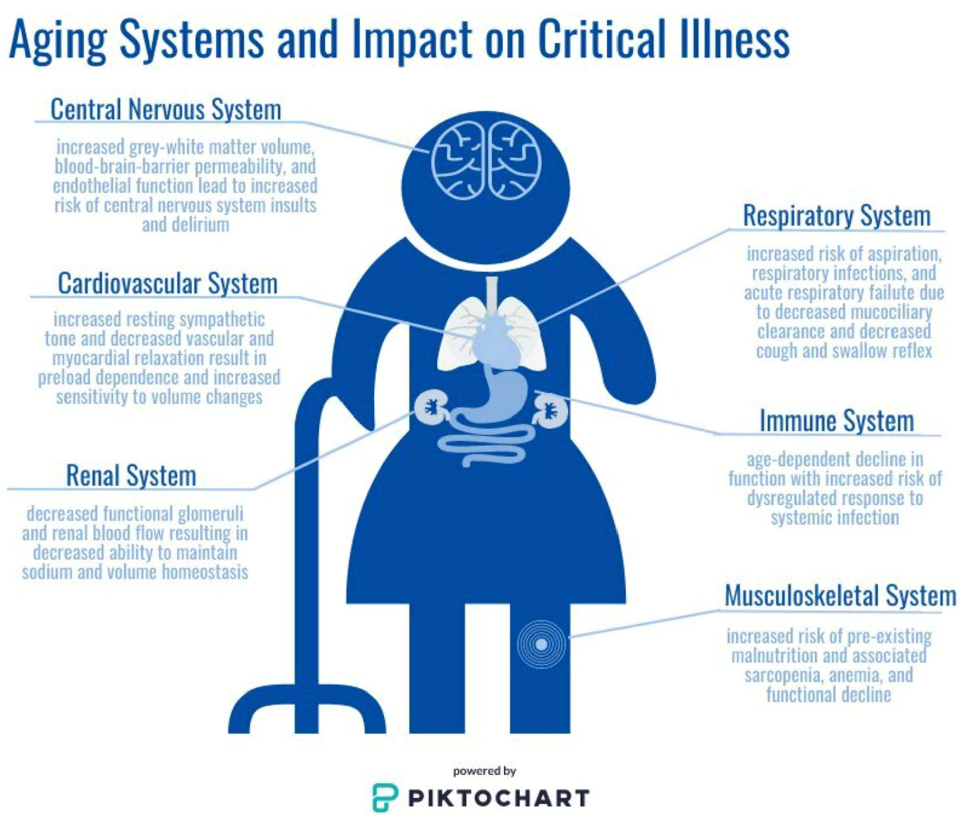

Figure 1 System-specific considerations for the critically Ill older adult patient. Age-related changes to the central nervous, cardiovascular, respiratory, musculoskeletal, renal, and immune systems are highlighted. Together these changes can impact overall patient health at baseline, and may be of particular concern during acute illness when physiologic homeostasis is particularly altered. Consideration of these changes should be made by all clinicians caring for older adults to help guide clinical decision making, family discussions, and overall goals of care. Image is powered by Piktochart.

neurotransmitters.[20,21] Further, endothelial cells lose function, and the blood–brain barrier becomes more permeable, exposing older adults to increased risk to the central nervous system from systemic insults.[22,23] Increasing age is also a risk factor for the development of cerebral microbleeds detected on MRI.[24] In a large population-based study, participants aged 60–69, 70–79, and 80–97 years old were found to have an 18.4%, 32.4%, and 38.1% incidence of microbleeds, respectively.[24] Higher microbleed burden is associated with increased physical frailty in a community dwelling adult population, and occurrence of microbleeds is associated with decline in cognitive function.[25,26] Loss of ability to perform activities of daily living and impaired cognition are not considered part of "normal aging" and warrant structured evaluation to identify and alleviate all modifiable factors.[27]

Acute brain dysfunction, or delirium, and long-term cognitive impairment are highly prevalent among ICU patients and survivors. Age is a well-established risk factor for both delirium and cognitive impairment. Routine screening with a validated assessment tool (ie, Confusion Assessment Method for the ICU [CAM-ICU] or Intensive Care Delirium Screening Checklist [ICDSC]) is essential as the diagnosis is often missed or delayed when relying on clinician identification alone. Application of routine screening has shown that a remarkable 60–80% of patients across medical, surgical, and trauma ICUs will develop delirium during their critical illness.[28,29] Early diagnosis is imperative as delirium is an independent predictor of increased duration of mechanical ventilation, duration of ICU and hospital stay, increased health care costs, long-term cognitive impairment, and mortality.[30–34]

Older adults admitted to the ICU with neurologic pathology such as traumatic brain injury, stroke, or postoperative neurosurgical intervention, may require specific neurologic care. These interventions include specialized monitoring electroencephalogram, intracranial pressure monitors, and serial neurologic exams. Serial hourly neurologic exams early in hospitalization may be beneficial for early detection of expanding intracranial hematoma or increasing cerebral edema requiring emergent intervention. Serial neurologic monitoring, however, requires frequent sleep interruptions and should be discontinued as soon as possible to mitigate sleep disruption.[35] Sleep disruption impacts several organ systems and has been found to be independently associated with delirium in the ICU.[36,37] Continuation of sleep disruption with hourly exams when no longer indicated may contribute to ICU delirium. Older age alone has been identified as a factor affecting sleep quality in the ICU.[38] One retrospective review of traumatic brain injury patients monitored with hourly neurologic exams found 20.2% of these patients were assessed hourly for greater than four days and had greater length of stay.[39] Given older age is associated with disrupted sleep in the ICU and sleep disruption associated increased risk delirium, the need for hourly neurologic exams should be assessed continually and interval increased as soon as possible.

Patients undergoing cardiac surgery are a unique population as they are often older and are placed at risk for delirium both from the surgery and from the often requisite ICU stay after surgery. Delirium develops in 20–50% of postoperative cardiac patients.[40,41] Risk factors for post-cardiac surgery delirium include advancing age, low ejection fraction, diabetes mellitus, postoperative atrial fibrillation, chronic kidney disease, and prolonged hospitalization.[40] Patients older than 65 years old undergoing cardiac surgery who had postoperative delirium were found to have prolonged hospitalization, prolonged ICU stays, and longer time on mechanical ventilation.[40] Delirium has also been shown to be an independent predictor of functional decline after cardiac surgery.[42]

There is currently no FDA-approved treatment for delirium. The best evidence for both prevention and management of delirium involves multi-component bundles of care, such as The Society of Critical Care Medicine's Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption (PADIS) Guidelines.[43] The PADIS Guidelines were designed to optimize care and minimize iatrogenic risk factors that contribute to poor outcomes after critical illness and are summarized into the ABCDEF implementation bundle. Each letter addresses a component of care associated with attempts to maintain brain health in the ICU: A, Assess, prevent and treat pain; B, perform Both spontaneous awakening and spontaneous breathing trials; C, Choose analgesic and sedative medications thoughtfully; D, perform frequent Delirium assessments and provide appropriate prevention and management; E, engage in Early mobility and exercise; F, encourage Family engagement.[44] Large-scale implementation studies of the ABCDEF bundle have demonstrated decreasing mortality, delirium, and coma with increased compliance with all components of the bundle.[45,46]

ABCDEF bundle implementation practices face hurdles and barriers for initiation, and Table 1 summarizes the bundle components, age-related barriers to implementation, and strategies for overcoming these barriers. Factors related to the structure of the ICU, implementation planning with training and staff support, and educational prompts may lead to

Table 1 ABCDEF Bundle Components and Age-Specific Barrier Guidance for Clinicians

Bundle Component		Bundle Intervention	Aging-Specific Barriers to Implementation	Specific Barrier Guidance for Older Adults
A	Assess, prevent, & manage pain	- assess pain with CPOT or BPS scales, NRS if patient able to self-report - use of regional analgesia and non-opioid adjuncts - analgesia-based sedation techniques with fentanyl	- cognitive or communication difficulties can make assessment more difficult - baseline pain conditions from immobility, joint disorders, or age-related degeneration -decreased muscle mass and metabolism can influence pharmacologic responses to medications and doses	Kirksey KM, McGlory G, Sefcik EF. Pain assessment and management in critically ill older adults. *Crit Care Nurs Q*. 2015;38(3):237–44. Klassen B, Liu L, Warren S. Pain management best practice with older adults: effects of training on staff knowledge, attitudes, and patient outcomes. *Phys Occup Ther Geriatr*. 2009;27:173–196. McLiesh P, Mungall D, Wiechula R. Are we providing the best possible pain management for our elderly patients in the acute-care setting? *Int J Evid Based Healthc*. 2009;7:173–180.
B	Both SAT & SBT	- daily linked SAT and SBT - interprofessional team coordination of care	- potential provider reluctance despite evidence of differences in SBT/weaning with age - daily pauses in sedation of particular importance given potential metabolic deficiencies	Aggarwal V, Singh R, Singh JB, Bawa J, Gaur N, Kumar S, Nagesh IV. Outcomes of mechanically ventilated critically ill geriatric patients in intensive care unit. *J Clin Diagn Res*. 2017;11(7):OC01-OC03. Stieff KV, Lim F, Chen L. Factors influencing weaning older adults from mechanical ventilation: An integrative review. *Crit Care Nurs Q*. 2017;40(2):165–177. Balas MC, Tate J, Tan A, Pinion B, Exline M. Evaluation of the perceived barriers and facilitators to timely extubation of critically ill adults: An interprofessional survey. *Worldviews Evid Based Nurs*. 2021;18(3):201–209.
C	Choice of sedation	- targeted light sedation when able - avoidance of benzodiazepines - dexmedetomidine if at high risk for delirium or weaning mechanical ventilation	- difficulty achieving light sedation due to increased sensitivity to medications - frequently continued after acute need; minimize high risk and potentially inappropriate prescribing for sedative medications during and following critical illness with frequent reconciliations for need	Pereira JV, Sanjanwala RM, Mohammed MK, Le ML, Arora RC. Dexmedetomidine versus propofol sedation in reducing delirium among older adults in the ICU: A systematic review and meta-analysis. *Eur J Anaesthesiol*. 2020;37(2):121–131. O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. *Age Ageing*; 44(2):213–8. By the 2019 American Geriatrics Society Beers Criteria Update Expert Panel. American Geriatrics Society Updated AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. *J Am Geriatr Soc*. 2019;67(4):674–694.
D	Delirium monitoring & management	- routine assessments with CAM-ICU, CAM-ICU-7, or ICDSC - non-pharmacologic interventions including sleep hygiene	- under-recognized when not routinely monitored (frequent hypoactive) - require emphasis on avoidance or dose reduction in high-risk medications - need for focus on nonpharmacologic methods for prevention (visual and hearing aids, sleep hygiene, reorientation)	Oh ES, Fong TG, Hshieh TT, Inouye SK. Delirium in Older Persons: Advances in Diagnosis and Treatment. *JAMA*. 2019;318(12):1161–1174, Lin WL, Chen YF, Wang J. Factors associated with the development of delirium in elderly patients in intensive care units. *J Nurs Res*. 2015;23(4):322–9. Chen L, Lim FA. Stuck inside a cloud: optimizing sedation to reduce ICU-associated delirium in Geriatric Patients. *Crit Care Nursing Q*. 2015;38(3):245–52.

(*Continued*)

Table 1 (Continued).

Bundle Component		Bundle Intervention	Aging-Specific Barriers to Implementation	Specific Barrier Guidance for Older Adults
E	Early mobility & exercise	- physical and occupational therapy assessment - coordinate activity with SAT or periods of no sedation - passive range of motion	- fear of causing harm or injury with physical activity - pre-existing immobility or frailty impairing participation - availability of staff	Bischoff-Ferrari HA, Vellas B, Rizzoli R, Kressig RW, da Silva JAP, et al. Effect of Vitamin D Supplementation, Omega-3 Fatty Acid Supplementation, or a Strength-Training Exercise Program on Clinical Outcomes in Older Adults: The DO-HEALTH Randomized Clinical Trial. *JAMA*. 2020; 10;324(18):1855–1868. Kitzman DW, Whellan DJ, Duncan P, Pastva AM, et al. Physical rehabilitation for older patients hospitalized for heart failures. *N Engl J Med*. 2021;385(3):203–216. Resnick B, Boltz M. Optimizing function and physical activity in hospitalized older adults to prevent functional decline and falls. *Clin Geriatr Med*. 2019;35(2):237–251.
F	Family engagement & empowerment	- unit orientation - education - emotional and verbal support - empowerment - participation in multidisciplinary rounds	- family reluctance or fear - illness in family members - unclear goals of care or understanding of potential/ expected clinical outcomes	Vincent JL, Creteur J. Appropriate care for elderly in the ICU. *J Intern Med*. 2022;291(4):458–468. Boltz M, Resnick B, Chippendale T, Galvin J. Testing a family-centered intervention to promote functional and cognitive recovery in hospitalized older adults. *J Am Geriatr Soc*. 2014;62(12):1298–407.

success of the ABCDEF bundle implementation.[47] High staff turnover, lack of continued education, and a culture that does not encourage multidisciplinary cooperation in quality improvement efforts may be barriers to bundle implementation.[47]

Cardiovascular

Physiologic changes of the aging cardiovascular system can make hemodynamic management challenging in older ICU patients. The autonomic nervous system becomes more imbalanced over time, with attenuated parasympathetic responses and increased resting sympathetic tone.[48] These imbalances predispose older adults to cardiovascular disease. The sinus node intrinsic rate and AV conduction slow, resulting in lower heart rates. Anatomic changes include valvular calcification and increased arterial and ventricular stiffness. In sum, these changes create higher preload dependence in older adults.[49] Intra-arterial and venous wall changes cause vessel stiffness and fragility, most notably in peripheral and coronary arteries. Thus, older adults are more vulnerable to the shifts in intravascular volume status that are common when critically ill.

The 2020 scientific statement from the American Heart Association reported increased incidence of myocardial infarction (MI) with age, both with type 1 MI due to plaque erosion and type 2 MI if blood supply and demand mismatch occur.[50] In older adults, less reserve and more demand resulting in type 2 MI were found to have five times increased risk of in-hospital mortality.[51] As such, demand ischemia from the acute critical illness insult is more likely to occur and complicate further management. Vascular changes contribute to the peak acute aortic dissection occurrences in the sixth and seventh decade of life;[52] however, management of Type A aortic dissection with open surgical repair remains high risk in the elderly. One meta-analysis found higher short-term mortality postoperatively in patients undergoing open aortic repair aged 70 years and older.[53] Postoperative in-hospital or 30-day mortality pooled incidence in older adults was 19.9% compared to 14.9% for younger adults, with a relative risk of 2.25 for the older adults.

The overall incidence of heart failure increases with age, and etiology is multifactorial with underlying causes including coronary artery disease (CAD), hypertension, and valvular disease.[54] In addition to increased incidence, mortality associated with heart failure also increases with age.[55] Development of congestive heart failure may result from increased left ventricle wall stiffness and decreased relaxation due to increased interstitial connective tissue within the left ventricle myocardium, myocyte hypertrophy, and changes in calcium channels in the sarcoplasmic reticulum.[54] This leads to reduced left ventricle early diastolic filling and decreased left ventricle compliance. The resultant decrease in cardiovascular reserve further contributes to older patients' sensitivity to changes in volume status, with hypovolemia resulting in decreased cardiac output. Conversely, hypervolemia in the setting of decreased cardiac compliance causes an increase in the left atrial stretch and pulmonary edema.[54]

Respiratory disorders, sepsis, or acute coronary syndrome may precipitate acute heart failure in older adults with limited cardiac reserve.[56] While intravascular depletion is detrimental in critically ill patients, resulting in hypotension and acute kidney injury, intravascular volume overload from intravenous fluid can also result in cardiac dysfunction and pulmonary edema with evidence for increased mortality in mechanically ventilated older patients with volume overload.[57]

Aging is also associated with an increased incidence of cardiac arrhythmias.[58,59] Cardiovascular changes with aging that can contribute to the development of arrhythmias include increased fibrous content resulting in dysfunction of the atrioventricular node and even atrioventricular block. The most common cardiac arrhythmia is atrial fibrillation, with an increased incidence in older adults and the most common arrhythmia in ICU patients.[60,61] In atrial fibrillation, the late diastolic filling of the left ventricle is lost. Along with impaired early filling as described earlier, this further increases the risk of hemodynamic compromise. Older adults may have chronic atrial fibrillation or may develop acute atrial fibrillation in the ICU, and atrial fibrillation is a predictor of mortality in critically ill patients regardless of chronicity.[62] For management of atrial fibrillation, the initial step is to recognize hemodynamic instability and if present proceed with emergent cardioversion. In the hemodynamically stable patient, treatment to control the ventricular response rate with beta blockade, calcium channel blockers, or amiodarone is administered.[63] Decreasing the heart rate allows for more left ventricle filling and improved stroke volume. Managing reversible causes of atrial fibrillation, such as volume overload and acute infection, must also be addressed. Associated morbidity with atrial fibrillation is cardioembolic stroke risk. Anticoagulation for atrial fibrillation has been associated with increased risk of bleeding complications in critically ill patients.[64] In the ICU or even after discharge, bleeding risk may preclude therapeutic anticoagulation in older patients due to other comorbidity and/or fall risk.

An early conversation for older patients in the ICU should involve code status in the event of cardiac arrest. The most common documented dysrhythmias in geriatric cardiac arrest are ventricular fibrillation and pulseless electrical activity.[65] Survival rates from in-hospital arrest and cardiopulmonary resuscitation (CPR) decrease with age. In one systematic review of in-hospital cardiac arrest for patients over age 90 years, the overall return of spontaneous circulation (ROSC) rate was 38.6%; the immediate survival rates of CPR for patients age 90 years and older was 11.6%, 15.4% for age 80–89 years, and 18.7% for age 70–79 years.[66] For elderly patients who survive in-hospital cardiac arrest and survive until hospital discharge, the risk-adjusted rate of 1-year survival was 63.7% for age 65–74 years, 58.6% for age 75–84 years, and 49.7% for age 85 years and older.[67] Out-of-hospital arrest survival rates after cardiac arrest and CPR are even lower. One-month survival for persons aged 85–94 years old was 0.59%, and 0.27% for ages >95 years old.[68] Careful attention is needed in administration of post-arrest management, as age is an independent predictor of underutilization of targeted temperature management. It is unclear if this is due to clinician bias or post-ROSC goals of care discussions.[50] One recent meta-analysis comparing hypothermic to normothermic management did not find a difference in 6-month mortality or functional outcomes using the Rankin score for both older and younger age groups.[69] While older age is associated with decreased survival after cardiac arrest, there is limited evidence on functional and neurologic outcomes specific to geriatric patients. This lack of data may impact code status discussions with patients and their family members and should be a goal of future studies.

Respiratory

Respiratory system changes with aging increase vulnerability to pulmonary infections and respiratory failure. Over time, mucociliary transport becomes dysfunctional which can contribute to difficulty with mucus and secretion clearance.[70] Connective tissue changes in the lung parenchyma lead to decreased elasticity, along with an overall reduced number of alveoli and increase in alveolar duct size. These changes cause an increase in the alveolar-arterial (A-a) gradient.[71] With kyphosis of the spine in addition to parenchymal changes, there is a decrease in forced expiratory volume (FEV) and a decrease in vital capacity.[72,73] In addition, age is associated with reduced muscular strength, reduced cough strength, and decreased ability to clear secretions.[74]

Physiologic changes of aging may also lead to increased risk of aspiration prior to, during, and after critical illness. Due to decrease in the cough and swallow reflex, chronic tracheal aspiration may go undetected until older patients present with aspiration pneumonia.[75,76] Cough and swallow reflexes have a sensory and motor component. The sensory limb seems to be more affected by aging and is the primary target for ongoing investigation to preserve cough and swallow reflexes.[77]

Advanced age is associated with an increased risk of acute respiratory failure.[78] The incidence of acute respiratory failure has been found to increase almost exponentially with each decade of life up to 85 years old.[78] With increased risk of respiratory failure and the growing aging population, more older adults with respiratory failure are being admitted to the ICU.[79] The incidence of mechanical ventilation requirement increases 10-fold from age 55 to 85 years old.[78] As the population ages and more geriatric patients require ICU care, there has been shown to be an increase in acute respiratory infection diagnoses and increase in number of hospitalizations for respiratory illness over the decade from 2006 to 2015.[79] The number of hospitalizations for patients age 75 years and older increased 1.6-fold, for age 85–90 by 2.5-fold, and for age 90 years and older by 2.1-fold. Older adults admitted to the ICU with respiratory failure are also at risk for complications including ventilator-induced lung injury and acute respiratory distress syndrome (ARDS).[80,81]

In respiratory failure requiring mechanical ventilation, increasing age is associated with increased mortality. In one study of patients aged 80 or older admitted to the ICU with acute respiratory illness, survival to hospital discharge was 75%.[82] When compared to a propensity score case-matched controls, the hospitalized cohort had a 10-fold increased risk of death 6 months post hospitalization. In mechanically ventilated older adults with acute lung injury and ARDS, adults aged 70 years and older had longer duration of mechanical ventilation, had longer stay in the ICU, and had higher mortality.[83] In this cohort, survival rate decreased for each increasing decade in age. Another observational study of patients age 65 and greater found decreasing survival with increasing age and also significant decrease in functional outcomes with increasing age.[84] For patients who survived one year, some functional recovery was regained. Increased mortality with age and potential functional recovery are both important considerations when caring for older adults with respiratory failure.

Respiratory changes with aging in addition to multiple comorbidities predisposed geriatric patients to develop severe infection and high mortality rates during the COVID pandemic.[85] In older adults, COVID may have atypical presentation of non-respiratory symptoms which can lead to delay in diagnosis and seeking supportive care; these symptoms can include fatigue, headache, diarrhea, and loss of sense and smell. A retrospective review of COVID hospitalizations in France during March 2020 found that age and history of cardiovascular disease were predictive of in-hospital mortality for patients hospitalized with severe SARS-CoV-2 infection.[86] The COVID international database to identify risk factors for mortality revealed that age >75 years, in addition to dementia, hypoxia, lymphopenia, and quick sequential organ failure assessment (qSOFA) score >1, was an independent predictor for mortality.[87]

Nutrition

Aging patients are at risk for preexisting malnutrition and inadequate dietary intake.[88] Malnutrition is associated with functional decline, sarcopenia, anemia, and poor wound healing.[89] Nutritional assessment may be useful in predicting complications; there is great variation in available assessment tools, however, and currently no consensus is available on the best tool for older adults in the ICU. The Geriatric Nutritional Risk Index was created to predict nutrition-related risk of morbidity and mortality in hospitalized older patients.[90] In a geriatric trauma patient population, the Geriatric Nutritional Risk Index was found to predict the length of stay and development of postoperative delirium in elderly patients.[91] According to the European Society for Parenteral and Enteral Nutrition (ESPEN), the Mini Nutrition Assessment (MNA) is the most commonly used and highly validated screening tool in older adults, though the requirement for anthropometric measurements and clinical history make implementation challenging in the ICU.[89,92] The Nutrition Risk in the Critically Ill (NUTRIC) score was designed specifically for use in the ICU, relies on clinical data not history or physical examination, and has been associated with increased duration of mechanical ventilation and 28-day mortality.[93]

While preexisting malnutrition may predispose patients to worse outcomes, nutrition requirements during critical illness also influence outcomes, and all critically ill patients are at risk for developing malnutrition. Critical illness is thought to have an acute phase with hemodynamic instability and early metabolic instability with a substantial increase in catabolism followed by later muscle wasting and stabilization of metabolic changes.[94] Current ESPEN guidelines recommend early implementation of oral or enteral feeding that slowly ramps up to full nutritional requirements within 3 to 7 days of admission and consideration of parenteral nutrition by days 3 to 7 if oral or enteral nutrition is contraindicated.[94] Enteral nutrition in older ICU patients preserves intestinal function.[95] While total parenteral nutrition (TPN) provides nutrition to patients with intestinal failure, it is associated with morbidity and mortality, and ESPEN guidelines should be followed with regard to initiation. In older adults, TPN use during hospitalization was associated with increased mortality when compared to younger adults.[96] All decisions on temporary and permanent procedures to supply nutrition to patients should be performed under the overall goals of patient care, as discussed within the Ethics section below.

Given the increased risk of baseline malnutrition, screening for refeeding syndrome and associated electrolyte abnormalities is also critical in the older population. Early screening for malnutrition and rapid steps to begin nutritional supplementation may improve outcomes in the particularly vulnerable population of older adults.

Renal

The kidneys undergo many physiologic changes with age. There is a decrease in renal mass due to loss of renal cortex.[97] This is in conjunction with a decrease in the number of functioning glomeruli and an increase in size of the remaining glomeruli.[98] The effective renal blood flow decreases up to 10% per decade of life.[99] When trending lab data, there is a variable decrease in glomerular filtration rate (GFR) with age, and many GFR calculations do not account for the physiologic changes of aging.[100] With increasing age, the physiologic changes to maintaining sodium homeostasis lead to decreased ability to concentrate urine and potential increased risk for volume depletion.[101]

Acute kidney injury (AKI) in critical illness is common.[102] Geriatric patients are at an increased risk of AKI due to the decrease in effective renal blood flow causing increased susceptibility to episodes of hypotension or reduced cardiac output. In combination with dehydration and disturbances in autoregulation, these episodes can lead to renal ischemia and AKI.[103] Using GFR and serum creatinine to diagnose AKI in older adults has limitations. Serum creatinine levels are less reliable, and an increase in serum creatinine can lag days behind the initial AKI insult.[104]

Acute renal failure in the setting of critical illness raises questions if elderly patients can tolerate the hemodynamic effects of renal replacement therapy (hemodialysis or hemofiltration). Acute illness with sequela of acute renal failure, along with renal replacement therapy, puts patients at risk of hemodynamic instability, decreased cardiac reserve, autonomic dysfunction, bleeding, and neurologic complications.[105] In one study, requirement of dialysis in older patients in the ICU was associated with higher risk of chronic dialysis than in younger patients.[106] Review of current evidence, however, does not show increase in mortality for older patients with acute renal failure requiring dialysis in the ICU when compared to younger patients.[107]

Geriatric patients are more likely to have chronic kidney disease (CKD) due to renal physiologic changes with aging. Geriatric patients on chronic dialysis have high annual mortality risk.[108,109] In the outpatient setting, for geriatric patients with chronic renal disease that progresses to renal failure, goals of care discussion should take place prior to initiating dialysis therapy.[107] Patient and family discussions and education about what chronic hemodialysis entails may help inform decision-making for unplanned hospitalizations or continued decline in renal function. In the acute setting, these goals should be readdressed if a patient declines to renal failure requiring dialysis as part of the holistic approach and prioritizing quality of life.

Infection and Immune System

Aging leads to an age-dependent decline in immune system effectiveness. Known as immunosenescence, these changes include higher level of proinflammatory cytokine secretion at baseline and a decrease in the ability to stimulate the immune response to antigens.[49] This results in chronic hyperstimulation of the immune system and likely higher risk of dysregulated systemic response to infection.

In older patients, respiratory infection is the most common source of sepsis. Patient's age, need for mechanical ventilation, need for renal replacement therapy, and need for inotropic support are all predictive of mortality in older adults with sepsis.[110] Sepsis from a urinary source is the second most common source of infection in septic older patients.[111] Presenting symptoms of urinary infection in geriatric patients can be atypical, leading to delays in diagnosis and often progression of infection prior to initiating appropriate treatments.[112] Finally, decline in immune system function in older patients increases their risk for secondary infections or hospital-acquired infections.

With increasing age, there is evidence that the gut microbiome also undergoes changes, with an increase in pro-inflammatory bacteria associated with inflammatory dysregulation and immunosenescence.[113] Changes in microbiota have been linked to increased intestinal permeability and age-associated inflammation, resulting in greater susceptibility to infections.[114] The microbiome is also affected by diet, lifestyle, medications, and overall health status, and there are many ongoing studies evaluating potential therapeutic targets. These changes in microbiome may also result in a reduction of essential amino acid production that may contribute to poor nutritional status and even sarcopenia in older adults.[113]

Musculoskeletal

Sarcopenia is an aging-related loss of muscle mass and function, which commonly impacts older adults presenting with critical illness.[115,116] In addition, structural and functional alterations in both muscles and nerves may occur throughout the course of critical illness and leave survivors with a new condition termed ICU-acquired weakness (ICUAW).[117,118] Nervous system changes include axonal degeneration, microvascular changes in the setting of sepsis, and channelopathies that all contribute to neuropathy.[119–122] Muscular changes in critical illness can begin early during hospitalization, including early atrophy from increased catabolism and decreased synthesis.[123] Many components of critical illness contribute to loss of muscle mass including inflammation, immobilization, endocrine stress responses, nutritional deficit, and impaired microcirculation.[124] Pro-inflammatory mediators such as TNF alpha, interleukin-1, interleukin-6, GDF-15, illness-induced sodium channel dysfunction, and altered intracellular calcium homeostasis have all been connected to muscle breakdown in critically ill patients.[125]

A retrospective observational study of outcomes in critically ill patients found increased age and sarcopenia were associated with increased hospital length of stay.[126] In addition, studies examining skeletal muscle mass measured on computed tomography imaging found that patients with lower muscle mass on admission to the ICU were more likely to have higher severity of illness during the ICU stay, longer duration of mechanical ventilation, increased length of ICU stay, and higher mortality.[127–130] Similarly, in older adults requiring cardiac surgery, sarcopenia diagnosed by psoas muscle area and handgrip strength predicted longer length of hospital stay.[131] The precise mechanism of developing ICUAW remains unknown; however, studies have shown that patients with increased severity of illness, including sepsis and shock, and increasing degree of multiorgan failure are more likely to develop ICUAW.[132,133]

Proposed methods to prevent muscle loss, sarcopenia, and ICUAW include maintaining normal glycemic levels during hospitalization, reducing duration of immobilization, using electrical muscle stimulation, and employing early enteral nutrition.[134–139] The early catabolic phase during critical illness, however, is not prevented by early parenteral nutrition.[138,139] Early mobilization of ICU patients has been a key area of interest and strategy for reducing the burden of physical decline after critical illness and potentially reducing muscle loss and dysfunction.[140,141] In mechanically ventilated patients, daily physical and occupational therapy sessions that were coordinated with interruption of sedation and initiated within 72 hours of mechanical ventilation improved the likelihood of being discharged with functional independence and reduced days of ICU delirium, days on the ventilator, and length of ICU and hospital stay.[142] Similar findings were reported in a study of early goal-directed mobility in surgical ICU patients.[143] A recent meta-analysis confirmed that physical rehabilitation in the ICU reduced ICU and hospital length of stay and improved physical function at discharge; however, there was no difference in physical function at 6-month follow-up.[144] Another recent meta-analysis comparing efficacy and safety of early mobilization and long-term outcomes found no effect on days alive and out of the hospital up to 6 months, but early mobilization was associated with improved physical function in survivors at

6-month follow-up.[145] In this meta-analysis, early mobilization, however, was also associated with an increase in adverse events potentially due to the mobilization, such as arrhythmia, blood pressure changes, and oxygen desaturation. Neither of these recent meta-analyses focused on outcomes specific to older adults. Future studies are needed to examine interventions that will improve long-term recovery, particularly in older and frailer adults and those with sarcopenia.

Oncologic

Cancer risk increases with age, and ICU admissions related to cancer, cancer treatments (ie, chemotherapy, radiation, surgery), and comorbid conditions are also increasing with the aging of the population. Data suggest that that approximately 20% of all ICU patients have underlying cancer diagnoses.[146] Breast, hematological, lung, colorectal, prostate, pancreatic and biliary, urinary tract, and sarcoma make up the majority of ICU admissions for cancer. The specific care associated with different cancer types, along with toxicities related to specific cancer therapies, is out of the scope of this manuscript. Although increasing age is a risk factor for many cancers, management is not different based on age but is rather centered around the oncologic pathology. Cancer and its therapies are additionally associated with immunosuppression, malnutrition, anemia, and frailty, which have all been previously discussed. A cancer diagnosis carries a slightly higher odds of death after accounting for additional risk factors, and cancer patients have a higher likelihood of death years after discharge following ICU admission.[147] As such, early goals of care and palliative discussions for oncology patients may be warranted, especially in the older patient population with limited neurologic or functional capacity or significant comorbid disease.

Post-Intensive Care Syndrome and Long-Term Outcomes

Post-intensive care syndrome includes the physical, neurocognitive, and psychological symptoms that frequently occur in survivors of critical illness.[148] Together, these symptoms can impact physical function, mental health, and overall quality of life for months to years after hospital discharge.[149–151] In older populations, it is often difficult to qualify deficits found following acute illness as secondary to the illness or attributed to premorbid status or aging. Surrogate markers of pre-illness disability and cognitive function are employed but limited by recall bias of both patients and family members.[152,153] Larger cohort studies have been constructed to understand the impact of critical illness on a population level, understanding that individual patients' experience can be variable.

Physical Disability

Baseline physical function status has been shown in several studies to be either associated with no change in post-discharge physical functional status[154–157] or associated with significant decline.[158–161] These results are limited in interpretation by the retrospective collection of preadmission functional status. Larger population-based studies investigating overall change in functional status have demonstrated that older mechanically ventilated patients have worsened functional status when compared to similar patients who did not require mechanical ventilation—indicating baseline functional impairment is likely associated with worse disability among older ICU survivors.[162] However, the overall link between pre-admission disability and post-survival physical dysfunction remains ill-defined.[163] Regardless of pre-admission functional status, survivors of critical illness experience physical deficits that impair their overall physical function and daily independence.[164] Identifying and optimizing modifiable factors associated with disability including optimizing nutritional status, early mobility, and incorporating care bundles have shown the best success in helping to mitigate the risk of physical disability among these patients.[140,142,165]

Neurocognitive Deficits

Cognitive impairments are prevalent, persistent, and can be severe among adult ICU survivors across all age groups, affecting up to 60% of survivors.[166–169] Baseline cognitive impairment, as well as advanced age, has been shown to be a strong predictor of long-term cognitive impairment among survivors.[169–172] While these strong predictors are non-modifiable, important modifiable factors have also been identified, introducing important targets for clinicians to potentially mitigate the downstream risk of cognitive impairment among older adults.

Delirium is the most prominent independent risk factor for cognitive impairment,[167,173–175] with up to 40% of cases during hospitalization deemed preventable.[176] The most effective strategies to date include multicomponent nonpharmacologic treatment bundles such as the ABCDEF bundle.[44,177–179] There are often barriers or perceived barriers that prevent incorporation of these bundles within the care of older adults. Table 1 outlines the ABCDEF bundle, age-related barriers, and strategies for mitigating these barriers for patients.

Sleep may play an important role in recovery, as sleep disruption has been shown to be associated with worse cognition in older ICU survivors[180] as well as worsened functional decline.[181] Further studies are necessary to define and understand these associations. While other modifiable risk factors have presented within the literature, evidence surrounding their correlation and causation remains mixed.

Older patients are vulnerable to medication side effects due to increased comorbid disease, decreased physiologic reserve, and impaired drug metabolism. Many common medications in the ICU used to treat anxiety, pain, and insomnia are centrally acting, including sedatives, analgesics, antipsychotics, and anticholinergics specifically identified by The American Geriatric Society as potentially inappropriate medications in older adults.[182] After leaving the ICU, these medications are frequently continued in up to a third of all patients, with an unclear understanding of how they may impact long-term health and recovery after the ICU.[183–185] Nonetheless, potentially inappropriate medications should be discontinued as soon as possible as their use is associated with lower quality of life, higher incidence of hospital readmission, worsening cognitive impairment, adverse drug events, and increased mortality in non-critically ill adults.[186–188]

Psychological Symptoms

Up to 30% of ICU survivors experience long-term psychological symptoms from the acute stress, trauma, and anxiety that accompanied their ICU stay.[149,189] These symptoms often include post-traumatic stress symptoms, anxiety, and depression that carry significant implications for patients,[151,190] ranging from impacting daily quality of life, employment, relationships, and worsening cognitive impairment to associated increases in patient mortality.[149,191–193] It can also lead to avoidance behaviors which may potentially impact willingness to continue necessary medical care after discharge.

ICU delirium is a risk factor for the development of neuropsychiatric disorders, perhaps in part due to the distorted memories and experiences that patients can experience while delirious.[151,194] Additional risk factors include socioeconomic status and isolation, both of which in older adults are associated with worsened mental health outcomes following ICU discharge.[195–197] Patient-centered approaches, including palliative aspects, to care such as ICU diaries, reorientation, cognitive and physical stimulation, and family involvement may reduce these psychological symptoms in older ICU survivors by emphasizing patient needs and quality of life goals.[198]

Overall Long-Term Outcomes

Prognosticating outcomes, including survival, is difficult across all patient groups, including older patients. Similar to other age groups, older adults (≥65 years) and very old (>85 years) adults with less comorbidities, lower severity of illness, and lower frailty index scores have shown better survival and function up to 1 year following hospital discharge.[199–203] Age in and of itself should not be a contraindication for ICU admission. The highest proportion of death occurs 6–12 months after hospital discharge, suggesting potential windows for optimum intervention and highlighting the impact of post-discharge impairments.[204] Future research should focus on identifying targets for improvement including post-ICU recovery clinics, rehabilitation, and therapeutic interventions to help identify modifiable factors and guide interventions to continue to improve outcomes among older ICU survivors.

Ethics and End-of-Life Discussions

Age alone is not a reliable predictor of mortality in the ICU, and other systems for assessing severity of illness and risk quantification should be validated and used to guide care-based decisions.[205–208] Acute illness, baseline comorbidities, and frailty should be interpreted alongside specific patient conditions and concerns to guide medical care, as illustrated in Figure 2. Along with defining goals of care, code status and end-of-life discussions are valuable to ensure care teams and families are communicating and informed on risks associated with acute illnesses as well as life-sustaining interventions,

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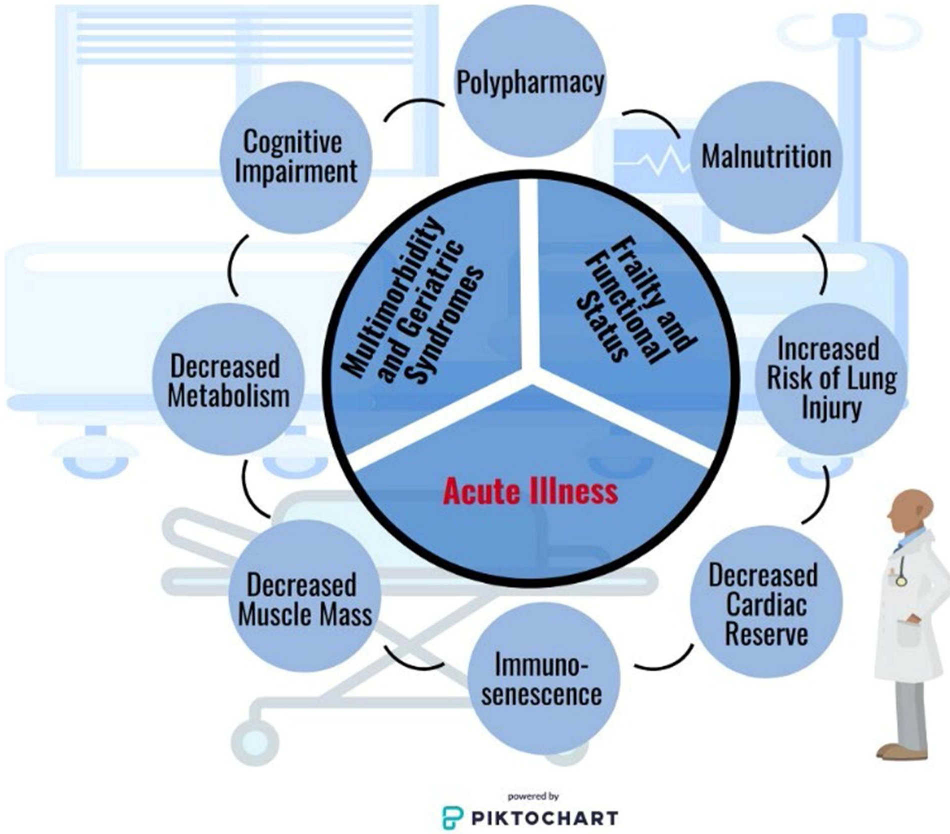

Figure 2 Conditions and concerns for older adults admitted to the intensive care unit. Older adults admitted to the intensive care unit present with a unique constellation of physiologic effects of aging that should be considered. In addition to their acute illness, baseline frailty/functional status, and geriatric syndromes/multimorbidities greatly impact outcomes. Additional influences that must be considered by the clinician includes presenting or iatrogenic polypharmacy and malnutrition as pose as potentially modifiable clinical factors. Physiologic conditions including cognitive impairment, alterations in metabolism, decreased muscle mass, immunosenescence, cardiac reserve, and an increased risk of lung injury are all common among older adults. Image is powered by Piktochart.

regardless of patient status on admission.[209–211] Care teams including social workers, case managers, interpreters, religious members, and palliative care teams can be helpful in aiding and facilitating these conversations within hospital settings with these ancillary teams readily available. Life-prolonging interventions that may not improve quality of life and should be discussed to delineate patient's goals of care may include mechanical ventilation, enteral feeding tube placement, TPN, and tracheostomy.

The ethical conflicts of withholding versus withdrawing care may be avoided by these early discussions.[212,213] Training in goals of care discussions is not ubiquitous in the many pathways to becoming an intensivist, and specific education in leading these discussions is imperative as the ICU patient population ages. The 5M approach is a proposed holistic framework for non-geriatricians to use when approaching care of an older adult. The 5M's: Mind, Mobility, Medications, Multicomplexity, and Matters Most incorporate unique characteristics of older patients in the ICU designed to remind clinicians to frame care goals around patient-specific values.[214] While this is good practice regardless of patient age, these conversations are particularly important in older critically ill adults who represent a higher proportion of mortalities attributed to withdrawal of care compared to younger cohorts.[215,216] This may in part be due to findings that the majority of older adults reported valuing quality of life over life extension—frequently preferring a shorter life expectancy over dying within an ICU.[217–219] Conversations surrounding prolonged mechanical ventilation with the patient, if able to participate, and their family should include tracheostomy procedure details, likely need for prolonged hospitalization, and potential need for long-term acute care facility. Additionally, most older adults reported viewing immobility and ventilator-dependence as equal to or worse than death.[220]

The American Thoracic Society has established five goals of clinician-family communication with the understanding that multiple strategies and organizations go into each and should be individualized to the situation and parties involved.

These goals include (1) establishing a trusting relationship, (2) providing emotional support to families, (3) helping families understand diagnosis, prognosis, and treatment options, (4) allowing clinicians to understand the patient as a person, and (5) creating conditions for careful deliberation about difficult conditions.[221] Strategies used to achieve these goals are often individualized and learned from either experience, colleagues, coursework, or other training as it is generally not yet integrated into medical studies. Patient goals remaining a focus of care is an overarching theme in these efforts. While not unique to older adults, these discussions are imperative within older populations as they experience high rates of both in-hospital and long-term mortality, along with the constellation of syndromes included within post-intensive care syndrome (PICS) that frequently require long-term caregiver support.[222] Together, these add social complexities to already medically complex patients.

Summary and Conclusion

Increasing age of the population means there will be increased demand for specialized geriatric care across medical and surgical specialties, including the ICU. Aging affects multiple organ systems, and these changes must be considered when caring for these patients. The multiorgan physiologic effects of aging, in addition to other complexities associated with geriatric patients, such as frailty and pre-existing comorbidities, all must be considered and incorporated into a greater holistic approach to caring for these patients in the ICU.

Many ICU trials identify mortality as primary outcome; in geriatric patients, however, morbidity and quality of life are often more important than survival. More studies are needed in older ICU patients with morbidity outcomes that affect quality of life. Finally, there is a well-described need for geriatric specific education and further implementation of geriatric knowledge via multidisciplinary ICU teams as the population ages and ICU admissions increase.

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