Editorial

Do hospitals need oncological critical care units?

Abby Koch, William Checkley

Division of Pulmonary and Critical Care, School of Medicine, Johns Hopkins University, Baltimore, MD, USA

Correspondence to: William Checkley, MD, PhD. Division of Pulmonary and Critical Care, Johns Hopkins University, 1800 Orleans Ave Suite 9121, Baltimore, MD 21287, USA. Email: wcheckl1@jhmi.edu.

Provenance: This is an invited Editorial commissioned by the Section Editor Xue-Zhong Xing [National Cancer Center (NCC)/Cancer Hospital, Chinese Academy of Medical Sciences (CAMS) and Peking Union Medical College (PUMC), Beijing, China].

Comment on: Soares M, Bozza FA, Azevedo LCP, *et al*. Effects of Organizational Characteristics on Outcomes and Resource Use in Patients with Cancer Admitted to Intensive Care Units. J Clin Oncol 2016;34:3315-24.

Abstract: Since the inception of critical care as a formal discipline in the late 1950s, we have seen rapid specialization to many types of intensive care units (ICUs) to accommodate evolving life support technologies and novel therapies in various disciplines of medicine. Indeed, the field has expanded such that specialized ICUs currently exist to address critical care problems in medicine, cardiology, neurology and neurosurgery, trauma, burns, organ transplant and cardiothoracic surgeries. Specialization does not only need new infrastructure, but also training and staffing of health care providers, ancillary staff, and development and implementation of processes of care. Oncology is another branch of medicine with growing ICU needs. Given the rise in cancer incidence worldwide and better survival rates alongside advances in chemotherapeutic and surgical options, more cancer patients are nowadays requiring advanced life support for cancer-related complications, treatment-related toxicities and severe infections. Here we provide a brief summary of the current evidence supporting the specialization of critical care and explore three different models of care for critically ill cancer patients, including the development of a specialized oncological ICU. Finally, we also discuss recently published and future research related to the care of critically ill cancer patients.

Keywords: Cancer; oncology; protocols; process improvement; specialty intensive care units

Submitted Jan 04, 2017. Accepted for publication Jan 20, 2017.
doi: 10.21037/jtd.2017.03.11
View this article at: http://dx.doi.org/10.21037/jtd.2017.03.11

Cancer patients admitted to an intensive care unit (ICU) have a unique set of critical care needs due to their underlying disease; time-point in treatment plan; and treatment-related toxicities leading to organ dysfunction, hemodynamic compromise, and infection. It is estimated that as high as 20% of patients admitted to ICUs hold a cancer diagnosis (1,2). New cancer incidence in the United States is estimated to reach 1.7 million in 2016 (3). Five-year survival has improved to 67% for all cancers (3) and recent studies have documented improved ICU survival rates in both solid tumor (4) and hematologic malignancies (5) from an average of 15% to about 50% in the last two decades (6). As cancer treatments improve and options evolve, the knowledge of the potential complications leading to critical illness needs to transcend from the oncology floor to the ICU. For example, anti-PD-1 inhibitor therapy and chimeric antigen receptor T-cell therapy are two new treatments with severe side effect profiles, including pneumonitis and cytokine storm that may lead to a higher rate of ICU admissions (7-9). Moreover the incidence of cancer is only expected to rise, therefore we believe that it is necessary to develop effective models of care for critically ill cancer patients. Several models currently exist but without published comparative effectiveness research studies. In large freestanding cancer hospitals, there may be an ICU for established patients. Some hospitals have distinct oncological ICUs where medical and surgical ICUs are also available. Yet other hospitals have general medical or surgical ICUs where cancer patients are treated alongside other critically ill patients. The question remains: Does the organization of

the ICU or its physical location affect outcomes for cancer patients? Is there a need for specialized oncological ICUs?

The era of specialized critical care

Since the inception of critical care as a formal discipline in the late 1950s (10,11), we have seen rapid specialization to many types of ICUs to accommodate evolving life support technologies and novel therapies. One of the first documented specialized units was developed at the Johns Hopkins Hospital in the 1920s by Walter Dandy, which housed three beds for post-operative neurosurgical patients. Early ICUs were built for close monitoring by physicians and nurses who remained geographically close to the patient to react quickly and provide care (10). As ICU care evolved it focused on providing newly developed supportive measures including advances in mechanical ventilation, renal replacement therapy, continuous hemodynamic monitoring, and extracorporeal support (12). From the growth of the ICU came the need for dedicated critical care physicians (13). Intensivists then brought change to include more patient-centered care and the realization that high-intensity staffing delivered the best care to patients (14-16). With the goal of improving outcomes, specialized ICUs began. Cardiology and Neurology are two clinical specialties that historically have had stand-alone ICUs. Nowadays, other specialized ICUs exist tailored to trauma, burns, organ transplant and cardiothoracic surgeries. But, are we certain that patients have better outcomes because they are treated in a specialized ICU? And if we see added benefit from ICUs organized by specialty, do we need to consider the development of specialized ICUs for cancer patients?

Few studies have examined the benefits of having specialized ICUs on clinical outcomes, and these have shown mixed results. Two small studies reviewed patients admitted to Neurology Critical Care Unit (NCCU) compared to the Medical Intensive Care Unit (MICU) for management of intra-cerebral hemorrhage; one had 1,038 patients (17) and the other had 125 (18). Both studies described lower mortality for patients admitted to an NCCU when compared to a MICU. One of the studies also found shorter hospital length of stay and lower costs of care when admitted to the NCCU (18). Another study reviewed 2,431 patients admitted to a Cardiac ICU managed by a cardiac intensivist or a general cardiologist, and found that patients with a dedicated cardiac intensivist had a lower mortality than those with a cardiologist who did not have specialty critical care training (19). A larger study including 84,182 patients in 124 ICUs across a diverse group of hospitals, however, compared outcomes of critically ill patients admitted to general or ideal specialty ICUs but found no differences in risk-adjusted mortality or ICU length of stay for complex conditions such as acute coronary syndrome, ischemic stroke, intracranial hemorrhage, abdominal surgery, or coronary-artery bypass graft surgery (20). Based on these findings, we still need to better understand the role of specialization in critical care and if it is a worthy investment.

Do patients in ICUs at cancer centers perform better than those in ICUs at general hospitals?

In a recent issue of the *Journal of Clinical Oncology*, Soares *et al.* described how ICU organizational characteristics might affect clinical outcomes and resource utilization in patients with cancer (21). In ORCHESTRA, the authors retrospectively reviewed 9,946 patients admitted to 70 ICUs in Brazil. Of those, 51 were in general hospitals and 19 were in cancer centers. The authors found that the presence of clinical pharmacists in the ICU, presence of ICU protocols, and daily meetings between oncologists and intensivists were associated with lower hospital mortality even after adjustment for hospital case volume (21). Protocols and daily meetings were also associated with more efficient resource utilization.

Do critically ill patients in ICUs at cancer centers perform better than those in ICUs at general hospitals after adjustment for severity? The findings in ORCHESTRA suggest that admission to an ICU in cancer centers was not associated with lower ICU mortality, hospital mortality or better resource utilization when compared to ICU admissions in general hospitals. Interestingly, the studied ICUs in a cancer center had a greater incidence of the measures that decreased mortality than in general hospitals. The presence of clinical pharmacists on daily rounds was 47% in ICUs of cancer centers when compared to 16% in general hospitals. A daily meeting between oncologists and intensivists for all patients was documented in 90% of cancer centers and in just 53% of general hospitals. Unmeasured confounders in the patient population or residual confounding may have affected their results. Using insurance as a surrogate for socioeconomic status and access to care, ICU patients treated at cancer centers more frequently had government-sponsored health insurance (31% *vs.* 7%, respectively) when compared to those in ICUs at general hospitals who more frequently had private health insurance (57% *vs.* 81%, respectively). Patients admitted to ICUs in cancer centers

appeared to be sicker on admission: they had higher SOFA scores when compared to those admitted in ICUs of general hospitals (median organ failures of 3 and 1, respectively) and were frequently on mechanical ventilation on day one of the ICU stay (24% *vs.* 17%, respectively). Other potential confounding variables in ICU organizational characteristics may have affected the mortality benefit of an ICU in a cancer center. The availability of palliative care services was more common in patients admitted to ICUs in cancer centers when compared to general hospitals (42% *vs.* 8%, respectively). Increased use of palliative care services may have led to increased discussion of goals of care and potential transition to comfort care measures. It is unclear if those patients made comfort care who did not survive to discharge were included in the reported hospital mortality. The use of regular multidisciplinary rounds was less frequent in cancer centers with 68% meeting >5 days per week compared to 90% of general hospitals. The lower frequency of multidisciplinary rounds in cancer centers may have contributed to the equivocal resource utilization when compared to general hospitals. Many of the protocols reviewed in this study affect all critically ill patients alike and were not specific to cancer patients. These were used in similar frequency in general hospital and cancer center ICUs with the exception of the cerebrovascular accident protocol, which was more prevalent in cancer center ICUs. Cancer specific protocols were used in 79% of cancer ICUs compared to 27% of general ICUs, and included febrile neutropenia, invasive fungal infection, and tumor lysis syndrome. In multilevel multivariable analysis, however, the presence of these cancer-specific protocols did not affect clinical outcomes. Perhaps the cancer specific protocols here did not address the needs of the patient population under study. Only 10% of the patients had hematologic malignancies, and the listed protocols address treatment and monitoring for common complications more frequently associated with hematologic malignancies rather than solid tumors.

Which model of oncological intensive care may be most cost-effective?

In light of the organizational characteristics reported by ORCHESTRA, we explore three models of care for critically ill cancer patient. First, we considered a model with admission to a distinct oncological ICU treating only patients with cancer, with critical care trained intensivists on staff who have daily meetings to collaborate with oncologists. Specialized oncological critical care ideally would lead to a more focused knowledge base, and experience with common disease processes and treatment complications. Higher volume of exposure leads to improved outcomes (22). The use of clinical pharmacists in daily rounds has previously been reported to improve outcomes and the study reviewed here supports the same (23-25). Staffing an oncological ICU with nurses and pharmacists focused on the concomitant oncology and critical care needs would likely have added benefit. Daily meeting between intensivists and oncologists improve mortality and is a similar structure change to those previously reported showing better communication strategies, including daily goal checklists and daily meetings between the attending and charge nurse (26). An oncological ICU may help to geographically facilitate daily meetings and ongoing collaboration of care. Palliative care services benefit many ICU patients and are frequently relevant to cancer patients. In this model those services can be organized into the daily structure of the ICU to help facilitate goals of care discussion with the oncology and the ICU team. However, while the specialized care provided by an oncological ICU might lead to improved care, it is also cumbersome and costly to develop, staff, and implement. There is no proven model that has been studied to implement an oncological ICU, which would lead to a long development time. Another potential downfall of a specialized ICU is the tunnel vision encountered with a narrowed scope of practice. If only seeing cancer patients one may be constantly looking for treatment related illness and overlook other general illnesses that affect our aging population. Generalized ICUs see a variety of illnesses that can be used as reference in the care of oncology patients.

Second, we considered a model with admission to a general ICU treating patients with a variety of illnesses including cancer, staffed by a critical care trained intensivist with an early, automated consult to oncology for patients with a cancer diagnosis. Perhaps a multidisciplinary approach to cancer critical care is more important than high volume exposure to the same disease process. In a high intensity-staffed general ICU, an automated consult to oncology may help facilitate co-management of the patients. Changing structure and processes of care in existing ICUs may be more cost effective than creating a specialized ICU for cancer patients, especially in smaller hospital networks. General intensivists have a broad multidisciplinary knowledge base and see a wide variety of disease processes. Clinical pharmacists are often already part of daily rounds in general ICUs. With the use of electronic medical records

and computerized patient order entry in many hospitals it would be easy to implement an automated consult based on admission diagnosis. Early consult would help organize daily meetings between oncologists and intensivists at the time of admission. This model could also be expanded to incorporate palliative care services by including them as a second automated consult at the time of admission. The concept of a consult according to diagnosis has been previously studied using *Staphylococcus aureus* bacteremia and infectious disease consultation. Several single center studies and a larger multi-center study have found that requesting an infectious disease consult based on documented *S. aureus* infection lead to improved diagnostic evaluation, guideline driven treatment, and lower hospital mortality (27-30). While consults for these studies were not automatically generated, they resulted in better clinical outcomes. Automation in this model as described above could lead to more frequent consultation to oncology and better outcomes, however it would be limited by proper documentation of a computerized problem list to trigger a consult. This approach would also place additional burden on the oncology consult service to accommodate. While less costly than adding an entire new ICU, it is still a resource rich model that may be difficult to implement widely. This model would also be less effective in low case volume hospital centers that do not see many critically ill cancer patients and do not have readily available oncologists to staff consults. Another limitation of this model is that pharmacists working in the general ICU may have less specialized knowledge of cancer specific treatments and adverse effects.

Third, we considered a final model with admission to a general ICU, treating patients with a variety of illnesses including cancer, staffed by a critical care trained intensivist but with fully implemented co-developed, ICU- and cancer-specific protocols. In this model an oncology and/or palliative care consult would be done at the discretion of the intensivist. Processes of care interventions like creating and implementing protocols are thought to alleviate provider variation in care and improve adherence to a pre-determined standard of care (31). The list of cancer specific protocols must be expanded as rapidly as cancer and ICU treatments evolve. Perhaps a novel set of cancer specific protocols when applied to the appropriate patient population would change outcomes. Authors of the recently published EMPIRICUS trial recommend against empirically treating ICU sepsis or *Candida* spp. colonization with echinocandins based on their findings (32,33). That study, however, did not include neutropenic or bone marrow transplant patients who are frequently placed on empiric anti-fungal coverage. This is an example of the need for awareness of both oncology and ICU studies and how different protocols should be used for different patient populations within a general ICU to avoid causing harm (31). The use of protocols co-developed by oncologists and intensivists may be the way to bridge the knowledge gap between medical specialties and improve outcomes for cancer patients in a general ICU while utilizing an existing infrastructure of high intensity staffing. Soares *et al.* did not see improved outcomes with cancer specific protocols (21). Perhaps this is due to the number of or the specific protocols used. There are conflicting data regarding whether a higher number of protocols is associated with improved clinical outcomes and resource use. Sevransky *et al.* of the United States Critical Illness and Injury Trials Critical Illness Outcomes Study reported a median of 19 protocols in United States ICUs, but having a higher number of protocols did not affect clinical outcomes or compliance with the use of those protocols (34). Authors of ORCHESTRA reported a mean of 7 protocols in Brazilian ICUs and having a higher number of protocols (as high as 10) showed improved resource use and patient mortality (1). This difference may represent protocol fatigue at levels greater than 19. We have not yet determined the most effective use of protocols in the ICU.

What kind of research is necessary to support the development of oncological ICUs?

Limitations of the study as reported by its authors provoke further questions. First, this study was done in Brazil. There is a known disparity in outcomes and ICU admission policies among international hospitals based on each countries global national income, and access to care in low resource settings (35,36), and as such this may not be translatable on a global level. Although these disparities make studies such as this one difficult to generalize to other ICUs, it is reasonable to use improvements in processes of care as a low cost method to decrease the differences among global ICUs. Second, Soares *et al.* did not evaluate if protocols were actually implemented and there was no evaluation of what was discussed in the daily meetings between oncologist and intensivists. The details of each intervention need to be further delineated to allow global implementation of these processes. Third, only 10% of patients had hematologic malignancies, a group with a high amount of treatment related critical illness and associated high mortality if admitted to the ICU (37). Because of the

small number of patients with hematologic malignancies, the study by Soares *et al.* may be underpowered to represent this group. Finally, the study included both medical and surgical patients. It is reasonable to believe that a surgical oncology patient post-operation from resection of a solid tumor is very different from a medical oncology patient having treatment related complications. A recent study of 69 ICUs in the United States showed that surgical ICU mortality was 5.6% lower than in medical ICUs (26) and lends support to the notion that surgical oncology patients who are critically ill may have a different hospital course.

Further research is needed to expand on the positive findings of this study. We need to determine which protocols work and which implementation processes lead to the highest compliance. Daily meetings between intensivists and oncologists, if implemented, should have strict guidelines on what points are discussed, and what should be included in the cancer patient specific ICU daily goals checklist. Future studies are needed to identify how cancer ICUs are currently organized, and the differences among them to truly determine if we can compare them directly to medical and surgical ICUs, which have been established for many years in general hospitals.

Conclusions

We support the need for cancer-specific guidelines for ICU admission and protocols for care that can be implemented in any ICU, general or cancer specific. If future studies show the added-value of an oncological ICU, then further evaluation should be done, based on regional cancer prevalence and geographic resources, to most effectively transfer those cancer patients needing ICU level of care to a center with the infrastructure of a dedicated high intensity staffed oncological ICU.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Soares M, Bozza FA, Angus D, et al. Organizational characteristics, outcomes, and resource use in 78 Brazilian intensive care units: The ORCHESTRA study. Intensive Care Med 2015;41:2149-60.
2. Encina B, Lagunes L, Morales-Codina M. The Immunocompromised oncohematologial critically ill patient: considerations in severe infections. Ann Transl Med 2016;4: 327-30.
3. SEER Stat Fact Sheet: Cancer of Any Site. Seer.cancer.gov. Accessed 12/24/2016.
4. Fisher R, Dangiosse C, Crichton S, et al. Short-term and medium-term survival of critically ill patients with solid tumors admitted to the intensive care unit: a retrospective analysis. BMJ Open 2016;6:e011363.
5. Bird GT, Farquar-Smith P, Wigmore T, et al. Outcomes and prognostic factors in patients with haematological malignancy admitted to a specialist cancer intensive care unit: a 5 yr study. British Journal of Anaesthesia 2012;108:452-9.
6. Azoulay E, Soares M, Darmon M, et al. Intensive care of the cancer patient: recent acheivements and remaining challenges. Annals of Intensive Care 2011;1:5.
7. Naidoo J, Wang X, Woo KM, et al. Pneumonitis in Patients Treated with Anti-Programmed Death-1/Programmed Death Ligand 1 Therapy. J Clin Oncol 2017;35:709-17.
8. Nishino M, Chambers ES, Chong CR, et al. Anti-PD1 Inhibitor-Related Pneumonitis in Non-Small Cell Lung Cancer. Cancer Immunol Res 2016;4:289-93.
9. Bonifant CL, Jackson HJ, Brentjens RJ, et al. Toxicity and Management in CAR T-cell therapy. Mol Ther Oncolytics 2016;3:16011.
10. Vincent JL. Critical care--where have we been and where are we going? Crit Care 2013;17 Suppl 1:S2.
11. Kelly FE, Fong K, Hirsch N, et al. Intensive Care Medicine is 60 Years Old: The History and Future of the Intensive Care Unit. Clin Med (Lond) 2014;14:376-9.
12. Rosengart MR, Pinsky MR. Origins of the Critically Ill: The Impetus For Critical Care Medicine. In: Scale DC, Rubenfeld GD. editors. The Organization of Critical Care: An Evidence Based Approach to Improving Quality. 2014, IX, 284P.
13. Safar P, Grenvik A. Critical care medicine. Organizing and staffing intensive care units. Chest 1971;59:535-47.
14. Manthous CA. Leapfrog and critical care: evidence- and reality-based intensive care for the 21st century. Am J Med 2004;116:188-93.
15. Wilcox ME, Chong CA, Niven DJ, et al. Do Intensivist Staffing Patterns Influence Hospital Mortality Following

ICU Admission? A Systematic Review and Meta-Analysis. Crit Care Med 2013;41:2253-74.
16. Gasperino J. The Leapfrog initiative for intensive care unit physician staffing and its impact on intensive care unit performance: a narrative review. Health Policy 2011;102:223-8.
17. Diringer MN, Edwards DF. Admission to a neurologic/neurosurgical intensive care unit is associated with reduced mortality rate after intracerebral hemorrhage. Crit Care Med 2001;29:635-40.
18. Mirski MA, Chang CW, Cowan R. Impact of a neuroscience intensive care unit on neurosurgical patient outcomes and cost of care: evidence-based support for an intensivist-directed specialty ICU model of care. J Neurosurg Anesthesiol 2001;13:83-92.
19. Na SJ, Chung CR, Jeon K, et al. Association Between Presence of a Cardiac Intensivist and Mortality in an Adult Cardiac Care Unit. J Am Coll Cardiol 2016;68:2637-48.
20. Lott JP, Iwashyna TJ, Christie JD, et al. Critical Illness Outcomes in Specialty versus General Intensive Care Units. Am J Respir Crit Care Med 2009;179:676-83.
21. Soares M, Bozza FA, Azevedo LCP, et al. Effects of Organizational Characteristics on Outcomes and Resource Use in Patients with Cancer Admitted to Intensive Care Units. J Clin Oncol 2016;34:3315-24.
22. Kahn JM, Goss CH, Heagerty PJ, et al. Hospital Volume and the Outcomes of Mechanical Ventilation. N Engl J Med 2006;355:41-50.
23. MacLaren R, McQueen RB, Campbell J. Clinical and Financial Impact of Pharmacy Services in the Intensive Care Unit: Pharmacist and Prescriber Perceptions. Pharmacotherapy 2013;33:401-10.
24. MacLaren R, Bond CA, Martin SJ, et al. Clinical and economic outcomes of involving pharmacists in the direct care of critically ill patients with infections. Crit Care Med 2008;36:3184-9.
25. Preslaski CR, Lat I, MacLaren R, et al. Pharmacist Contributions as Members of the Multidisciplinary ICU Team. CHEST 2013;144:1687-95.
26. Checkley W, Martin GS, Brown SM, et al. Structure, process and annual intensive care unit mortality across 69 centers: United States Critical Illness and Injury Trials Group Critical Illness Outcomes Study (USCIITG-CIOS). Crit Care Med 2014;42:344-56.
27. Bai AD, Showler A, Burry L, et al. Impact of Infectious Disease Consultation on Quality of Care, Mortality, and Length of Stay in Staphylococcus aureus Bacteremia: Results From a Large Multicenter Cohort Study. Clin Infect Dis 2015;60:1451-61.
28. Robinson JO, Pozzi-Langhi S, Phillips M, et al. Formal Infectious Disease Consultation is Associated with Decreased Mortality in Staphylococcus aureus Bacteremia. Eur J Clin Microbiol Infect Dis 2012;31:2421-8.
29. Lahey T, Shah R, Gittzu J, et al. Infectious Diseases Consultation Lowers Mortality from Staphylococcus aureus Bacteremia. Medicine (Baltimore) 2009; 88:263-7.
30. Suanderson RB, Gouliouris T, Nickerson EK, et al. Impact of routine bedside infectious disease consultation on clinical management and outcome of Staphylococcus aureus bacteraemia in adults. Clin Microbiol Infect 2015;21:779-85.
31. Chang SY, Sevransky j, Martin GS: Protocols in the Management of Critical Illness. Critical Care 2012;16:306-11.
32. Timsit JF, Azoulay E, Schwebel C, et al. Empirical Micafungin Treatment and Survival Without Invasive Fungal Infection in Adults with ICU-Acquired Sepsis, Candida Colonization, and Multiple Organ Failure: The Empiricus Randomized Clinical Trial. JAMA 2016;316:1555-64.
33. Siddharthan T, Karakousis PC, Checkley W. Empirical Antifungal Therapy in Critcally Ill Patients With Sepsis: Another Case of Less is More in the ICU. JAMA 2016;316:1549-50.
34. Sevransky JE, Checkley W, Herrera P, et al. Protocols and Hospital Mortality in Critically Ill Patients: The United States Critical Illness and Injury Trials Group Critical Illness Outcomes Study. Crit Care Med 2015;43:2076-84.
35. Vincent JL, Marshall JC, Namendys-Silva SA, et al. Assessment of the worldwide burden of critical illness: the intensive care over nations (ICON) audit. Lancet Respir Med 2014;2:380-6.
36. Miele CH, Checkley W. Defining ICU Structure and Process: Working Toward a Worldwide Agenda. Critical Care Medicine 2016;44:1952-3.
37. Jackson K, Mollee P, Morris K, et al. Outcomes and prognostic factors for patients with acute myeloid leukemia admitted to the intensive care unit. Leukemia & Lymphoma 2014;55:97-104.

Cite this article as: Koch A, Checkley W. Do hospitals need oncological critical care units? J Thorac Dis 2017;9(3):E304-E309. doi: 10.21037/jtd.2017.03.11

