Published in final edited form as:

J Intensive Care Med. ; : 885066617748874. doi:10.1177/0885066617748874.

Outcomes of ICU Admission of Patients With Progressive Metastatic Gastrointestinal Cancer

Andrew S. Epstein, MD¹, Andrew Yang, MD², Lauren E. Colbert, MD, MSCR³, Louis P. Voigt, MD¹, Jason Meadows, MD¹, Jessica I. Goldberg, NP⁴, and Leonard B. Saltz, MD¹

¹Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA

²Department of Medicine, Brown University School of Medicine, Providence, RI, USA

³Department of Radiation Oncology, MD Anderson Cancer Center, Houston, TX, USA

⁴Department of Nursing, Memorial Sloan Kettering Cancer Center, New York, NY, USA

Abstract

Background: Data on the outcomes of intensive care unit (ICU) admissions for patients with advanced incurable chemoresistant solid tumor malignancies, and the benefits of subsequent/post-ICU anticancer treatments are limited but have end-of-life and ethical implications.

Methods: An institutional database was queried to identify patients of the gastrointestinal (GI) medical oncology service of Memorial Sloan Kettering Cancer Center with 1 ICU admission during 2014. Records were reviewed for evidence of cancer control from cancer treatment after the ICU admission.

Results: Twenty-eight patients who had progressed beyond at least first-line chemotherapy for metastatic GI adenocarcinoma were admitted to the ICU for sequelae of progressive clinical deterioration. The most frequent reasons for ICU admission were sepsis (39%) and acute respiratory failure (29%). Ten patients died in the ICU, 3 died during the same hospitalization after ICU discharge, and 15 were discharged from the hospital. Of these 15, the median survival from hospital discharge was 2.2 months and 6 received further chemotherapy but with no evidence of clinical benefit. Of these 6, 3 lived over 5 months but the treatment of 5 entailed recycling of previously ineffective chemotherapy agents (3) or those originally used in the adjuvant setting (2). Two of these patients received liver-directed therapy without benefit.

Conclusions: Admissions to the ICU in this cancer population were associated with high morbidity and mortality and did not result in benefit from subsequent cancer treatment. These data can be used to help establish realistic expectations and care goals in previously treated patients having metastatic GI cancer with clinical deterioration.

Corresponding Author: Andrew S. Epstein, Department of Medicine, Memorial Sloan Kettering Cancer Center, 300 E. 66th Street, Room 1013, New York, NY 10065, USA., epsteina@mskcc.org.

Authors' Note

This work was presented in abstract form at the annual meeting of the American Society of Clinical Oncology (ASCO), in Chicago, 2016.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Keywords

cancer; end-of-life care; intensive care

Introduction

One in 5 people in the United States receives care at least once in an intensive care unit (ICU) at the end of life.¹ This resource utilization is more than twice as common in the United States than several other developed countries and with no clear relative overall survival benefit.² Moreover, the US' ICU utilization makes up a significant proportion of the Medicare expenditures in the last year of life.³ Intensive care unit care at the end of life has drawbacks in that it can sometimes result in burdensome, nonbeneficial, and potentially detrimental care.⁴ In addition, family members of patients with cancer admitted to an ICU in the last 30 days of life are less likely to report high-quality, end-of-life care compared to a simultaneous cohort of family members of patients with cancer who had not been admitted to an ICU.⁵ The same study also demonstrated correlations between both earlier hospice referrals and not dying in a hospital, with better end-of-life care ratings.⁵

Although it is widely assumed that benefits of ICU care are more likely to be realized by patients with reversible conditions, and less so for patients with progressive and treatment-refractory cancers, there are only limited data regarding outcomes in patients with cancer, and further data are needed to adequately assist clinicians in triaging patients in whom ICU care is being considered. Furthermore, such data would provide a tool for clinicians to more effectively (both more clearly and compassionately) explain to such patients with cancer and their loved ones why ICU care would, or would not, be a reasonable approach to matching medical care to an individual patient's goals. This would also contribute to ethically sound care being delivered as well.

One common hope for patients with cancer and their loved ones, especially for those whose illnesses are worsening despite cancer treatments, is that future cancer treatments be administered, with the goal of improving quality and length of life. It is however unclear whether ICU admissions result in long-term survival or the ability to administer subsequent cancer treatments and whether such treatments benefit patients. In this study, we hypothesized that ICU admissions for patients with complications of progressive gastrointestinal (GI) cancers are associated with not only poor prognoses but also a lack of benefit from future cancer treatment. We therefore examined the ICU admissions over the course of 1 year at a comprehensive cancer center of patients with advanced GI cancers, which is a large and heterogeneous patient population.

Methods

We queried our institution's electronic database to identify those patients who were admitted to the GI medical oncology inpatient service of Memorial Sloan Kettering Cancer Center (MSKCC) from January 1, 2014, to December 31, 2014, and who were admitted to the ICU during the course of their admission.

Data abstracted included MSKCC medical record number, name, age, sex, marital status, race, type of cancer, date and reason for ICU admission and subsequent ICU stay, sources of admissions (emergency department vs hospital wards), intubation and use of vasopressors in the ICU, Mortality Probability Model II score⁶ on ICU admission, date of discharge from the ICU, date of discharge from the hospital, date of death, and the dates of their next oncology appointment and next chemotherapy.

For the purposes of this study, and as in Figure 1, we excluded any patient with multiple malignancies, patients with well-differentiated neuroendocrine tumors, patients who did not have metastatic disease, patients who were cancer treatment naive or on first-line cancer therapy, and patients admitted to the ICU for postprocedural (surgical, endoscopic, or interventional pulmonology or radiology) complications or acute GI bleeding. Our rationale for this was that postprocedural complications, and GI bleeds are often events that are able to be reversed or at least temporized with ICU-level care.

With the approval of the institutional review board of MSKCC, we performed an analysis with the purpose of identifying the extent of clinical benefit derived from posthospital discharge chemotherapy in this specific subgroup of patients. To this extent, charts were reviewed in detail independently by 3 study authors (A.Y., as well as A.S.E. and L.E.C., who are both GI medical oncologists) for all patients who survived to hospital discharge and who went on to receive chemotherapy. A clinical benefit from chemotherapy was defined as radiographic evidence of either disease stability or regression as well as if patients' symptoms and functional status were documented to have improved with post-ICU chemotherapy. We also analyzed receipt and benefit from nonchemotherapy cancer treatments such as liver-directed therapies.

Results

We identified 118 patients with GI cancer admitted to the ICU from January 1, 2014, to December 31, 2014. We excluded 26 patients with nonmetastatic or locally advanced (inoperable) disease, 3 patients with multiple malignancies, 5 patients with well-differentiated neuroendocrine tumors, 36 patients who were cancer treatment naive or on first-line cancer therapy only, 6 patients admitted to the ICU for postoperative monitoring only, 13 patients admitted solely for GI bleeding, and 1 patient who was admitted for a chemotherapy-related hypersensitivity reaction. Ultimately, 28 patients with progressive cancers despite first-line chemotherapy were analyzed (Figure 1).

Of these patients, the median age was 62 years (range 38–80), the most common cancers were colon (36%) and pancreatic (32%), and the median number of lines of prior chemotherapy was 2 (Table 1). The most common reasons for ICU admission were sepsis (39%) and acute respiratory failure (29%). Intensive care unit mortality was 36% (n = 10), and overall hospital mortality (death during the same hospitalization after discharge from the ICU) was 47% (n = 13); 15 (53%) patients were discharged alive from the hospital. Of the 18 who survived to ICU discharge, 1 (6%) was intubated during the admission, 32% received vasopressors during their ICU stay, and 32% were admitted from a medical floor. In contrast, of those who did not survive their ICU stay (n = 10), 30% were intubated on

admission to the ICU, 80% received vasopressors during the course of their ICU stay, and 80% were admitted from a medical floor (Table 2). None of the 28 patients underwent hemodialysis.

Of the 15 patients who survived to hospital discharge, the median overall survival was 68 days (range 10–302), 6 (40%) were alive at 3 months, 2 (13%) were alive at 6 months, and the median number of readmissions to MSKCC was 1 (range 0–9). Of these 15 patients, 2 were readmitted not only to MSKCC but also to the MSKCC ICU (each 3 times).

Of the 15 patients surviving to hospital discharge, 6 (21%) received further chemotherapy after discharge, but none showed evidence of clinical benefit (Table 3). Of these 6, 3 patients underwent treatment that entailed a recycling of chemotherapy agents that had previously resulted in disease progression, and 2 were retreated with agents originally used in the adjuvant setting. The medical records reflected in 3 of these 6 patients that their medical treatment teams had recommended a transition to comfort-directed care through hospice but that these recommendations had been declined. Two of these 6 patients received liver-directed therapy: One was hepatic artery chemotherapy infusion for a patient with diffusely metastatic colon cancer whose metastases were originally confined to the liver, and the other was yttrium-90 microsphere-selective internal radiotherapy for a patient with cholangiocarcinoma whose metastases were predominantly in the liver. Neither of these patients experienced radiographic disease stability or improvement. Agreement of lack of benefit was unanimous by all 3 independent reviewers for all post-ICU cancer treatments.

Discussion

Intensive care unit care places a substantial physical and emotional burden on patients and their families.^{4,5,7} Presumably, the expectation of such ICU care for patients with cancer would be prolonged survival. This seems to be related, at least in part, to patients' hope for reinitiation of effective anticancer therapy. Our data indicate that these expectations were not met for the patients in our study. Of the 28 patients in our study, only 2 were alive at 6 months from ICU discharge, and none received chemotherapy or anticancer treatment that showed evidence of efficacy. These data do not support the use of ICU care as a means to achieve further effective chemotherapy in this patient population.

These data, while at first glance small in number (28 patients), are important because they can be used to help establish realistic expectations and care goals in a specific but common population, namely, previously treated patients having metastatic GI cancer with clinical deterioration not attributable to a recent procedure and not focally treatable such as for GI bleeding. Such patients and their families deserve clear and compassionate guidance about the fact that such clinical decline is associated with high morbidity and mortality, where most patients die in less than 6 months and none ultimately ever receive cancer treatment that benefits them. For these patients, a transition to best supportive care, away from cancer testing and treatment, can be advocated, and hospice can be described in full and recommended, as an additional layer of support on top of the oncology team's primary support, which can continue as much as needed. A clearly stated direction (e.g. "we know from many prior experiences that further cancer treatment will not help someone in your

situation live longer or better”) is made possible by these data, liberating all parties involved (patients, families and clinicians) of the uncertainty that often manifests in statements such as “it’s unclear if further cancer treatment will help, or not.” Such uncertainty, as well as an oft-perceived “terrible choice”⁸ of either continuing cancer-directed therapy or transitioning to best supportive care via the hospice insurance benefit, is one of the most challenging aspects in clinical oncology. Furthermore, recent data show that bereaved family members of patients with advanced cancer perceive lower quality end-of-life care when patients are in an ICU close to death, die in a hospital, or have a hospice length of stay <3 days.⁵ The prognostic and predictive value of our data may serve as an adjunct tool to improve the end-of-life care experience in patients with progressive cancer.

These findings have ethical implications relating to ethical principles, including doing no harm. It can also help with the delivery of optimally just care by ensuring resources in the ICU are being allocated to the patients most likely to benefit. Finally, by aiding clinicians in assessing what patients and families are hoping for and how certain medical treatments will and will not result in certain outcomes, our results can enhance beneficence by facilitating transitions in care for patients with progressive cancer at the end of life.

Our data are in line with and add to the recent literature on the subject of ICU care for patients with cancer. While we did not analyze what proportion of our center’s total patients with cancer was represented by our cohort, recent data describe that approximately 1 in 20 patients with a solid tumor is admitted to an ICU within the first 2 years of their diagnosis,⁹ and our study provides the site- and episode-specific information about such solid tumor ICU admissions that has been called for¹⁰ in the wake of such cancer registry data research.⁹ A different US institution recently presented the characteristics of their ICU admissions for patients with cancer and found that most deaths in the ICU consisted of advanced disease and/or poor clinical performance status,¹¹ that center’s experience agrees with our findings, and that the outcomes of patients with cancer in ICUs entail high morbidity and mortality. Those investigators’ findings also suggest that almost half of their ICU admissions were potentially avoidable,¹¹ although no specific criteria exist for such preventability of ICU admissions. Ongoing investigations into which patients would most benefit from ICU care, and what advance care planning is needed upstream of the ICU to best evaluate patient and family values is therefore needed such that subsequent care delivered can be married to such goals and expectations. Such early assessment of “the patient’s voice” has recently been described as a strategy for critically ill patients with cancer in whom ICU care is being considered,¹² and our study contributes to this strategy. If a patient or family is hoping for more cancer treatment in order to live longer and better, then our data can be used as a tool to clearly and compassionately guide the patient’s hope toward an attainable goal.

Our study has limitations, one being its retrospective methodology, thereby limiting certainty about patient clinical characteristics and important outcomes such as quality of life for the patients and families in our study. However, the authors uniformly agreed on the lack of benefit (on radiographic and/or symptom grounds) for the patients who ultimately received cancer treatment after ICU stay, an important outcome which we identified prestudy. While it would be unlikely for clinical benefit to be obtained and not documented in the medical record, it is nonetheless possible that such occurred. Also, it was not possible to ascertain

through chart review exactly what was discussed between clinicians, patients, and their loved ones regarding the potential benefits and harms of ICU admission. Finally, while it would have been helpful for us to know which patients were considered for but ultimately not admitted to the ICU, we focused on those patients who were in order to most specifically answer our main question about what happens to this population in and after ICU, including if post-ICU cancer treatment is beneficial.

Additionally, our study was limited to patients at a single cancer center with cancers of the GI system only. Other practice settings such as other cancer centers, or noncancer center community practices, may have different results than seen in this population. The population with GI cancer is a large and heterogeneous one, and thus generalizability may be better in this setting using detailed, patient-level data rather than large data base studies. For instance, a recent retrospective study¹³ of outcomes in patients with solid tumors over 65 years of age admitted to the ICU was larger than ours and demonstrated ICU mortality similar to that seen in our population, but the heterogeneity of the all solid tumor population precluded clear conclusions (despite the study's multivariate analyses) about the utility of ICU care in one specific population subset.

Despite these limitations, and while future studies would be helpful to further address the validity and generalizability of our findings, these data nonetheless at least currently suggest that patients with progressive GI cancers will not benefit from further cancer treatment after an ICU stay for nonreversible medical deterioration. Instead, ICU resources need to be reserved for patients who might benefit, such as those with acute decompensation from GI bleeding or periprocedural complications. Patients with progressive and nonreversible sequelae of their advanced cancers may be better managed on general medical floors with ongoing discussions with patients and families about goals of care. Communication between oncologists and intensivists about ICU patients with cancer has recently been shown¹⁴ to be one of the organizational characteristics associated with decreased mortality in ICUs serving patients with cancer. We did not analyze this characteristic in our study, but future quality improvement research could examine this aspect of care, both for patients once they are admitted to the ICU and earlier, such as when patients on the wards or emergency departments are being evaluated for a potential ICU admission. We therefore hope that our data serve as a communication tool to facilitate optimally ethical and shared decision-making for all persons involved, rather than a perceived barrier for patients and families struggling with the end-of-life realities of a progressive cancer.

Acknowledgments

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This research was funded in part through the NIH/NCI Cancer Center Support Grant P30 CA008748.

References

1. Angus DC, Barnato AE, Linde-Zwirble WT, et al. Robert Wood Johnson Foundation ICU End-Of-Life Peer Group. Use of intensive care at the end of life in the United States: an epidemiologic study. *Crit Care Med* 2004;32(3):638–643. [PubMed: 15090940]

2. Bekelman JE, Halpern SD, Blankart C, et al. International Consortium for End-of-Life Research (ICELR). Comparison of site of death, health care utilization, and hospital expenditures for patients dying with cancer in 7 developed countries. *JAMA* 2016;315(3):272–283. [PubMed: 26784775]
3. Riley GF, Lubitz JD. Long-term trends in Medicare payments in the last year of life. *Health Serv Res* 2010;45(2):565–576. [PubMed: 20148984]
4. Wright AA, Zhang B, Ray A, et al. Associations between end-of-life discussions, patient mental health, medical care near death, and caregiver bereavement adjustment. *JAMA* 2008;300(14): 1665–1673. [PubMed: 18840840]
5. Wright AA, Keating NL, Ayanian JZ, et al. Family perspectives on aggressive cancer care near the end of life. *JAMA* 2016; 315(3):284–292. [PubMed: 26784776]
6. Salluh JIF, Soares M. ICU severity of illness scores: APACHE, SAPS and MPM. *Curr Opin Crit Care* 2014;20(5):557–565. [PubMed: 25137401]
7. Wright AA, Keating NL, Balboni TA, Matulonis UA, Block SD, Prigerson HG. Place of death: correlations with quality of life of patients with cancer and predictors of bereaved caregivers' mental health. *J Clin Oncol* 2010;28(29):4457–4464. [PubMed: 20837950]
8. Casarett DJ, Fishman JM, Lu HL, et al. The terrible choice: reevaluating hospice eligibility criteria for cancer. *J Clin Oncol* 2009;27(6):953–959. [PubMed: 19114698]
9. Puxty K, McLoone P, Quasim T, Sloan B, Kinsella J, Morrison DS. Risk of critical illness among patients with solid cancers: a population-based observational study. *JAMA Oncol* 2015;1(8): 1078–1085. [PubMed: 26313462]
10. Todd KH. Critical care utilization for those with cancer: how much is enough? *JAMA Oncol* 2015;1(8):1085–1086. [PubMed: 26313203]
11. Daly B, Hantel A, Wroblewski K, et al. No exit: identifying avoidable terminal oncology intensive care unit hospitalizations. *J Oncol Pract* 2016;12(10):e901–e911. [PubMed: 27601514]
12. Von Roenn JH. Critically ill patients' preferences regarding aggressive medical interventions: can we hear the patient's voice? *JAMA Oncol* 2016;2(1):83–84. [PubMed: 26468919]
13. Auclin E, Charles-Nelson A, Abbar B, et al. Outcomes in elderly patients admitted to the intensive care unit with solid tumors. *Ann Intensive Care* 2017;7(1):26. [PubMed: 28265980]
14. Soares M, Bozza FA, Azevedo LC, 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(27): 3315–3324. [PubMed: 27432921]

Figure 1.
Patient inclusion characteristics.

Table 1.

Patient Demographics.

	Number (N = 28 Total)	%
Age (median, years)	62 (range, 38–80)	NA
Alive ^a	0	0
Dead	28	100
Cancer type		
Colon	10	36
Pancreatic	9	32
Gastric	4	14
Other ^b	5	18
Median lines of therapy	2 (2–7)	NA
<2 lines of therapy	14	50
>2 lines of therapy	14	50

^aAs of September 1, 2015.

^bEsophageal, cholangiocarcinoma, and rectal.

Table 2.**Hospitalization and ICU Admission Characteristics.**

	Number (N = 28 total)	%
Admitted to ICU from		
Medical Floor	14	50
Emergency department	14	50
Reason for admission		
Sepsis	11	39
Respiratory failure	9	32
Other (non-GI bleed)	8	29
Intubated on admission to ICU	4	14
Intubated during hospitalization	12	43
Vasopressors on admission to ICU	7	25
Vasopressors during ICU course	13	46
MPM II ^a score >80	4	14
Survived to ICU discharge	18	64
Survived to hospital discharge	15	54
Hospital discharge destination		
Died as inpatient	13	46
Home	12	43
Hospice	3	11
Outpatient oncology follow-up	10	36
More chemotherapy	6	21

Abbreviations: GI, gastrointestinal; ICU, intensive care unit; MPM, Mortality Probability Model II.⁶

Table 3.

Descriptive Characteristics of Patients Receiving Post-ICU Cancer Treatment.

Age ^a , years, Gender	Metastatic Cancer Type	Pre-ICU Cancer Treatment	Post-ICU Cancer Treatment	Survival, days ^b
39, F	Colon	HAI chemotherapy “pump” had been placed for disease originally metastatic to liver only. At extrahepatic disease progression, systemic chemotherapy had been given, with subsequent disease progression. ICU admission for sepsis	During a hospital readmission where she was found radiographically to have more disease progression, she was given more HAI and systemic chemotherapy (prior disease progression on the same agents). Brisk disease progression was thereafter documented radiographically	52
40, M	Gastric	Disease progression through all available standard lines of chemotherapy for metastatic disease over several years, then ICU admission for altered mental status from severe hyponatremia	Platinum-containing chemotherapy recycled (prior disease progression on a different platinum), with subsequent disease progression	169
37, M	Colon	Adjuvant platinum-containing chemotherapy. At disease recurrence, all standard systemic chemotherapies given but disease progressed on all. ICU admission for sepsis	Platinum-containing chemotherapy recycled, with subsequent disease progression	87
68, F	Pancreas	Platinum-containing chemotherapy with disease progression, then ICU admission for severe pneumonitis while on second-line gemcitabine-containing chemotherapy	Erlotinib given for approximately 1 month before hospital readmission for overall clinical decline (debility, anasarca, pain, dyspnea)	44
70, F	Cholangiocarcinoma	Initial disease progression on gemcitabine-containing chemotherapy, then intolerance of platinum-containing chemotherapy. ICU admission for sepsis	Disease progression on irinotecan-containing chemotherapy, then intolerance of taxane chemotherapy. Disease progression on yttrium-90 microsphere-selective internal radiotherapy for still liver dominant disease	289
57, F	Colon	Disease progression through all available lines of chemotherapy for metastatic disease over several years, then ICU admission for sepsis	EGFR inhibitor recycled (prior disease progression on the same EGFR inhibitor), with subsequent disease progression	303

Abbreviations: EGFR, epidermal growth factor receptor; F, female; HAI, hepatic arterial infusion; ICU, intensive care unit; M, male.

^aAt time of ICU admission.^bFrom date of ICU hospital discharge to death.