SUBMITTED 2 JUL 24
REVISIONS REQ. 4 AUG & 11 SEP 24; REVISIONS RECD. 26 AUG & 8 OCT 24
ACCEPTED 23 OCT 24
ONLINE-FIRST: OCTOBER 2024
DOI: https://doi.org/10.18295/squmj.10.2024.058

Characteristics and Outcomes of Cancer Patients Admitted to the Hospital with Community-Acquired Pneumonia

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Abstract

Objectives: Community-Acquired Pneumonia (CAP) is associated with high risk of complications in cancer patients. Few studies evaluated hospitalized cancer patients with CAP. Therefore, we aimed to evaluate the characteristics and outcomes of cancer patients admitted with CAP. ***Methods:*** A retrospective study that included patients admitted to King Hussein Cancer Center in Jordan with the diagnosis of CAP (January 2021-August 2022). CAP was defined based on the Infectious Diseases Society of America guidelines criteria. Patients' characteristics, microbiological cultures, length of hospital stay, transfer to the intensive care unit (ICU), and all-cause mortality were recorded. We also assessed early clinical stability, defined as temperature ≤37.8°C, heart rate ≤100/min, respiratory rate ≤24/min, systolic blood pressure ≥90mmHg, and oxygen saturation ≥90% at room air on the third day of admission. ***Results:*** We evaluated 632 cancer patients admitted with CAP. The mean age was 60 (±13.9 SD) years; 55% were males, breast cancer was the most prevalent malignancy (23%) and 49% had received cancer-related treatment within 2 months. Positive blood and sputum cultures were detected in 12% and 30% of the patients, respectively. Early clinical stability was achieved in 49% of the patients, and 89% were discharged home after a median of 6 days (range: 1-48) in the hospital. Among the

included patients, 3% required ICU transfer and 11% died. ***Conclusions:*** Early clinical stability was achieved in about half the patients and the majority were discharged home. Future research should be conducted to identify interventions to improve clinical outcomes of CAP in cancer patients.

Keywords: Pneumonia, Community-Acquired, Infections, Immunocompromised, Cancer, Hospitalization.

Advances in Knowledge

- This study provides novel insights into the clinical characteristics and outcomes of cancer patients hospitalized with community-acquired pneumonia (CAP).
- By evaluating a relatively large cohort of patients, the study highlights the prevalence of breast cancer in this group and the significant rate of microbiological positivity.
- The study identifies metrics of early clinical stability and hospital outcomes, which can help in the clinical assessment and management of high-risk population.
- The findings of this study underscore the importance of further research and potential interventions to improve outcomes in cancer patients with CAP.

Application to Patient Care

- This study underscores the importance of monitoring and tailored treatment of cancer patients with community acquired pneumonia (CAP).
- The identification of indicators for early clinical stability can guide clinicians in making decisions regarding the site of patient care, which can reduce the need for hospital admission and its associated complications.
- This study suggests that certain patients might be safely managed as outpatients, potentially shortening hospital stays and enhancing overall patient outcomes.
- These findings can enhance the clinical management of CAP in cancer patients, leading to improved outcomes and more efficient use of healthcare resources.

Introduction

Community-acquired pneumonia (CAP) refers to an acute lung infection that is acquired outside the hospital.[1,2] The clinical manifestations of CAP vary depending on the patient's condition and risk factors, ranging from mild symptoms such as cough and fever to severe manifestations such as respiratory failure and sepsis. Hospitalization may be necessary for patients with severe CAP, those with underlying comorbid conditions, and those who are unable to take oral medications. The decision regarding hospital admission depends on multiple factors and may vary according to institutional practices.[1] CAP requiring hospitalization is linked to a clinical burden that contributes to worldwide morbidity and mortality.[3,4]

Risk factors and severity of CAP should be assessed for differential diagnosis and proper management. Several risk factors, such as advanced age, pre-existing lung diseases, smoking, and immunosuppression, contribute to the severity and outcomes of CAP.[5]Cancer patients or those undergoing active immunotherapy or chemotherapy are particularly susceptible to pneumonia due to their immunocompromised status, leading to a high risk of complications and mortality.[6-9]

Though CAP is common in cancer patients, there are limited studies that evaluated this patient population, those studies were conducted in United States, Europe, Australia, Spain, Thailand, and China.[5,10-12] In addition, the guidelines published by the Infectious Diseases Society of America (IDSA) for CAP did not include specific treatment recommendations in immunocompromised patients, including those with cancer who are actively receiving chemotherapy. [1] Therefore, we conducted this study to evaluate the characteristics and outcomes of CAP that resulted in hospital admission in a large cohort of patients with cancer. The goal was to provide a better understanding of this common and serious disease in cancer patients.

Methods

This was a retrospective observational study conducted at King Hussein Cancer Center (KHCC), located in Amman, Jordan. KHCC is a 350-bed comprehensive cancer center that treats adult and pediatric patients with various types of malignancies in the inpatient and outpatient settings.

The study included adult (aged ≥18 years) patients with cancer admitted to the medical wards with the diagnosis of CAP, between January 2021 and August 2022. Patients with a hospital admission diagnosis of CAP were identified using the electronic database of the medical records at our institution. Subsequently, the investigators verified each case to ensure it met the IDSA definition of CAP at the time of admission, which included the presence of pulmonary infiltrates on chest radiographs (computed tomography (CT) chest scan and/or chest X-ray), along with at least one of the following clinical manifestations: fever (temperature ≥38°C), cough, chest pain, shortness of breath, elevated white blood cell count, or elevated C-reactive protein levels.[1] Patients who developed pneumonia after ≥48 hour of hospital admission, or patient with recurrent admission with pneumonia within 48 hour of discharge date were excluded, as this falls under the IDSA definition of hospital acquired pneumonia. Additionally, patients who had an admission diagnosis of CAP but did not meet the criteria for CAP were excluded. Patients with non-infectious causes of pulmonary infiltrates, such as pulmonary edema and drug-induced pneumonitis were also excluded. The information was retrieved using the Computerized Patient Record System (CPRS).

The CPRS was also used to collect data upon admission, including patients' baseline characteristics, clinical presentation, vital signs (including blood pressure, temperature, pulse, and respiratory rate), laboratory findings (including complete blood cell count with differentials, C- reactive protein, and procalcitonin), and the antimicrobial regimens initiated upon admission per our institutional clinical practice guidelines. Additionally, we recorded the microbiological data, including sputum and blood cultures, which was obtained before the initiation of antimicrobial therapy as per our institutional polices and

procedure, as well as the length of hospital stay (LOS). We also assessed the clinical outcomes of CAP, which included transfer to the intensive care unit (ICU), all-cause mortality, and early clinical stability. Early clinical stability was defined as temperature ≤ 37.8°C, heart rate ≤ 100/min, respiratory rate ≤ 24/min, systolic blood pressure ≥ 90 mmHg, and oxygen saturation ≥ 90% while breathing room air on the third day of admission.[13] The study was performed in accordance with Declaration of Helsinki and approved by the Institutional Review Board of KHCC on (Sep 2022), and was granted the waiver of informed consent, given the retrospective nature of the study.

Statistical analysis

Categorical data was presented as counts and percentages, while continuous data was presented as mean with standard deviation, and/or median with range. Univariate and multivariate analysis were performed to identify predictors associated with early clinical stability and all-cause mortality. Factors included in the univariate analysis were baseline characteristics, the antimicrobial agents initiated upon admission, vital signs, and laboratory data upon admission. Nominal data were tested with $\chi 2$ test or Fisher exact test, and continuous variables were tested with Student t-test or non-parametric test, depending on the assumptions required for each test. Multivariate logistic regression was performed for factors that were significant in the univariate analysis. A $p \leq 0.05$ was considered statistically significant. All analyses were performed using SAS version 9.4 (SAS Institute Inc, Cary, NC).

Results

During the study period, 1642 patients with cancer were admitted with a diagnosis of pneumonia among whom 632 (38%) met the IDSA criteria for CAP. The included patients had a mean age of 60 years (±13.9 SD), with 349 (55%) being male, and 283 (45%) females. Additionally, 159 (25%) were active smokers, and 67 (11%) had chronic lung diseases. Among the included patients, breast cancer was the most common type of malignancy (n=144, 22.9%), and 307 (49%) had received antineoplastic agents within two months prior to admission. Patients' baseline characteristics are summarized in Table 1.

The most common clinical presentation upon admission was shortness of breath, reported in 404 (64%) patients, while fever >38C was reported in 228 (36.1%) patients with mean of 37.1C (±0.75 SD). Key laboratory findings were Neutropenia with mean of 10212 (±31978 SD), and in patient who has Procalcitonin level mean was 3.3 (±11 SD). The clinical presentation of patients upon admission, as well as the vital signs and laboratory findings are presented in Table 2. For diagnosis of CAP diagnosis, radiographic imaging was used to confirm cases. This included both chest CT scans and X-rays, with 239 patients (38%) undergoing both, 17 patients (27%) diagnosed using only chest CT imaging, and 419 (35%) were diagnosed by chest Xray.

Blood culture samples were obtained from 434 (69%) patients. Among the collected blood cultures, 54 (12.5%) tested positive. Out of these positive blood cultures, 35 (65%) were composed of gram-positive bacteria. Sputum culture samples were collected from 140 (22.2%) patients, of which, 42 (30%) were positive. This included 17 (40%) cases of gram-negative bacteria, 15 (36%) cases of gram-positive bacteria, and 10 (24%) cases of fungus, with 100% of Candida. Blood and sputum culture results among the collected samples presented in Figure 1. Among patients tested for COVID-19 (N= 489), COVID-19 was confirmed by polymerase chain reaction in 102 (16%) cases.

During the study period, 312 (50%) patients received two antimicrobial agents upon admission, while 168 (26%) and 149 (24%) received a single agent and a combination of three agents, respectively. Based on the pharmacologic categories, the most prescribed empiric agents were piperacillin/tazobactam and amoxicillin/clavulanate, which were administered to 505 (80%) patients, followed by fluoroquinolones, which were given to 420 (67%) patients. Among the included patients, 45 (7%) received antifungal therapy, of whom, 9 (1.4%) were neutropenic.

Early clinical stability by the third day of admission was achieved in 309 (49%) patients. Among the included patients, 562 (89%) were discharged home, with a median length of

hospital stay of 6 days (range 1-48). During hospitalization, 20 (3%) patients were transferred to the ICU, with a mean age 60 years (±17.5 SD), and 11 (55%) were female. The median duration of stay in the medical ward before transfer of 2 days (range 1–15). The primary causes of ICU transfer included respiratory failure and septic shock, accounting for 10 (50%) and 6 (30%) patients, respectively. The remaining transfers were due to electrolyte imbalances and cardiac causes. The most common clinical presentation upon admission for ICU transfers was shortness of breath. Additionally, four patients (20%) had positive blood cultures, and two (10%) had positive sputum cultures. In this study, 69 (11%) patients died with a median duration from admission to death of 8 days (range 1-42).

In the univariate analysis, absolute neutrophil count (ANC) levels below 1000 cells/microL (P=0.004), procalcitonin levels <0.1ng/ml (P=0.044), the use of single empiric agent upon admission (P=0.004), the use of azithromycin as an empiric antimicrobial therapy upon admission (P=0.001), and an increase in respiratory rate upon admission (P=0.035), were significantly associated with achieving clinical stability on the third day of admission. Elevated WBC levels above the upper normal range, the use of piperacillin/tazobactam and amoxicillin/clavulanate as an empiric antimicrobial therapy upon admission, and recent hospital visits within 90 days of admission were inversely associated with achieving clinical stability on the third day of admission. The presence of metastasis (P=0.044), the decrease in temperature (P=0.0003), the use of glycopeptides (vancomycin or teicoplanin) as an empiric antimicrobial therapy upon admission (P=0.004) and an elevated WBC count (P=0.013) were significantly associated with all-cause mortality.

In the multivariate analysis, ANC levels below 1000 cells/micoL, the use of single empiric antimicrobial agent, and a history of hospital visits of more than 90 days were independently associated with achieving early clinical stability on the third day of admission (Table 3). The decrease in temperature, the use of glycopeptides (vancomycin

or teicoplanin) as an empiric antimicrobial therapy upon admission, and the presence of metastasis were independently associated with all-cause mortality (Table 4).

Discussion

In this study, we evaluated a relatively large cohort of cancer patients admitted to the hospital with CAP. The most common type of malignancy was breast cancer and about half of the patients had been on active anti-neoplastic therapy within 2 months of admission. Interestingly, the majority of patients were non-smokers, which is a finding that requires further investigation given the association between smoking and developing CAP.[14]

Aliberti et al (2009) evaluated the outcomes of cancer patients with CAP.[15] Among 310 patients with solid and hematological malignancies, lung cancer was the most common, followed by prostate and breast cancer. In a similar study by Wang et al (2020) that evaluated CAP in 149 patients with cancer, lung cancer was the most common.[16] In our study, CAP was mostly observed in patients with breast cancer, followed by lung cancer (21%), which might reflect the higher incidence of breast cancer in our institution.

In our study, almost half of the patients had received antineoplastic agents within the last two months prior to admission, which may have contributed to immune suppression and an increased risk of infections, including pneumonia. Pasquale et al (2019) conducted a study that enrolled patients with various types of immunocompromised conditions, including patients with hematological and solid malignancies and 22% of the study cohort had received chemotherapy within the last three months.[5] In a study by Certan et al (2022) which assessed the incidence and predictors of CAP among hematological malignancies, 15% of the patients had received chemotherapy within the past month.[17] Similarly, Aramrat et al. (2023) reported that 20% of cancer patients admitted with CAP had received chemotherapy within 4 weeks of admission. [12] Given that being on active cancer-related treatments was common in our study and other similar studies, further research should study more closely the association between the treatment type, timing, and the

likelihood of developing CAP to develop prediction models and proactive measures to reduce the incidence and severity of CAP that results in hospitalization.

Considering comorbidities such as lung disorders place patients at risk for CAP hospitalization, it is crucial to evaluate and consider the implications of chronic lung disease in the development of CAP in cancer patients. In a large study conducted in the US (2015) that included 2320 non-cancer patients hospitalized with CAP, about half had chronic lung disease.[11] In our study, only 11% of patients had chronic lung diseases. This could be related to the underreporting of chronic lung diseases such as COPD, given that our study was conducted retrospectively.

The clinical presentations of CAP vary across studies. Carlota et al. (2016) found that among neutropenic patients with cancer who were diagnosed with CAP, two-thirds of patients presented with fever, whereas in Wang et al study (2020), 73% of patients presented with cough.[10,16] In our study, shortness of breath was the most common presentation among patients with CAP. This variability could be related to underreporting of patient's signs and symptoms upon presentation due to the retrospective nature of the study.

Our study highlights the microbiological diversity of pathogens causing pneumonia in cancer patients. In our findings, 12.5% of the collected blood samples exhibited bacteremia, with gram-positive bacteria being the most frequently isolated microorganism. In contrast, Carlota et al (2016) reported gram-negative microorganisms as the most prevalent, accounting for two-thirds of blood cultures.[10] This emphasizes the importance of tailored empiric antibiotic therapy that covers a broad spectrum of potential microorganisms according to the institutional antibiogram. The predominance of gram-positive bacteria in our study highlights the need for further studies in this area to optimize empiric antimicrobial therapy. It’s notable that 16% of patients who were screened for COVID-19 tested positive, warranting a comprehensive approach for a diagnosis of patients who are at high risk for synchronized bacterial and viral infections.

Our study revealed a median of 3 days of hospital stay after clinical stabilization which is comparable to a study that evaluated hospitalized non-cancer patients with CAP (1998), which showed a median of 4 days of hospital stay after achieving clinical stability at day 3 of admission.[18] A study by Mortensenet al (2002), which evaluated causes of death in 208 (9%) died by 90 days out of 1343 admitted patients with CAP, found a 50% of deaths occurred due to underlying comorbid conditions, including neurological conditions, lung cancer, and cardiac ischemia rather than pneumonia itself.[19] Similar to our study revealed an 11% all-cause mortality rate during hospitalization. Conversely, Certan et al (2022), reported higher all-cause mortality rate reaches 34% among 275 patients with hematological malignancies.[17] Mortality rate discrepancy could be explained by the differences in primary tumors.

We identified independent predictors of early clinical stability, including ANC below 1000 cells/micoL, the use of single antimicrobial agent, and a history of hospital visits of more than 90 days from the admission. Unlike our results, Aliberti et al (2005) found no significant difference in the time to clinical stability between neutropenic and non-neutropenic patients.[15]Our results could be explained by physicians aggressively manage CAP in neutropenic patients which could provide faster clinical stability. Our findings point to the necessity of conducting a prospective study to assess the contribution of neutropenia to the severity of CAP.

This study has several limitations. First are those related to the retrospective design of the study, and being conducted in a single center. In addition, we did not evaluate certain cancer and chemo-related characteristics, such as the stage of malignancy, goals of care, performance status, type of chemotherapy, number of cycles, and CAP burden on patient's caregivers. Moreover, we have missing data related to the detailed microbiology results. Such variables would be important to evaluate in future studies to provide a better understanding about the outcomes of cancer patients admitted with CAP that can guide management, as well as identify prognostic markers.

In our study, we ensured to evaluate each patient admitted with a pneumonia diagnosis to confirm that they met the IDSA definition and criteria for CAP, and to exclude any cases that fall under hospital-acquired pneumonia; which is defined as pneumonia not incubating at the time of hospital admission and occurring 48 hours or more after admission.[20] The use of clear criteria of CAP, helped to employ objective measures in assessing each patient with CAP, thereby avoiding bias associated with the misdiagnosis of the included cases of CAP.

Our study stands out for its inclusion of substantial sample size of patients. This is an important aspect of our study as studying CAP in patients with solid tumors is limited in the literature. Moreover, our study evaluated multiple clinical outcomes during hospitalization. In addition, we investigated the association between patient's characteristics and the clinical outcomes. In contrast to previous studies that focused on hematological malignancies, our study highlighted the clinical stability of patients with solid tumors requiring hospitalization. Furthermore, we presented the microbiological patterns among cancer patients with CAP, which provides an insight about the possible causative microorganisms in this cohort of patients and emphasizes the need for individualized management strategies.

Conclusions

Among cancer patients hospitalized with CAP, about half achieved early clinical stability, and the majority were discharged home. Early clinical stability was significantly associated with neutropenia, history of hospitalization of more than 90 days from the admission and the use of single empiric antimicrobial agent. This might help in identifying patients with high risk for complications. Our study contributes to the understanding of pneumonia in cancer patients. Future multicenter studies of prospective settings should be conducted to identify predictors for patients who may be treated as outpatients and may help in shortening hospital stays and associated complications, ultimately improving their outcomes.

Authors' Contribution

AA-S and NF conceptualized and designed the study. AA-S, DH and SD collected the data. AA-S and NF analysed the data. AA-S, NF and DH drafted the manuscript. AA-S and NF revised and edited the manuscript. All authors approved the final version of the manuscript.

Conflict of Interest

The authors declare no conflicts of interest.

Funding

No funding was received for this study.

References

1 Metlay JP, Waterer GW, Long AC, Anzueto A, Brozek J, Crothers K, et al. Diagnosis and treatment of adults with community-acquired pneumonia. Am J Respir Crit Care Med 2019;200(7). https://doi.org/10.1164/rccm.201908-1581ST.

2 Baden LR, Swaminathan S, Angarone M, Blouin G, Camins BC, Casper C, et al. Prevention and treatment of cancer-related infections, version 2.2016, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 2016;14(7):882-913. https://doi.org/10.6004/jnccn.2016.0093.

3 Rozenbaum MH, Mangen MJ, Huijts SM, van der Werf TS, Postma MJ. Incidence, direct costs, and duration of hospitalization of patients hospitalized with community-acquired pneumonia: a nationwide retrospective claims database analysis. Vaccine 2015;33(28):3193-9. https://doi.org/10.1016/j.vaccine.2015.05.001.

4 Ramirez JA, Wiemken TL, Peyrani P, Arnold FW, Kelley R, Mattingly WA, et al. Adults hospitalized with pneumonia in the United States: incidence, epidemiology, and mortality. Clin Infect Dis 2017;65(11):1806-12. https://doi.org/10.1093/cid/cix647.

5 Di Pasquale MF, Sotgiu G, Gramegna A, Radovanovic D, Terraneo S, Reyes LF, et al. Prevalence and etiology of community-acquired pneumonia in immunocompromised patients. Clin Infect Dis 2019;68(9):1482-93. https://doi.org/10.1093/cid/ciy722.

6 Lim WS, Woodhead M; British Thoracic Society. British Thoracic Society adult community-acquired pneumonia audit 2009/10. Thorax 2011;66(6):548-9. https://doi.org/10.1136/thx.2010.145912.

7 Novosad SA, Winthrop KL. Beyond tumor necrosis factor inhibition: the expanding pipeline of biologic therapies for inflammatory diseases and their associated infectious sequelae. Clin Infect Dis 2014;58(11):1587-98. https://doi.org/10.1093/cid/ciu146.

8 Zheng Y, Chen Y, Yu K, Yang Y, Wang X, Yang X, et al. Fatal infections among cancer patients: a population-based study in the United States. Infect Dis Ther 2021;10(2):871-95. https://doi.org/10.1007/s40121-021-00414-5.

9 Williams AM, Baran AM, Meacham PJ, Feldman MM, Valencia HE, Newsom-Stewart C, et al. Analysis of the risk of infection in patients with chronic lymphocytic leukemia in the era of novel therapies. Leuk Lymphoma 2018;59(3):625-32. https://doi.org/10.1080/10428194.2017.1348782.

10 Gudiol C, Royo-Cebrecos C, Laporte J, Ardanuy C, Garcia-Vidal C, Antonio M, et al. Clinical features, aetiology, and outcome of bacteraemic pneumonia in neutropenic cancer patients. Respirology 2016;21(8):1411-8. https://doi.org/10.1111/resp.12830.

11 Jain S, Self WH, Wunderink RG, Fakhran S, Balk R, Bramley AM, et al. Community-acquired pneumonia requiring hospitalization among US adults. N Engl J Med 2015;373(5):415-27. https://doi.org/10.1056/NEJMoa1500245.

12 Aramrat C, Ratanasiri T, Gomutbutra P. Is aggressive care appropriate for patients with cancer complicated by pneumonia? A retrospective chart review in a tertiary hospital. BMC Palliat Care 2023;22(1):1-8. https://doi.org/10.1186/s12904-023-01107-8.

13 Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis 2007;44(Supplement_2). https://doi.org/10.1086/511159.

14 Almirall J, Bolibar I, Balanzo X, Gonzalez CA. Risk factors for community-acquired pneumonia in adults: a population-based case-control study. Eur Respir J 1999;13(2):349-55. https://doi.org/10.1183/09031936.99.13234999.

15 Aliberti S, Myers JA, Peyrani P, Blasi F, Menendez R, Rossi P, et al. The role of neutropenia on outcomes of cancer patients with community-acquired pneumonia. Eur Respir J 2009;33(1):142-7. https://doi.org/10.1183/09031936.00072708.

16 Wang X, Zhang H, Zhang T, Pan L, Dong K, Yang M, et al. Etiology of community-acquired pneumonia requiring hospital admission in adults with and without cancers: a single-center retrospective study in China. Infect Drug Resist 2020;13:1607-17. https://doi.org/10.2147/IDR.S258048.

17 Certan M, Garcia Garrido HM, Wong G, Heijmans J, Grobusch MP, Goorhuis A, et al. Incidence and predictors of community-acquired pneumonia in patients with hematological cancers between 2016 and 2019. Clin Infect Dis 2022;75(6):1046-53. https://doi.org/10.1093/cid/ciab874.

18 Halm EA, Fine MJ, Marrie TJ, Coley CM, Kapoor WN, Obrosky DS, et al. Time to clinical stability in patients hospitalized with community-acquired pneumonia: implications for practice guidelines. JAMA 1998;279(18):1452-7. https://doi.org/10.1001/jama.279.18.1452.

19 Mortensen EM, Coley CM, Singer DE, et al. Causes of death for patients with community-acquired pneumonia: Results from the Pneumonia Patient Outcomes Research Team Cohort Study. Arch Intern Med. 2002;162(9):1059-64. https://doi.org/10.1001/archinte.162.9.1059.

20 Kalil AC, Metersky ML, Klompas M, Muscedere J, Sweeney DA, Palmer LB, et al. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 clinical practice guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis 2016;63(5). https://doi.org/10.1093/cid/ciw353.

Table 1: Baseline characteristics of patients admitted with community-acquired pneumonia according to achieving early clinical stability.

Patient's Characteristic	**Total Number (%)**	**Patients who achieved early**	**Patients who didn't achieve**

		clinical stability, N (%)	early clinical stability, N (%)
Age, mean (SD), years	60 ±13.9		
Male	349 (55.2%)	172 (55.7%)	177 (54.8%)
Female	283 (45%)	137 (44.3%)	146 (45.2%)
Cancer type			
Breast	145 (22.9%)	71 (23.0%)	74 (22.9%)
Lung	130 (20.6%)	66 (21.4%)	64 (19.8%)
Genitourinary	85 (13.4%)	41 (13.3%)	44 (13.6%)
Gastrointestinal	84 (13.3%)	37 (12.0%)	47 (14.6%)
Lymphoma	55 (8.7%)	32 (10.4%)	23 (7.1%)
Head and Neck	37 (5.9%)	15 (4.9%)	22 (6.8%)
Central nervous system	26 (4.1%)	11 (3.6%)	15 (4.6%)
Others	69 (10.9%)	35 (11.3%)	34 (11%)
Metastasis	427 (67.6%)	204 (66.0%)	223 (69.0%)
Lung Involvement	277 (43.8%)	129 (41.7%)	148 (45.8%)
Smoking status			
Smoker	159 (25.2 %)	84 (27.2%)	75 (23.2%)
Non- Smoker	306 (48.4 %)	153 (49.5%)	153 (47.4%)
Ex-Smoker	167 (26.4 %)	72 (23.3%)	95 (29.4%)
Recent Chemotherapy or Immunotherapy (within the last 2 months from admission date)	307 (48.6 %)	150 (48.5%)	157 (48.6%)
Comorbidities			

Hypertension	286 (45.3%)	142 (46.0%)	144 (44.6%)
Diabetes	246 (38.9 %)	118 (38.2%)	128 (39.6%)
Cardiovascular diseases	157 (24.8 %)	78 (25.2%)	79 (24.5%)
Chronic kidney disease	55 (8.7 %)	23 (7.4%)	32 (9.9%)
COPD	31 (4.9 %)	17 (5.5%)	14 (4.3%)
Asthma	20 (3.2 %)	8 (2.6%)	12 (3.7%)
Other lung diseases	19 (3.0 %)	9 (2.9%)	10 (3.1%)
Liver disease	14 (2.2 %)	7 (2.3%)	7 (2.2%)
Recent hospital visit (within 90 days of admission date)	532 (84.2 %)	245 (79.3%)	287 (88.9%)

414 COPD: chronic obstructive pulmonary disease; early clinical stability: temperature ≤
415 37.8°C, heart rate ≤ 100/min, respiratory rate ≤ 24/min, systolic blood pressure ≥ 90 mmHg,
416 and oxygen saturation ≥ 90% while breathing room air on the third day of admission.

417 **Table 2:** Clinical presentation, vital signs, and laboratory results of patients with
418 community-acquired pneumonia upon admission.

Clinical Presentation	Number (%)
Shortness of breath	404 (63.9 %)
Productive cough	260 (41.1 %)
Fever >38 C	228 (36.1 %)
Nonproductive cough	122 (19.3 %)
Chest pain	96 (15.2 %)
Vital signs upon admission, mean (SD)	
Diastolic blood pressure	70.5 ± 11.5
Systolic blood pressure	120.3 ± 21.7
Pulse	102.8 ± 20.4
Respiratory rate	18.9 ± 3.6

Temperature	37.1 ± 0.7
Laboratory data	Number (%)
Elevated White Blood Count (above upper normal range)	209 (33.1 %)
Absolute Neutrophil Count < 1000 cells/microL	41 (6.5 %)
C-Reactive Protein (total N= 337), mean ±SD	144.8 ± 95.8
Procalcitonin level (total N= 270)	
Level < 0.10	48 (17.8%)
Level between 0.10 to 0.25	63 (23.3%)
Level > 0.25 to 0.50	36 (13.3%)
Level > 0.50	123 (45.6%)

Table 3: Multivariate analysis of early clinical stability.

Effect	Odds ratio	95% Wald Confidence Limits		p-value
Hospital visits for more than 90 days from admission	1.941	1.236	3.048	0.0040
ANC < 1000 cells microL	2.942	1.459	5.929	0.0026
Single agent for empiric treatment	1.625	1.127	2.345	0.0094
Increase in respiratory rate upon admission	1.000	0.956	1.045	0.9873

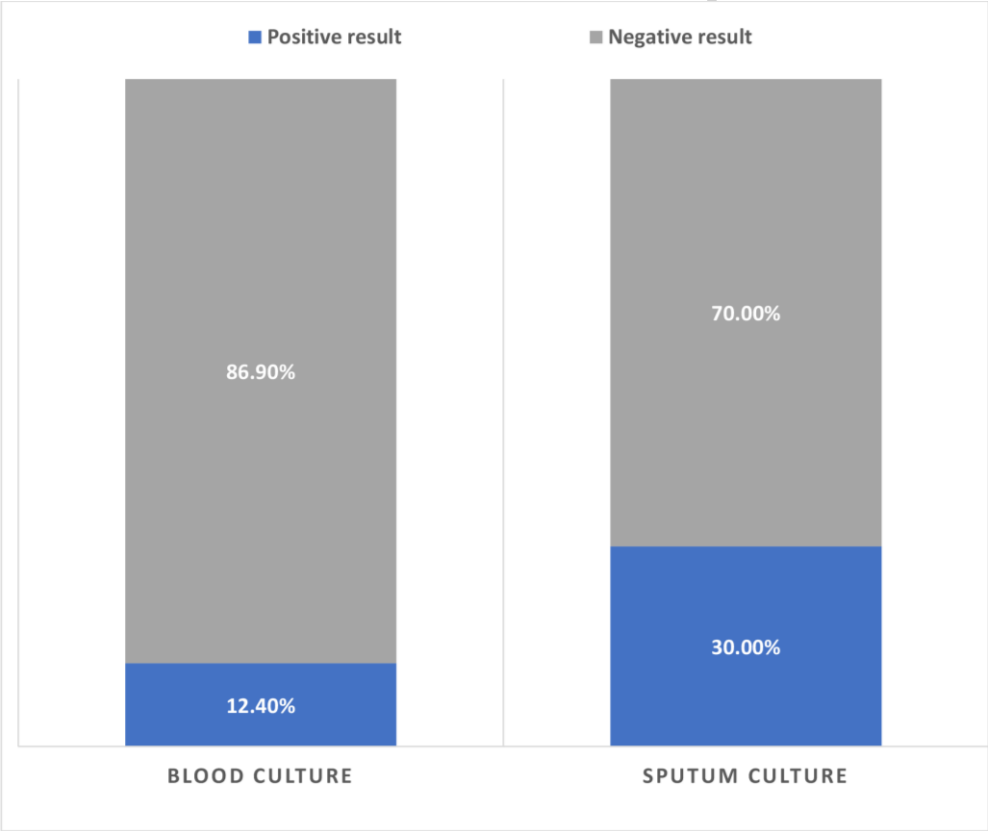
ANC: absolute neutrophil count.

Table 4: Multivariate analysis of all-cause mortality.

Effect	Odds ratio	95% Wald Confidence Limits		p-value
Metastasis	1.886	1.026	3.468	0.0412
Elevated WBC from upper normal limit	1.624	0.967	2.727	0.0667
Use of glycopeptides (vancomycin\teicoplanin) as empiric antimicrobial agents	2.129	1.252	3.621	0.0053
Decrease in temperature upon admission	0.543	0.341	0.865	0.0103

423 WBC: white blood count.

424



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426 **Figure 1:** Blood and sputum culture results among the collected samples.