The Diagnosis of Community-Acquired Pneumonia

Subjects: Emergency Medicine
Contributor: Sedat Ozbay , Mustafa Ayan , Orhan Ozsoy , Canan Akman , Ozgur Karcioglu

Community-acquired pneumonia (CAP) is among the most common causes of death and one of the leading healthcare concerns worldwide. It can evolve into sepsis and septic shock, which have a high mortality rate, especially in critical patients and comorbidities. The diagnosis of CAP generally necessitates an infiltration on Chest X-rays (CXR) in a patient with fever, dyspnea, cough, and sputum.

pneumonia bacteremia sepsis

1. The Diagnosis of CAP

The diagnosis of CAP generally necessitates an infiltration on CXR in a patient with fever, dyspnea, cough, and sputum.

While S. pneumonia is the most commonly isolated agent, *S. aureus*, *Haemophilus influenzae*, *Enterobacteriaceae*, *Legionella pneumophila*, *Mycoplasma pneumoniae*, and *Chlamydophila pneumonia* are among the culprits in patients with CAP. A Swedish study disclosed that in hospitalized patients with CAP, Pneumococci are the dominant agent, followed by *Haemophilus influenzae* and *Mycoplasma pneumonia* [1][2]. On the other hand, elderly patients have a different order of frequency of culprit agents in CAP (**Table 1**) [3][4]. **Table 2** summarizes the differential diagnosis in patients presenting with cough.

Table 1. Frequency of etiologic agents of community-acquired pneumonia (CAP) in elderly patients.

Streptococcus pneumoniae	Up to 50%
Atypical (*Legionella pneumophila* and others)	Up to 25%
Haemophilus influenzae	0–13%
Staphylococcus aureus	0–7%
Methicillin-resistant *Staphylococcus aureus* (MRSA)	0–6%
Gram-negative bacilli including *Pseudomonas aeruginosa*	Up to 27%
Virus	0–8%

Aspiration pneumonia	10%

Table 2. Differential diagnosis of patients with cough. These entities commonly masquerade as CAP.

Pulmonary embolism
Cryptogenic organizing pneumonia
Tuberculosis, *Actinomycosis*
Pulmonary vasculitis, lupus pneumonitis and hypersensitivity pneumonitis, acute or chronic eosinophilic pneumonia
Sickle cell syndrome, sickling crisis
Acute hemorrhage in the alveoli
Radiation pneumonitis
Leukemia and neoplasms such as bronchogenic carcinoma
Drug-induced pulmonary infiltration

2. Radiological Findings

2.1. Chest X-rays

Chest X-rays (CXR, PA and lateral) can mostly be adequate for decision-making in suspected patients, which render CT scans not necessary in selected situations. The diagnosis of CAP is generally based on the presence of predefined clinical properties and is supported by simple imaging modalities, mostly by CXR [5]. In this regard, CAP presents as one of three patterns as follows:

1. Focal nonsegmental or lobar pneumonia.

2. Bronchopneumonia in multiple foci or lobular pneumonia.

3. Patterns compatible with interstitial pneumonia (focal or diffuse).

False-negative CXR can be seen in the initial stage of pneumonia in some situations, including patients with neutropenia, dehydration, and immunocompromise. A special example is *Pneumocystis carinii* pneumonia (PCP, a.k.a. *Pneumocystis jirovecii* pneumonia), in which spiral CT scans can be needed to adequately visualize findings suggestive of infection.

High-resolution computed tomography (HRCT) usually demonstrates the pattern and distribution of pneumonia more accurately than the CXR [6][7]. It is not routinely ordered in the diagnosis of patients with suspected CAP because of cost-effectiveness principles. Instead, HRCT can be ordered as an adjunct to CXR in selected cases. For example, HRCT has been postulated to be a useful alternative to RT–PCR in the diagnosis of COVID pneumonia, in which a negative test can rule out the diagnosis of COVID pneumonia [8].

2.2. Ultrasonography (USG)

Lung USG has been employed more commonly in the last decade to diagnose pneumonia with inappreciable diagnostic value in the patients *in extremis* who are hard to be transferred to the radiology unit. The sensitivity of lung USG was reported to be between 80 and 90%, and the specificity between 70 and 90% [9][10].

3. Microbiological Work-Up

3.1. Sputum Gram Stain

A systematic review and Bayesian meta-analysis pointed out that a gram stain was adequately accurate to diagnose *S. pneumoniae* and *H. influenzae* in those with CAP [11]. With good-quality specimens, it can form a basis of clinical actions for specified antibiotic therapies for certain pathogens.

3.2. Blood Count

An increased WBC count (up to 30,000/mm^3) and a leftward shift are common findings, whereas leukopenia is suggestive of a poor outcome. The co-existence of fever, cough, tachycardia, and crackles had a sensitivity below 50% when CXR was used as a reference standard [12]. *Legionella* spp., Influenza A and B, MERS–CoV and SARS–CoV, and community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) are among these organisms.

3.3. Blood Cultures

Blood cultures (BCs) and sputum gram stains and cultures should be obtained and studied in severe, hospitalized patients. BCs are expected to be positive in around one-fifth of patients. Patients with severe CAP requiring ICU admission, especially, should have BCs, *Legionella* and pneumococcus urinary antigen tests, and sputum culture. BCs are recommended in severe and critical patients with CAP because positive results indicate the specific microbial diagnosis in most cases [13]. False-positive BCs can be encountered in one-tenth of the patients [14]. Studies pointed out that positive BCs rarely result in a change of antibiotic treatment regimens [15].

3.4. Molecular Methods

The potential advantages of molecular methods are speed and enhanced sensitivity and specificity [16][17]. These methods are available in most centers to elucidate viral agents and some bacteriae, including *M. pneumoniae* and

Legionella pneumophila. Polymerase chain reaction (PCR) boosts the accuracy of the microbiological tests for patients with CAP with its rapid turnaround time [1][18]. Since PCR specimens can be contaminated by the airway flora, a quantitative or semiquantitative PCR assay is needed in most cases [1][19][20].

4. Biomarkers

4.1. Lactate

Lactate is another biomarker with diagnostic and prognostic value in most severe infections [21]. Research disclosed that lactate was able to predict poor outcomes in CAP patients in the acute setting and augmented the predictive power for death [22]. High lactate value is associated with mortality of up to one-third of the samples in patients with CAP. An elevated lactate level suggests hypoperfusion and a marker for grave clinical course [23][24]. In accordance with the updated criteria for sepsis, both hypotension, which prompted inotropic infusions, and high lactate (>2 mmol/L) are necessary for the recognition of septic shock [25].

A recent study analyzed the impact of adding lactate levels to the Rapid Emergency Medicine Score (REMS) system to predict death and prognosis in the middle-aged and elderly (>40 years of age), who were admitted to the ED with dyspnea [26]. The REMS + L score ($p < 0.001$) was found to be more accurate than REMS ($p < 0.001$) and lactate values ($p < 0.001$) in the prediction of death.

4.2. Monocyte Human Leukocyte Antigen—DR Isotype (mHLA–DR)

Zhuang et al. evaluated the expression of monocyte human leukocyte antigen–DR (mHLA–DR) measured within 24 h after admission in the prediction of short-term survival, and mHLA–DR levels were reported to be higher in patients with mortality when compared to survivors [27].

4.3. C–Reactive Protein (CRP)

As an important marker of the inflammatory process, CRP has a value in the diagnosis of pneumonia to some extent. A CRP level above 40 mg/L has a sensitivity of 70% to 73%, and a specificity of 90% to 65% in diagnosing bacterial pneumonia [28]. Another study by Boussekey et al. cited that CRP had lower sensitivity when compared to PCT for the recognition of bacterial respiratory infection [29].

In the outpatient conditions, CRP levels can supply meaningful information to exclude pneumonia. In this group, the evaluation of signs and symptoms identified diagnostic risks accurately in around one-fourth of patients [30]. On the other hand, with the majority of patients in whom diagnostic doubt remained, CRP levels were useful to exclude pneumonia.

The predictive power of CAP was improved by adding biomarkers, such as CRP, to the other well-known scores. Menendez et al. reported that the added value of CRP to PSI, CURB–65, or CRB–65 augmented the prediction of death for hospitalized patients [31]. These combinations retained a sensitivity of 0.77 and a specificity of 0.78.

Therefore, it can be valued as a prognostic instrument, hampered by a lack of sensitivity and/or specificity in individual decision-making. A recent meta-analytic study disclosed that CRP has been found to be the most reliable marker (AUC = 0.8), together with leukocytosis (0.77) and PCT (0.77) [32]. For CRP, LR+ and LR− were 2.08 and 0.32 (cutoff: 20 mg/L), 3.64 and 0.36 (cutoff = 50 mg/L), and 5.89 and 0.47 (cutoff: 100 mg/L), respectively. For PCT, LR+ and LR− were 2.50 and 0.39 (cutoff: 0.10 µg/L), 5.43 and 0.62 (cutoff: 0.25 µg/L), and 8.25 and 0.76 (cutoff: 0.50 µg/L), respectively. On the other hand, the combination of CRP > 49.5 mg/L with PCT > 0.1 µg/L had an LR+ of 2.24 and LR− of 0.44.

4.4. P–Calprotectin

P–calprotectin has been recently reported to be a useful aid in sepsis-suspected patients. This biomarker has been found to be significantly elevated in critical patients after an assessment by a multidisciplinary team [33]. P–calprotectin was superior to traditional biomarkers in predicting the need for intensive care.

4.5. Procalcitonin (PCT)

PCT, on the other hand, is a 116-amino acid precursor polypeptide for calcitonin produced in C cells of the thyroid, which is expressed in reaction to microbial toxins and pro-inflammatory mediators such as IL-1B (interleukin-1beta, TNF-α, and IL-6), bacterial products (e.g., lipopolysaccharides) and necrotic tissue cells, and immune-reactive calcitonin [34]. They act as factors to reduce serum calcium levels, and their levels can be detected in healthy adults that rapidly rise 1000-fold with severe disease states [35]. PCT also responds to modulate immunity-related functions, vasomotility, and microcirculation, as well as changes in cytokine expression during hypoperfusion states mediated by endotoxins [36]. PCT is expressed and converted to calcitonin in the C-cells in the thyroid glands of healthy people without inflammation, presenting very low PCT levels (<0.1 ng/mL) [37].

PCT is a widely used serum biomarker, which is closely related to bacterial structure and severity of the infection. It is most specific to infections incited by bacteria, as it is attenuated by INF9 expressed in response to viral infections [38]. The metabolic response to elevated PCT in critical diseases has not been explained so far. The inflammatory response is critical to understand metabolic changes during extreme stress [39].

PCT is accepted as a valuable inflammatory biomarker to discern bacterial from viral, and other causes of pneumonia [16][40]. Besides acute bacterial infections, PCT helps to identify various medical conditions, including post-surgical anastomotic leaks, acute kidney injury, and consequences of intracerebral hemorrhage [41]. Research revealed that PCT levels rise in correlation with bacteremia and severe infection and predict death in patients with CAP and sepsis [42][43]. Studies from Northern Europe pointed out a link between elevated PCT readings and pneumonia severity [44]. PCT is not routinely worked up in the diagnostic process of CAP as its predictive accuracy is only moderate. Most clinicians order a PCT level at the time of diagnosis and serially to help decide the most beneficial duration of antibiotics.

4.6. Comparisons of PCT with CRP and Other Markers

Some investigations highlighted its diagnostic value in different clinical scenarios. PCT was more accurate than CRP to predict bacteremia, for discriminating bacterial from nonbacterial infections, and for determining bacterial species (i.e., AUC of PCT and CRP were 0.79 and 0.66, respectively) [45]. The optimal cutoff value for PCT was 0.5 mcg/L (sensitivity 70% and specificity 70%), whereas it was 50.0 mg/L for CRP (sensitivity 63% and specificity 65%). Using these cutoff values as a reference, the OR was 71.11 and the hazard ratio was 6.27 for PCT > 2.0 mcg/L, and the rate of BC positivity was markedly elevated.

Some studies advocated CRP against PCT in specific subgroups. For example, CRP was better than PCT at predicting pneumonia, as demonstrated in a retrospective study of elderly patients with comorbid diseases [46]. Zhang et al. compared patients with sepsis and those with local inflammatory diseases admitted to the ICU in China [47]. The combined AUC was significantly larger than the sum of IL–10, IL–17, and PCT. A clinical decision curve analysis disclosed that the three combined tests performed better than the individual tests with regard to the total clinical benefit rate. It was concluded that there was a considerable net therapeutic benefit ranging from 3 to 87%.

The analyses of soluble interleukin-2 receptor (sIL-2R), tumor necrosis factor-a (TNF-a), and PCT were found to carry a considerable benefit in the recognition of septic course in closed abdominal trauma complicated with severe multiple injuries [48]. The high concentrations of PCT and TNF-a can be used as valuable predictors of sepsis.

References

1. Johansson, N.; Kalin, M.; Tiveljung-Lindell, A.; Giske, C.G.; Hedlund, J. Etiology of community-acquired pneumonia: Increased microbiological yield with new diagnostic methods. Clin. Infect. Dis. 2010, 50, 202–209.
2. Strålin, K.; Olcén, P.; Törnqvist, E.; Holmberg, H. Definite, probable, and possible bacterial aetiologies of community-acquired pneumonia at different CRB-65 scores. Scand. J. Infect. Dis. 2010, 42, 426–434.
3. Vila-Corcoles, A.; Ochoa-Gondar, O.; Rodriguez-Blanco, T.; Raga-Luria, X.; Gomez-Bertomeu, F.; EPIVAC Study Group. Epidemiology of community-acquired pneumonia in older adults: A population-based study. Respir. Med. 2009, 103, 309–316.
4. Viasus, D.; Núñez-Ramos, J.A.; Viloria, S.A.; Carratalà, J. Pharmacotherapy for community-acquired pneumonia in the elderly. Expert Opin. Pharmacother. 2017, 18, 957–964.
5. Franquet, T. Imaging of Community-acquired Pneumonia. J. Thorac. Imaging 2018, 33, 282–294.
6. Nyamande, K.; Lalloo, U.G.; Vawda, F. Comparison of plain chest radiography and high-resolution CT in human immunodeficiency virus infected patients with community-acquired pneumonia: A sub-Saharan Africa study. Br. J. Radiol. 2007, 80, 302.

7. Claessens, Y.E.; Debray, M.P.; Tubach, F.; Brun, A.L.; Rammaert, B.; Hausfater, P.; Naccache, J.M.; Ray, P.; Choquet, C.; Carette, M.F.; et al. Early Chest Computed Tomography Scan to Assist Diagnosis and Guide Treatment Decision for Suspected Community-acquired Pneumonia. Am. J. Respir. Crit. Care Med. 2015, 192, 974.
8. Murtaza, H.G.; Javed, N.; Iqbal, A.; Ramzan, M.; ul haq Lodhi, O.; Majid, S.; Abbas, K.; Rehman, A.; Murtaza, H.G. Comparison of High-Resolution Computed Tomography and Real-Time Reverse Transcriptase Polymerase Chain Reaction in Diagnosis of COVID-19 Pneumonia in Intensive Care Unit Population. Cureus 2021, 13, e13602.
9. Long, L.; Zhao, H.T.; Zhang, Z.Y.; Wang, G.Y.; Zhao, H.L. Lung ultrasound for the diagnosis of pneumonia in adults: A meta-analysis. Medicine 2017, 96, e5713.
10. Llamas-Álvarez, A.M.; Tenza-Lozano, E.M.; Latour-Pérez, J. Accuracy of Lung Ultrasonography in the Diagnosis of Pneumonia in Adults: Systematic Review and Meta-Analysis. Chest 2017, 151, 374.
11. Furukawa, Y.; Luo, Y.; Funada, S.; Onishi, A.; Ostinelli, E.; Hamza, T.; Furukawa, T.A.; Kataoka, Y. Optimal duration of antibiotic treatment for community-acquired pneumonia in adults: A systematic review and duration-effect meta-analysis. BMJ Open 2023, 13, e061023.
12. Metlay, J.P.; Kapoor, W.N.; Fine, M.J. Does this patient have community-acquired pneumonia? Diagnosing pneumonia by history and physical examination. JAMA 1997, 278, 1440.
13. Musher, D.M.; Montoya, R.; Wanahita, A. Diagnostic value of microscopic examination of Gram-stained sputum and sputum cultures in patients with bacteremic pneumococcal pneumonia. Clin. Infect. Dis. 2004, 39, 165.
14. Corbo, J.; Friedman, B.; Bijur, P.; Gallagher, E.J. Limited usefulness of initial blood cultures in community acquired pneumonia. Emerg. Med. J. 2004, 21, 446.
15. Chalasani, N.P.; Valdecanas, M.A.L.; Gopal, A.K.; McGowan, J.E., Jr.; Jurado, R.L. Clinical utility of blood cultures in adult patients with community-acquired pneumonia without defined underlying risks. Chest 1995, 108, 932.
16. File, T.M., Jr. New diagnostic tests for pneumonia: What is their role in clinical practice? Clin. Chest Med. 2011, 32, 417–430.
17. Cho, M.C.; Kim, H.; An, D.; Lee, M.; Noh, S.A.; Kim, M.N.; Chong, Y.P.; Woo, J.H. Comparison of sputum and nasopharyngeal swab specimens for molecular diagnosis of Mycoplasma pneumoniae, Chlamydophila pneumoniae, and Legionella pneumophila. Ann. Lab. Med. 2012, 32, 133.
18. Templeton, K.E.; Scheltinga, S.A.; Van Den Eeden, W.C.; Graffelman, W.A.; Van Den Broek, P.J.; Claas, E.C. Improved diagnosis of the etiology of community-acquired pneumonia with real-time polymerase chain reaction. Clin. Infect. Dis. 2005, 41, 345.

19. Park, H.K.; Lee, H.J.; Kim, W. Real-time PCR assays for the detection and quantification of Streptococcus pneumoniae. FEMS Microbiol. Lett. 2010, 310, 48.
20. Resti, M.; Micheli, A.; Moriondo, M.; Becciolini, L.; Cortimiglia, M.; Canessa, C.; Indolfi, G.; Bartolini, E.; de Martino, M.; Azzari, C. Comparison of the effect of antibiotic treatment on the possibility of diagnosing invasive pneumococcal disease by culture or molecular methods: A prospective, observational study of children and adolescents with proven pneumococcal infection. Clin. Ther. 2009, 31, 1266.
21. Besen, B.A.M.P.; Romano, T.G.; Nassar, A.P.; Taniguchi, L.U.; Azevedo, L.C.P.; Mendes, P.V.; Zampieri, F.G.; Park, M. Sepsis-3 definitions predict ICU mortality in a low–middle-income country. Ann. Intensive Care 2016, 6, 107.
22. Frenzen, F.S.; Kutschan, U.; Meiswinkel, N.; Schulte-Hubber, B.; Ewig, S.; Kolditz, M. Admission lactate predicts poor prognosis independently of the CRB/CURB-65 scores in community-acquired pneumonia. Clin. Microbiol. Infect. 2017, 24, 306-e1.
23. Dellinger, R.P.; Levy, M.M.; Rhodes, A.; Annane, D.; Gerlach, H.; Opal, S.M.; Sevransky, J.E.; Sprung, C.L.; Douglas, I.S.; Jaeschke, R.; et al. Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock: 2012. Crit. Care Med. 2013, 41, 580–637.
24. Howell, M.D.; Donnino, M.; Clardy, P.; Talmor, D.; Shapiro, N.I. Occult hypoperfusion and mortality in patients with suspected infection. Intensive Care Med. 2007, 33, 1892–1899.
25. Singer, M.; Deutschman, C.S.; Seymour, C.W.; Shankar-Hari, M.; Annane, D.; Bauer, M.; Bellomo, R.; Bernard, G.R.; Chiche, J.D.; Coopersmith, C.M.; et al. The third international consensus definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016, 315, 801–810.
26. Vargun, P.; Yilmaz, S.; Tatliparmak, A.C.; Karcioglu, O. Should lactate levels be combined with rapid emergency medicine scores (REMS) to predict outcomes of patients with dyspnea. Signa Vitae 2023, 19.
27. Zhuang, Y.; Li, W.; Wang, H.; Peng, H.; Chen, Y.; Zhang, X.; Chen, Y.; Gao, C. Predicting the Outcomes of Subjects with Severe Community-Acquired Pneumonia Using Monocyte Human Leukocyte Antigen-DR. Respir. Care 2015, 60, 1635–1642.
28. Holm, A.; Nexoe, J.; Bistrup, L.A.; Pedersen, S.S.; Obel, N.; Nielsen, L.P. Aetiology and prediction of pneumonia in lower respiratory tract infection in primary care. Br. J. Gen. Pract. 2007, 57, 547.
29. Boussekey, N.; Leroy, O.; Alfandari, S.; Devos, P.; Georges, H.; Guery, B. Procalcitonin kinetics in the prognosis of severe community-acquired pneumonia. Intensive Care Med. 2006, 32, 469.
30. van Vugt, S.F.; Broekhuizen, B.D.; Lammens, C.; Zuithoff, N.P.; de Jong, P.A.; Coenen, S.; Ieven, M.; Butler, C.C.; Goossens, H.; Little, P. Grace Consortium. Use of serum C reactive protein and

procalcitonin concentrations in addition to symptoms and signs to predict pneumonia in patients presenting to primary care with acute cough: Diagnostic study. BMJ 2013, 346, f2450.

31. Menéndez, R.; Martínez, R.; Reyes, S.; Mensa, J.; Filella, X.; Marcos, M.A. Biomarkers improve mortality prediction by prognostic scales in community-acquired pneumonia. Thorax 2009, 64, 587–591.
32. Ebell, M.H.; Bentivegna, M.; Cai, X.; Hulme, C.; Kearney, M. Accuracy of Biomarkers for the Diagnosis of Adult Community-acquired Pneumonia: A Meta-analysis. Acad. Emerg. Med. 2020, 27, 195–206.
33. Parke, Å.; Unge, C.; Yu, D.; Sundén-Cullberg, J.; Strålin, K. Plasma calprotectin as an indicator of need of transfer to intensive care in patients with suspected sepsis at the emergency department. BMC Emerg. Med. 2023, 23, 16.
34. Lee, H. Procalcitonin as a biomarker of infectious diseases. Korean J. Intern. Med. 2013, 28, 285–291.
35. Maruna, P.; Nedelnikova, K.; Gurlich, R. Physiology and genetics of procalcitonin. Physiol. Res. 2000, 49 (Suppl. 1), S57–S61.
36. Hoffmann, G.; Czechowski, M.; Schloesser, M.; Schobersberger, W. Procalcitonin amplifies inducible nitric oxide synthase gene expression and nitric oxide production in vascular smooth muscle cells. Crit. Care Med. 2002, 30, 2091–2095.
37. Vijayan, A.L.; Vanimaya; Ravindran, S.; Saikant, R.; Lakshmi, S.; Kartik, R.; Kartik, R. Procalcitonin: A promising diagnostic marker for sepsis and antibiotic therapy. J. Intensive Care 2017, 5, 51.
38. Philipp, S.; Werner, A.; Beat, M. Procalcitonin for diagnosis of infection and guide to antibiotic decisions: Past, present and future. BMC Med. 2011, 9, 107.
39. Kobayashi, H.; Amrein, K.; Lasky-Su, J.A.; Christopher, K.B. Procalcitonin metabolomics in the critically ill reveal relationships between inflammation intensity and energy utilization pathways. Sci Rep. 2021, 11, 23194.
40. Upadhyay, S.; Niederman, M.S. Biomarkers: What is their benefit in the identification of infection, severity assessment, and management of community-acquired pneumonia? Infect. Dis. Clin. N. Am. 2013, 27, 19–31.
41. Choi, J.J.; McCarthy, M.W. Novel applications for serum procalcitonin testing in clinical practice. Expert Rev. Mol. Diagn. 2018, 18, 27–34.
42. Christ-Crain, M.; Stolz, D.; Bingisser, R.; Muller, C.; Miedinger, D.; Huber, P.R.; Zimmerli, W.; Harbarth, S.; Tamm, M.; Muller, B. Procalcitonin guidance of antibiotic therapy in community-acquired pneumonia: A randomized trial. Am. J. Respir. Crit. Care Med. 2006, 174, 84–93.

43. Jensen, J.U.; Heslet, L.; Jensen, T.H.; Espersen, K.; Steffensen, P.; Tvede, M. Procalcitonin increase in early identification of critically ill patients at high risk of mortality. Crit. Care Med. 2006, 34, 2596–2602.
44. Johansson, N.; Kalin, M.; Backman-Johansson, C.; Larsson, A.; Nilsson, K.; Hedlund, J. Procalcitonin levels in community-acquired pneumonia-correlation with aetiology and severity. Scand. J. Infect. Dis. 2014, 46, 787–791.
45. Nishikawa, H.; Shirano, M.; Kasamatsu, Y.; Morimura, A.; Iida, K.; Kishi, T.; Goto, T.; Okamoto, S.; Ehara, E. Comparison between procalcitonin and C-reactive protein in predicting bacteremias and confounding factors: A case-control study. Clin. Chem. Lab. Med. 2017, 55, 1043–1052.
46. Nouvenne, A.; Ticinesi, A.; Folesani, G.; Cerundolo, N.; Prati, B.; Morelli, I.; Guida, L.; Lauretani, F.; Maggio, M.; Aloe, R.; et al. The association of serum procalcitonin and high-sensitivity C-reactive protein with pneumonia in elderly multimorbid patients with respiratory symptoms: Retrospective cohort study. BMC Geriatr. 2016, 16, 16.
47. Zhang, W.; Wang, W.; Hou, W.; Jiang, C.; Hu, J.; Sun, L.; Hu, L.; Wu, J.; Shang, A. The diagnostic utility of IL-10, IL-17, and PCT in patients with sepsis infection. Front. Public Health 2022, 10, 923457.
48. Zhai, G.H.; Zhang, W.; Xiang, Z.; He, L.Z.; Wang, W.W.; Wu, J.; Shang, A.Q. Diagnostic Value of sIL-2R, TNF-α and PCT for Sepsis Infection in Patients with Closed Abdominal Injury Complicated with Severe Multiple Abdominal Injuries. Front Immunol. 2021, 12, 741268.