**Supplementary Table 1:** Standard definitions used to adjudicate secondary infections (developed after 48 hours of hospital admission) among COVID-19 patients.

|  |  |  |  |
| --- | --- | --- | --- |
| **Type of Secondary Infection** | **Proven** | **Probable** | **Possible** |
| Hospital-acquired bacterial pneumonia | Timing criteria:  - Period of stability/improvement in supplemental oxygen settings/device; AND  - Worsening of oxygenation  Clinical criteria:  - Temp >38°C or <36°C AND WBC ≥12,000a; AND  - Chest imaging with new/worsening findings  Microbiologic criteria:  - Endotracheal aspirate/BALb/sputum with potential pathogen | Meets timing AND clinical criteria AND clinical improvement on antibiotics within 48-72 hours | New onset fever, hypoxia/worsening hypoxia, OR new/worsening radiographic evidence of pneumonia |
| Ventilator-associated pneumonia | Timing criteria:  - ≥3 days of mechanical ventilation; AND  - Period of stability/improvement in vent settings for ≥2 days preceding event; AND  - Increase in FiO2 >0.2 and/or minimum daily PEEP >3 sustained for ≥2 days  Clinical criteria:  - Temp >38°C or <36°C AND WBC ≥12,000a; OR  - Chest imaging with new/worsening findings  Microbiologic criteria:  - Endotracheal aspirate/BALb with potential pathogen | Meets timing AND clinical criteria AND clinical improvement on antibiotics within 48-72 hours | Meets clinical or microbiologic criteria |
| Fungal respiratory infection | Microscopic analysis of tissue consistent with hyphae/yeast AND evidence of associated tissue damage | Host factorc, clinical features, AND mycologic evidence.  Clinical features:  - Lower respiratory tract fungal disease  - ≥1 on CT chest: dense well-circumscribed lesions, air-crescent sign, cavity  Mycological criteria:  - Recovery of a mold in culture or of fungal elements from a respiratory source; OR  - Indirect testd | - Appropriate host factors and clinical features but no mycologic support; OR  - Evidence of positive fungal indirect testd/fungal culture with unclear supporting clinical features |
| Viral/atypical respiratory infection | - Positive nucleic acid amplification test for respiratory virus (excluding SARS-CoV-2)  - Positive NP swab/BALb for *Mycoplasma*  - Positive *L. pneumophila* urinary antigen test/BALb with *L. pneumophila* | N/A | N/A |
| Bloodstream infection | - Blood culture with bacteria/yeast  - Not deemed a contaminante | N/A | N/A |
| Urinary tract infection | - Signs/symptoms of UTI; AND  - Pyuria (>10 wbc/hpf) on urinalysis; AND  - Urine/blood culture with a typical pathogen | N/A | N/A |
| *Clostridioides difficile* infection (CDI) | - Clinical picture compatible with CDI; AND  - Positive *C. difficile* nucleic acid amplification test (NAAT) | N/A | N/A |
| Skin and Soft Tissue Infection (SSTI) | Timing criteria:  - admitted for at least 3 days  Clinical criteria:  - Unilateral or localized area of erythema, tenderness on exam,  AND/OR  - A wound with surrounding erythema and purulent discharge  OR  - An abscess on imaging  Microbiologic criteria:  - Positive culture with recovery of an organism from a deep culture | Meets the criteria for timing and clinical characteristics |  |

a Leukopenia was not considered, as leukopenia and lymphopenia are commonly seen with COVID-19 infections.

b Bronchoalveolar lavage

c Host factors include: Recent history of neutropenia (<500 PMN/mm3) for >10 days temporally related to the onset of fungal disease, hematologic malignancy, receipt of an allogeneic stem cell or solid organ transplant, receipt of a solid organ transplant, prolonged use of corticosteroids with mean minimum dose 0.3 mg/kg/day of prednisone equivalent for >3 weeks, treatment with other recognized T cell immunosuppressants (such as cyclosporine, TNF-α blockers, specific monoclonal antibodies (such as alemtuzumab), or nucleoside analogs) during the past 90 days, or inherited severe immunodeficiency

d Indirect fungal tests include positive serum or BAL galactomannan ≥0.5, fungal pathogen identified in culture and/or fungal elements identified in microscopic analysis of sterile material, cryptococcal antigen, *Pneumocystis* direct fluorescent antigen and/or PCR

e Contamination was determined based on several factors including number of positive cultures, if vascular hardware present, consultant’s opinion, and/or documentation of such in the patient’s chart

**Supplementary Table 2:** Hospital-acquired infections among COVID-19 adult patients.

|  |  |
| --- | --- |
| Hospital-acquired infections | **Number of patients**  **N=206 (%)** |
| Hospital-acquired pneumonia  Proven  Probable  Possible | 133 (65)  6 (3)  10 (5)  117 (57) |
| Ventilator-associated pneumonia  Proven  Probable  Possible | 73 (35)  9 (4)  7 (3)  57 (28) |
| Viral pneumonia | 0 |
| Respiratory fungal infection\*  Probable  Possible | 8 (4)  2 (1)  6 (3) |
| Bloodstream infection | 22 (11) |
| Urinary tract infection | 19 (9) |
| Skin and soft tissue infection  Proven  Probable | 9 (4)  1  8 (4) |
| *Clostridioides* *difficile* infection | 5 (2) |

\*All pulmonary aspergillosis.

**Supplementary table 3.** Organisms isolated from microbiology cultures in other proven/probable infections developed >48 hours of hospitalization in patients with COVID-19.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Total** | **HAP** | **VAP** | **Fungal respiratory infections** | **BSI** | **UTI** | **SSTI** |
| **Monomicrobial** | 47 | 4 | 7 | 1 | 19 | 16 | -- |
| **Polymicrobial** | 14 | 3 | 5 | -- | 3 | 2 | 1 |
| **Organisms** | 77 | 10 | 18 | 1 | 26 | 20 | 2 |
| **Gram-negative bacteria (%)** | 41 (53.2) | 3 (30.0) | 12 (66.7) | -- | 9 (34.6) | 16 (80.0) | 1 (50.0) |
| *Klebsiella* spp. | 13 (16.9) | 1 (10.0) | 5 (27.8) | -- | 5 (19.2) | 2 (10.0) | -- |
| *Escherichia coli* | 8 (10.4) | -- | 1 (5.6) | --- | -- | 7 (35.0) | -- |
| *Proteus* spp. | 5 (6.5) | -- | -- | -- | 1 (3.8) | 3 (15.0) | 1 (50.0) |
| *Pseudomonas aeruginosa* | 5 (6.5) | -- | 2 (11.1) | -- | -- | 3 (15.0) | -- |
| *Citrobacter* spp. | 2 (2.6) | -- | 2 (11.1) | -- | -- | -- | -- |
| *Serratia* spp. | 2 (2.6) | -- | -- | -- | 1 (3.8) | 1 (5.0) | -- |
| Other\* | 6 (7.8) | 2 (20.0) | 2 (11.1) | -- | 2 (7.7) | -- | -- |
| **Gram-positive bacteria (%)** | 31 (40.3) | 7 (70.0) | 6 (33.3) | -- | 15 (57.7) | 2 (10.0) | 1 (50.0) |
| *Staphylococcus aureus*  MSSA  MRSA | 17 (22.1)  11  6 | 5 (50.0)  3  2 | 6 (33.3)  3  3 | -- | 6 (23.1)  5  1 | -- | -- |
| *Enterococcus* spp. | 6 (7.8) | -- | -- | -- | 3 (11.5) | 2 (10.0) | 1 (50.0) |
| Coagulase-negative staphylococci | 4 (5.2) | -- | -- | -- | 4 (15.4) | -- | -- |
| *Streptococcus* spp.\* | 3 (3.9) | 1 (10.0) | -- | -- | 2 (7.7) | -- | -- |
| *Corynebacterium* spp. | 1 (1.3) | 1 (10.0) | -- | -- | -- | -- | -- |
| **Fungi (%)** | 5 (6.5) | -- | -- | 1 (100.0) | 2 (7.7) | 2 (10.0) | -- |
| *Aspergillus* spp. | 1 (1.3) | -- | -- | 1 (100.0) | -- | -- | -- |
| *Candida* spp. | 4 (5.2) | -- | -- | -- | 2 (7.7) | 2 (10.0) | -- |

Abbreviations: BSI = Bloodstream infection; ESBL = Extended-spectrum beta-lactamase; HAP = Hospital-acquired pneumonia; SSTI = Skin and soft tissue infection; UTI = Urinary tract infection; VAP = Ventilator-associated pneumonia.

\**Achromobacter xylosoxidans* (1), *Bacteroides* spp. (1), *Enterobacter cloacae* complex (1), *Prevotella bivia* (1), *Raoultella ornithinolytica* (1), and *Stenotrophomonas maltophilia* (1).

\*\**Streptococcus bovis* group (1), *Streptococcus* group C/G (1), and *Viridans streptococcus* group (1).