# Outcomes and Risk Factors Associated with the Development of Pneumonia in Lung Transplant Recipients in the Year after Transplant

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## BACKGROUND

Lung transplant patients experience considerable infection-related morbidity and mortality, including from pneumonia. We strove to evaluate the incidence of and factors associated with pneumonia in the year after transplant.

## METHODS

This was a retrospective cohort study of all patients who received a lung transplant at TUH in 2018-19. Patients were identified from our transplant database and records were reviewed from the pre-transplant period to 1-year after transplant for data pertinent to comorbidities, transplantation characteristics and complications, donor organ cultures, immunosuppression, prophylactic and therapeutic antibiotic regimens, pathogens, and outcomes. Development of pneumonia was the primary outcomes; episodes of pneumonia were evaluated by two ID physicians using standard criteria.

Patients who developed pneumonia during the year post-transplant were compared with those who did not. Factors associated with the development of pneumonia with a p<0.2 and comprised more than 15% of the total population were entered into a backwards stepwise logistic regression model.

## RESULTS – PATIENT CHARACTERISTICS

| Patient Characteristic | Total (n=291) | Pneumonia (n=98) | No pneumonia (n=193) | p-value |
|---|---|---|---|---|
| Age, years | 64.71 ± 8.64 | 63.23 ± 9.49 | 65.47 ± 8.11 | 0.037 |
| Sex, male | 197 (67.7) | 66 (67.3) | 131 (67.9) | 0.927 |
| Comorbidities (PMH) | | | | |
| Asthma | 31 (10.7) | 11 (11.2) | 20 (10.4) | 0.822 |
| COPD | 136 (46.7) | 45 (45.9) | 91 (47.2) | 0.842 |
| Obesity | 60 (20.6) | 24 (24.5) | 36 (18.7) | 0.245 |
| DM | 83 (28.5) | 31 (31.6) | 52 (26.9) | 0.402 |
| ILD | 87 (29.9) | 34 (34.7) | 53 (27.5) | 0.203 |
| IPF | 149 (51.2) | 49 (50.0) | 100 (51.8) | 0.770 |
| HTN | 137 (47.1) | 42 (42.9) | 95 (49.2) | 0.304 |
| CF | 3 (1.0) | 2 (2.0) | 1 (0.5) | 0.263 |
| History of VATS | 30 (10.3) | 11 (11.2) | 19 (9.8) | 0.714 |
| Atrial fibrillation | 33 (11.3) | 18 (18.4) | 15 (7.8) | 0.007 |
| Lung nodules | 20 (6.9) | 4 (4.1) | 16 (8.3) | 0.180 |
| Depression / anxiety | 68 (23.4) | 26 (26.5) | 42 (21.8) | 0.364 |
| Malignancy | 48 (16.5) | 12 (12.2) | 36 (18.7) | 0.164 |
| Pulmonary HTN | 78 (26.8) | 27 (27.6) | 51 (26.4) | 0.838 |
| Prior history of MAC | N=288 24 (8.3) | N=97 8 (8.2) | N=191 16 (8.4) | 0.970 |
| Prior history of MDR 90 days prior to lung transplant | N=287 18 (6.3) | N=97 11 (11.3) | N=190 7 (3.7) | 0.011 |

## RESULTS – TRANSPLANT CHARACTERISTICS

| #(%) or median [IQR] | Total (n=291) | Pneumonia (n=98) | No Pneumonia (n=193) | P-Value |
|---|---|---|---|---|
| Year of transplant | | | | |
| 2018 | 145 (49.8) | 42 (42.9) | 103 (53.4) | 0.090 |
| 2019 | 146 (50.2) | 56 (57.1) | 90 (46.6) | |
| Type of transplant | | | | |
| Left | 110 (37.8) | 28 (28.6) | 82 (42.5) | 0.021 |
| Right | 120 (41.2) | 44 (44.9) | 76 (39.4) | 0.366 |
| Dual | 61 (21) | 26 (26.5) | 35 (18.1) | 0.096 |
| CMV Risk | | | | |
| Low (D- / R-) | 56 (19.2) | 14 (14.3) | 42 (21.8) | 0.126 |
| Intermediate (D+ / R+) | 173 (59.5) | 61 (62.2) | 112 (58.0) | 0.489 |
| High (D+ / R-) | 62 (21.3) | 23 (23.5) | 39 (20.2) | 0.521 |
| EBV Risk | | | | |
| Low (D- / R-) | 4 (1.4) | 1 (1.0) | 3 (1.6) | 1.000 |
| Intermediate (D+ / R+) | 264 (90.7) | 91 (92.9) | 173 (89.6) | 0.371 |
| High (D+ / R-) | 15 (5.2) | 5 (5.1) | 10 (5.2) | 0.977 |
| Unable to determine | 8 (2.7) | 1 (1.0) | 7 (3.6) | 0.274 |
| Induction immunosuppression | N=289 | N=98 | N=191 | |
| Basiliximab | 161 (55.7) | 60 (61.2) | 101 (52.9) | 0.176 |
| Alemtuzumab | 128 (44.3) | 38 (38.8) | 90 (47.1) | |
| Intraoperative complications | N=288 | N=98 | N=190 | |
| Required blood transfusions | 9 (3.1) | 6 (6.1) | 3 (1.6) | 0.066 |
| Lung cutdown performed | 1 (0.3) | 1 (1.0) | 0 (0) | 0.340 |
| Adhesions | 22 (7.6) | 13 (13.3) | 9 (4.7) | 0.010 |
| Afib requiring cardioversion | 8 (2.8) | 2 (2.0) | 6 (3.2) | 0.720 |
| Hypotension | 12 (4.2) | 5 (5.1) | 7 (3.7) | 0.550 |
| Significant bleeding | 6 (2.1) | 3 (3.1) | 3 (1.6) | 0.413 |
| ECMO | 28 (9.7) | 15 (15.3) | 13 (6.8) | 0.022 |
| Other arrhythmias | 15 (5.2) | 6 (6.1) | 9 (4.7) | 0.616 |
| Post-operative immunosuppression | | | | |
| Tacrolimus | 286 (98.3) | 95 (96.9) | 191 (99.0) | 0.339 |
| Sirolimus | 1 (0.3) | 1 (1.0) | 0 (0) | 0.337 |
| Mycophenolate | 260 (89.3) | 82 (83.7) | 178 (92.2) | 0.025 |
| Prednisone / methylpred | 288 (99.0) | 97 (99.0) | 191 (99.0) | 1.000 |
| Cyclosporine | 8 (2.7) | 5 (5.1) | 3 (1.6) | 0.124 |

All patients received pre-operative antibacterial, antifungal, and antiviral prophylaxis with a variety of regimens. Most common antibiotics were vancomycin (93.1%), piperacillin-tazobactam (81.4%), cefazolin (23%), and ciprofloxacin (12%). The mean duration was 7.45 ± 3.73 days.

## RESULTS – POST-OP RISK FACTORS

| Variable #(%) or median [IQR] | Total (n=291) | Pneumonia (n=98) | No Pneumonia (n=193) | P-Value |
|---|---|---|---|---|
| Re-intubated within 7 days post-op | N=288 36 (12.5) | N=98 18 (18.4) | N=190 18 (9.5) | 0.031 |
| Development of rejection during immediate post-transplant period | N=288 8 (2.8) | N=97 5 (5.2) | N=191 3 (1.6) | 0.124 |
| Bronchial stent within 1-year post-transplant | N=288 24 (8.3) | N=96 19 (19.8) | N=192 5 (2.6) | <0.001 |

## RESULTS - PNEUMONIA

Pneumonia developed in 98/291 (33.7%) patients at a median of 66 days after transplant (IQR 15-142). Most frequent pathogens >10 cases were *P. aeruginosa* (n=36), *S. aureus* (16), and *K. pneumoniae* (13). The most common viral cause was RSV (5) and 3 patients had fungal pneumonia with different pathogens.

Patients with pneumonia had significantly lower 1-year survival rates than those without (79/98 (80.6%) vs. 180/193 (93.3%), p<0.001). They also had more readmissions after transplant (3.39 ± 2.96 vs 1.84 ± 2.42, p<0.001) and more acute rejection episodes (0.29 ± 0.61 vs 0.13 ± 0.42, p<0.026).

## RESULTS – PREDICTORS

| Variables associated with protection from pneumonia | aOR | 95% CI | P-Value |
|---|---|---|---|
| Basiliximab induction therapy | 0.535 | 0.307-0.932 | 0.27 |
| Mycophenolate used as immunosuppression | 0.425 | 0.189-0.954 | 0.038 |
| Piperacillin-tazobactam used as pre-operative prophylaxis | 0.513 | 0.269-0.977 | 0.042 |
| Trimethoprim-sulfamethoxazole used as opportunistic infection prophylaxis | 0.506 | 0.294-0.870 | 0.014 |

## CONCLUSIONS

In our population, pneumonia occurred in about a third of patients and was associated with increased 1-year mortality. Several factors were associated with protection from pneumonia.

## FUNDING