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Donor-Derived Mollicute Infections in Lung Transplant Recipients: a Prospective Study of Donor Respiratory Tract Screening and Recipient Outcomes

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Background

- Mollicutes are fastidious bacteria that can cause both pulmonary and extrapulmonary donor-derived infections after lung transplant
- Best practice for donor screening and recipient surveillance is unknown

OBJECTIVE: To assess the performance of donor respiratory tract Mollicute screening in lung transplant recipients

Methods

- **Prospective analysis** of all lung transplant recipients between **10/5/20 – 9/25/21** at a single academic transplant center
- Donor BAL performed at time of transplant was tested for the presence of urogenital *Mycoplasma* spp. and *Ureaplasma* spp. using culture and PCR (screening)
- Screening results were blinded to treating clinicians
- Clinical infection was defined as any microbiological study submitted and positive for *M. hominis* or *Ureaplasma* spp. post-transplantation
- Donor and recipient characteristics, treatment courses, and outcomes were analyzed with a follow-up period **up to 1 year after transplant**

Figure. Clinical courses of 9 lung transplant recipients who acquired post-transplant *Mycoplasma hominis* or *Ureaplasma* spp.

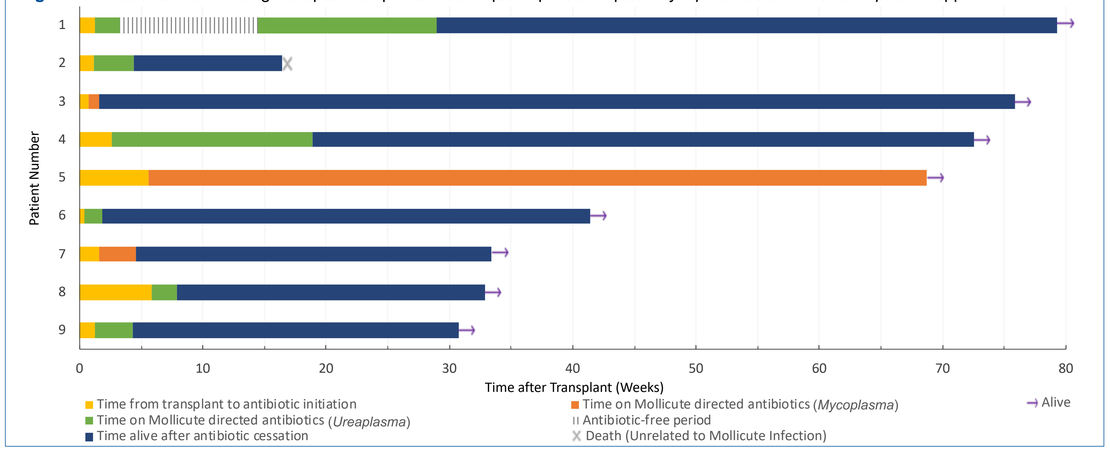

Table 1. Characteristics of 9 lung transplant recipients who developed Mollicute colonization or infection

Patient Number	Age and Gender	Positive Donor Screening Tests	Donor Species Detected	Positive Tests for Recipient Diagnosis	Recipient Species Detected	Site of Mollicute Detection	Hyperammonemia Syndrome[a]	Weeks of Mollicute Antimicrobial Therapy	Outcome
1	64 M	PCR and culture	*M. hominis* and *U. urealyticum*	Culture	*U. urealyticum*	Pulmonary and extrapulmonary (mediastinal)	No	16.5 weeks	Clinical cure
2	69 M	PCR and culture	*U. parvum* and *U. urealyticum*	Culture	*Ureaplasma* sp.	Pulmonary	No	3 weeks	Death (unrelated)[b]
3	66 F	Culture	*Mycoplasma* sp.	Culture	*Mycoplasma* sp.	Pulmonary	Possible	1 week	Clinical cure
4	72 M	PCR and culture	*U. parvum*	PCR and Culture	*U. parvum*	Pulmonary and extrapulmonary (pleural)	Definite	16 weeks	Clinical cure
5	74 M	Culture	*M. hominis*	Culture	*M. hominis*	Extrapulmonary (mediastinal)	No	63 weeks (ongoing)	Long-term antibiotic suppression[c]
6	51 M	Negative screen	N/A	Culture	*Ureaplasma* sp.	Pulmonary	No	1.5 weeks	Clinical cure
7	43 F	PCR	*M. hominis*	Culture	*M. hominis*	Pulmonary	No	3 weeks	Clinical cure
8	27 F	Negative screen	N/A	PCR	*Ureaplasma* sp.	Pulmonary	No	2 weeks	Clinical cure
9	58 F	PCR and culture	*Ureaplasma* sp.	Culture	*Ureaplasma* sp.	Pulmonary	No	3 weeks	Clinical cure

[a]Definite hyperammonemia syndrome was defined by altered mentation and a corresponding serum ammonia level ≥100 µmol/L. Possible hyperammonemia syndrome required altered mentation and ammonia levels of 51-99 µmol/L. [b]Death for Patient 2 was due to an unrelated infection. [c]Long-term antibiotic suppression for Patient 5 is due to hardware-associated mediastinal *M. hominis* infection.
Abbreviations: *M.*, *Mycoplasma*; PCR, polymerase chain reaction; *U.*, *Ureaplasma*.

Results

- **115 patients** underwent lung transplantation
- **99/115 (86%)** of lung transplant recipients had donor BAL tested for Mollicutes with Mollicute-specific culture and PCR at time of transplant
- **8/99 (8%) donors had culture-positive** samples, and **15/99 (15%) had PCR-positive samples** for Mollicutes during screening at time of transplant
- **9/99 (9%) patients** developed clinical Mollicute infection post-transplant (Figure)
  - Recipients were diagnosed a **median of 6 days after transplant (IQR 4-15 days)**
  - 6 patients had isolated pulmonary infection and 3 patients had extrapulmonary infection
- Of these 9 patients, **1 death** occurred which was unrelated to Mollicute infection (Table 1)
- Donor BAL **culture sensitivity was 6/9 (67%)** and **PCR sensitivity was 5/9 (56%)** in predicting recipient Mollicute infection**. Positive predictive value (PPV) was 6/8 (75%) for donor culture** and **5/15 (33%) for PCR** (Table 2)

Conclusions

- In our single center cohort, donor BAL screening via culture predicted all serious recipient Mollicute infections and had better PPV than PCR
- Given the limitations of either donor screening method, clinicians should maintain a high index of suspicion for Mollicute infection after lung transplant despite a negative screening test

Table 2. Performance of donor BAL screening methods in predicting Mollicute infection among 99 lung transplant recipients

Donor Screening Method	Sensitivity		Specificity		Positive Predictive Value		Negative Predictive Value	
PCR	5/9	(56)	80/90	(89)	5/15	(33)	80/84	(95)
Culture	6/9	(67)	88/90	(98)	6/8	(75)	88/91	(97)
PCR and culture[a]	7/9	(78)	78/89	(88)	7/18	(39)	78/81	(96)

Data are presented as No. (%). [a]For the combined PCR and culture method, if either the PCR or culture detected a Mollicute, the donor screening test was considered to be positive. If both studies were negative, the screening test was negative. Abbreviations: PCR, polymerase chain reaction.

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