Respiratory Virus Infections and Airflow Obstruction after Allogeneic Hematopoietic Cell Transplantation

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Background

- Respiratory viruses are readily detectable in hematopoietic cell transplant (HCT) recipients in the molecular diagnostic era.
- The association of respiratory virus infections with acute and chronic airflow obstruction (AFO) is poorly defined.

Objective

- To prospectively characterize the spectrum and temporal pattern of respiratory virus infections, their initial clinical presentation as well as their association with airflow obstruction, including temporary and late airflow obstruction phenotypes, in subjects undergoing HCT.

Methods

- Prospective cohort study of allogeneic HCT recipients of all ages
- PCR surveillance: weekly testing of nasal wash/throat swabs testing by multiplex PCR for 11 viruses for the first 100 days and every 3 months and with respiratory symptoms thereafter.
- Pulmonary function testing in those over 6 years of age
  - Weekly handheld spirometry throughout one year after HCT
  - Standard pulmonary function testing occurred at recommended intervals.
- Symptom survey: 16 question
- Airflow obstruction phenotypes
  - Short-term AFO: 2- or 4-week decline (↓) of 1 second forced expiratory volume (FEV1) >10% by handheld spirometry
  - Late AFO: FEV1/forced vital capacity [FVC] < lower limit normal predicted and FEV1 decline >10% from baseline at 3 years
  - Bronchiolitis obliterans syndrome (BOS): FEV1 <75%, FEV1/FVC <0.7, and FEV1 ↓ >10% from baseline) by 3 years after HCT
  - Late AFO and BOS were assessed by standard pulmonary function testing.
- Statistical analysis: Cox proportional hazard models were used to correlate longitudinal symptomatic respiratory tract viral infections with AFO phenotypes
- Fred Hutchinson Cancer Research Center IRB approved the study.

Results

- Overall, 7,091 PCR tests were performed in 471 symptomatic and asymptomatic patients
- 70% of patients had ≥1 respiratory virus detected.
- Among 437 patients who survived >4 weeks
  - Decline of FEV-1 for 2 weeks 11.9%
  - Decline of FEV-1 for 4 weeks 7.1%
  - Late AFO 15.6%
  - BOS 3.9%

Short-term FEV-1 Decline

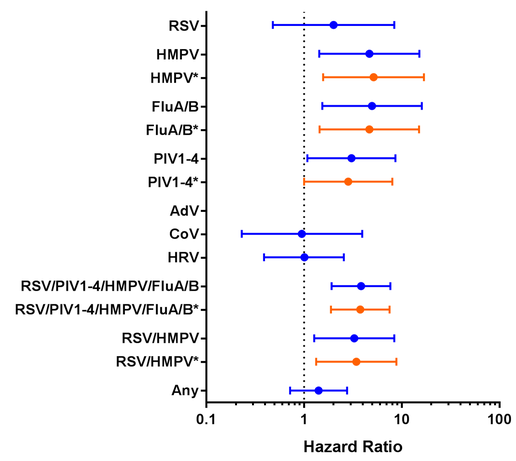

Figure 1. Association of first respiratory virus upper respiratory tract infection (URI) with 2-week airflow decline by handheld spirometry. Results from univariate (blue) and multivariable models (*orange; separate for each virus category; adjusted for recipient sex) are shown (categories without HRs have too few events to fit the model).

Conclusions

- Development of AFO after HCT is common.
- Respiratory viruses are significantly associated with both short-term airflow decline and long-term airflow obstruction.
- Interventional strategies that target multiple viruses are warranted.

Results

Late Airflow Obstruction and BOS

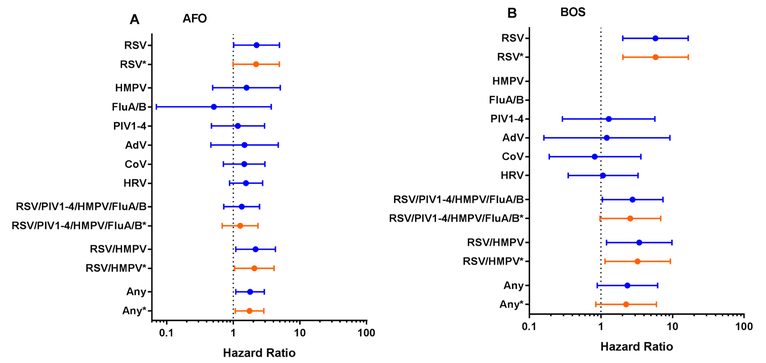

Figure 2. Association of respiratory virus URIs with late AFO (A) and BOS (B). Results from univariate (blue) and multivariable models (*orange; separate for each virus category) are shown. AFO estimates were adjusted for recipient age, recipient race and intensity of the conditioning regimen; BOS estimates were adjusted for recipient race and intensity of the conditioning regimen (categories without HRs have too few events to fit the model).

Impact of Lower Tract Viral Disease

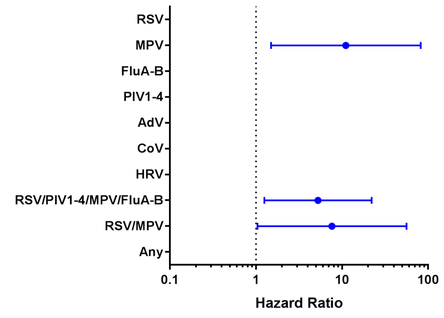

Figure 3. Association of respiratory virus lower respiratory tract disease with 2 week airflow decline, adjusted for sex. There was no statistically significant association with AFO and BOS.

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