Bile Acid Aspiration is Associated with Airway Infections: A Targeted Metabolomic Approach

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OBJECTIVE

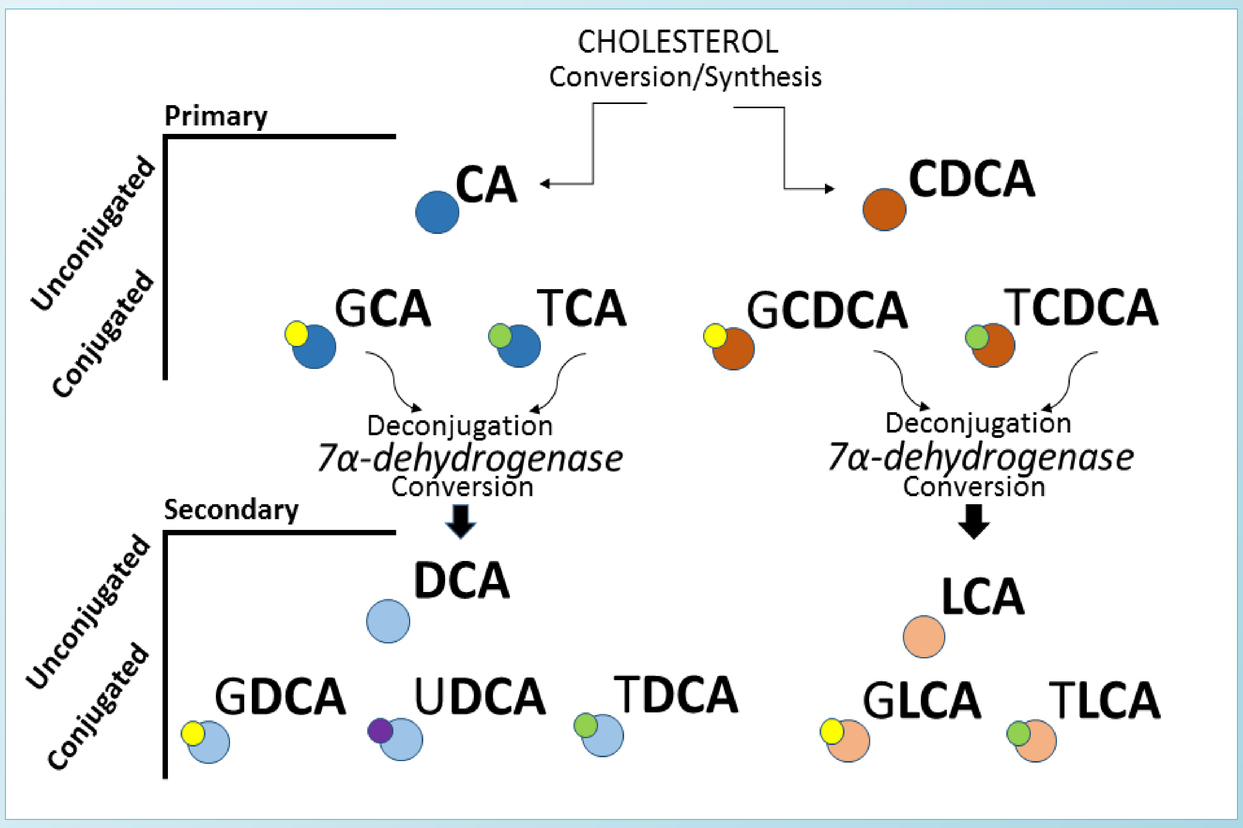
- Gastroesophageal reflux and bile acids (BAs) aspiration is a risk factor for chronic lung allograft dysfunction.
- BAs may compromise the broncho-alveolar innate immunity by deranging the lipid surface barrier and/or by direct modulation of macrophage activity.
- Targeted BAs metabolomics and bacterial, fungal and viral cultures were investigated in post lung transplant surveillance bronchial washings (BW).

METHODS

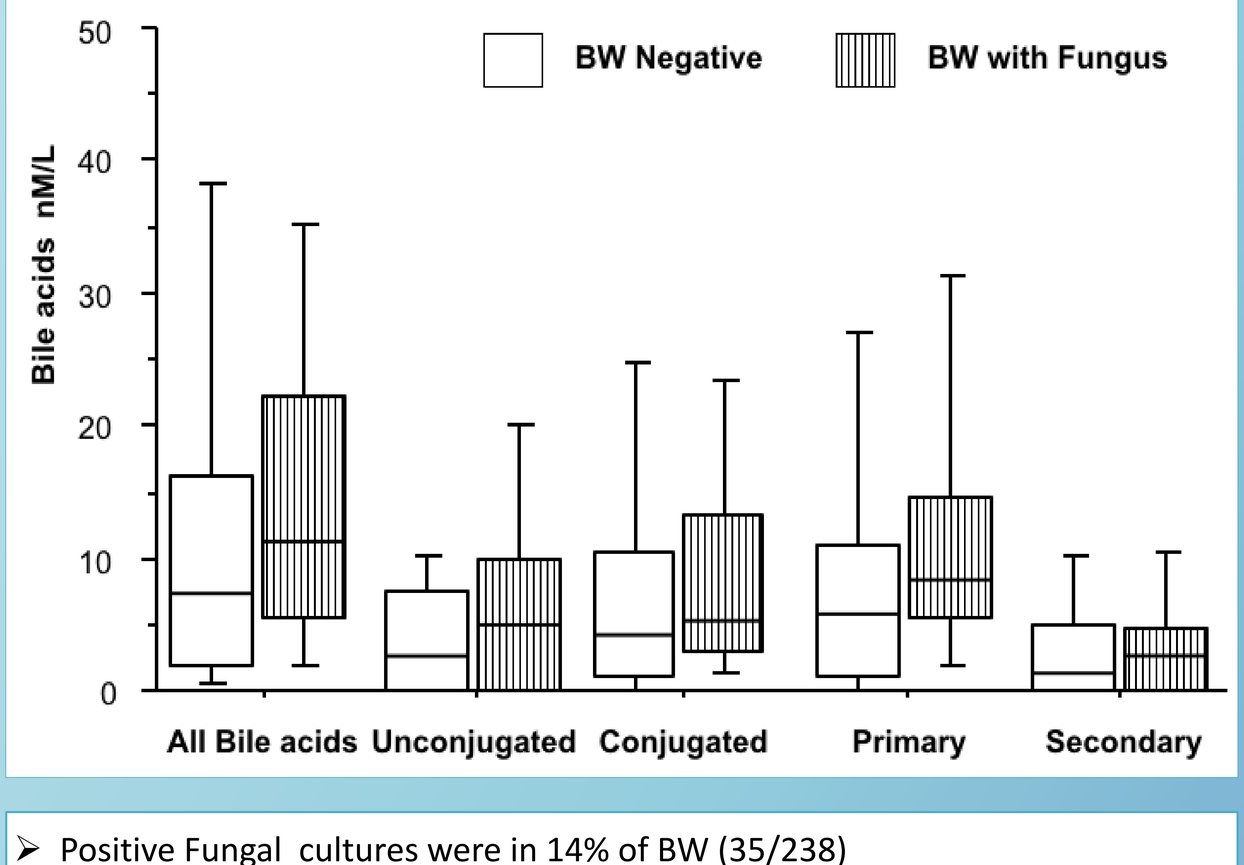
- BW (238 samples) prospectively collected from 111 lung-Tx patients were retrospectively assayed by liquid chromatography-mass spectrometry for primary and secondary BAs
- BW cultures for bacterial, fungal or viral infection were monitored.
- Statistical analysis was performed via Mann Whitney test. Data shown as 25th to 75th percentile boxplot, with bars representing 10th and 90th percentile.

RESULTS

BAs Synthesis & Conversion Flow Chart



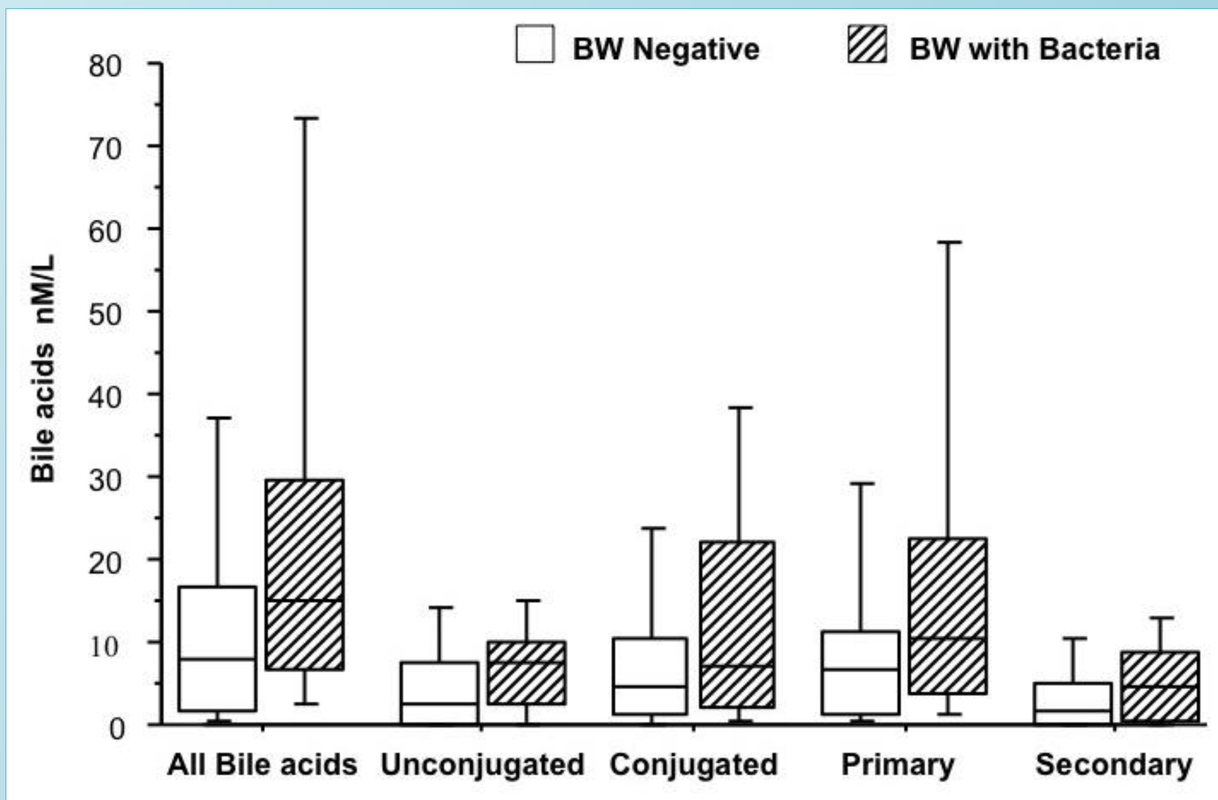
Fungal Infections



- BAs were in present in 94% of BW samples (224/238)

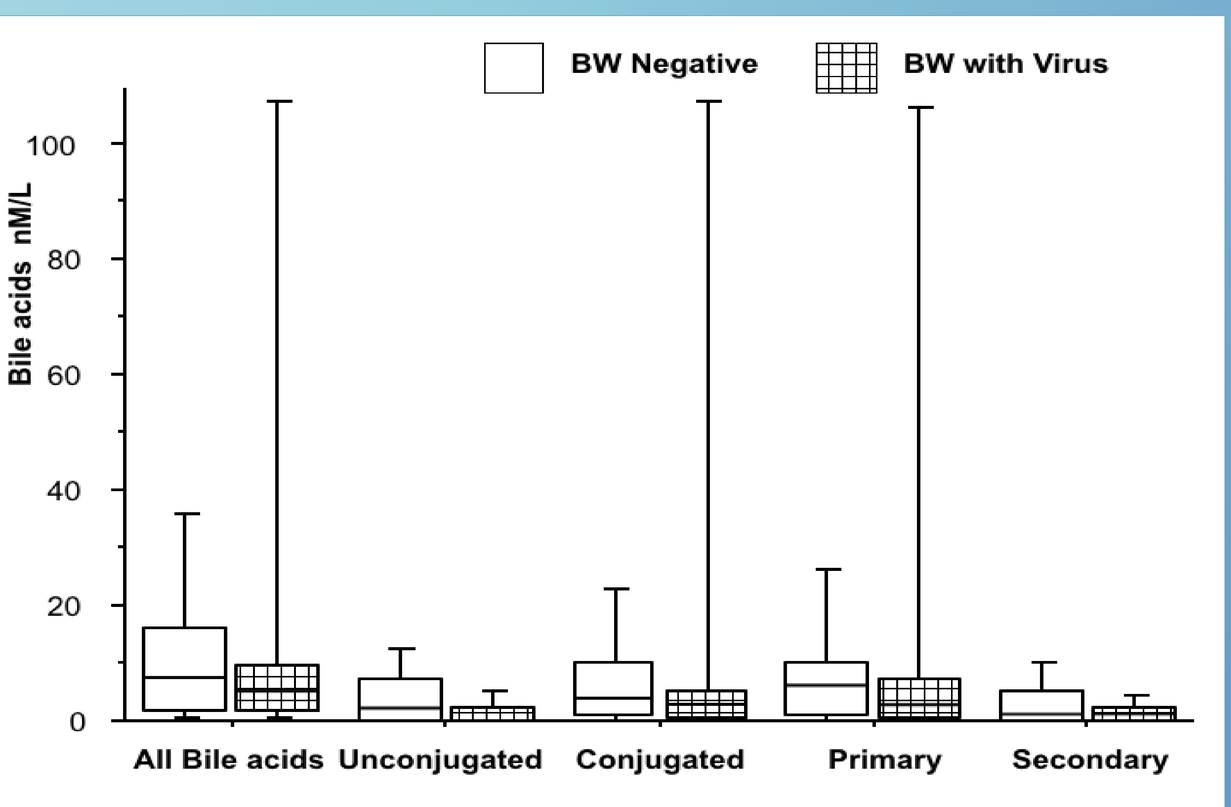
- Positive Fungal cultures were in 14% of BW (35/238)
- Only Primary BAs were greater in BW with fungal infection (p=0.045)

Bacterial Infections



- Positive Bacterial cultures were in 71% of BW (170/238)
- BW with bacteria had greater levels of BAs:
  All BAs (p=0.0003); Unconjugated (p=0.0002); Conjugated (p=0.01);
  Primary (p=0.0015); Secondary (p=0.002).

Viral Infections



- Positive Viral cultures were in 6% of BW (15/238)
- No difference noted for BAs levels.

CONCLUSIONS

- BAs aspiration is associated with airway infection
- BW positive for bacterial cultures had greater levels of BAs, with a stronger association to unconjugated BAs.
- We speculate BAs may inhibit macrophage activity via TGR5 receptor in lung affecting its broncho-alveolar innate immunity, thus facilitating bacterial and possibly fungal infections.

REFERENCES

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