Outcomes of Latent Tuberculosis Screening and Therapy in Transplant Candidates and Recipients over a 10 Year Period

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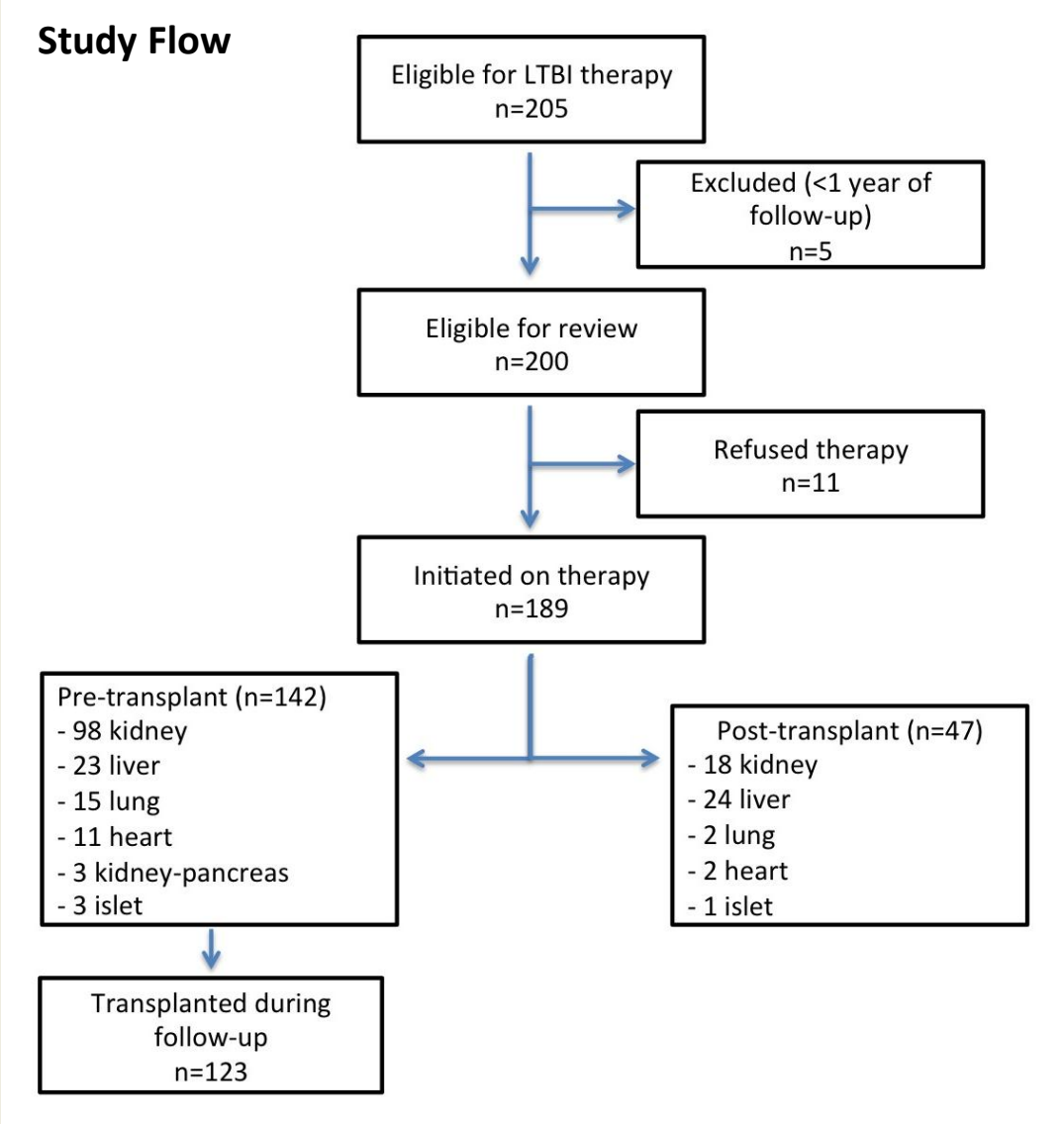
Tuberculosis in Solid Organ Transplant (SOT)

- Active infection rate 20-74 times higher than population endemic rate
  - Fatal in up to 30%
  - More treatment-related morbidity
    - Drug interaction leading to reduced immunosuppression level (calcineurin inhibitors, MMF)
    - Graft dysfunction, rejection in up to 1/3 on TB treatment
- Optimal timing/type of LTBI therapy not established
  - Most controversial in liver transplant
  - Lack of data on tolerability of INH vs. rifampin in solid organ transplant

Transplantation 1997; 63: 1278–1286
Chest 1994; 106: 435–439
Transplantation 2007;83: 1557–1562
Liver Transpl 2012; 18(9): 1110-7

Objectives and Methods

- Retrospective review of all SOT candidates/recipients in Alberta with LTBI 2001-2010
- To determine:
  - Risk factors for therapy intolerance
  - Effect(s) of timing, type of therapy
  - Outcomes in liver patients vs. other organs
  - Rate of active TB in our population



Results: Patient/Treatment Characteristics

Patient Characteristic	Number (n=200)
Mean age (SD)	53.65 (11.9)
Male gender (%)	127 (63.5%)
Ethnicity/country of origin (%)	
Canadian	75 (37.5%)
Canadian – Aboriginal	28 (14.0%)
Asian	59 (29.5%)
African	17 (8.5%)
European/Other	15 (7.5%)
Central/South American	6 (3.0%)
Method of LTBI diagnosis (%)	
Tuberculin skin test	182 (91.0%)
Interferon-gamma release assay	1 (0.5%)
Chest radiograph	13 (6.5%)
Other/clinical diagnosis	4 (2.0%)

Table 1.Baseline characteristics of 200 SOT patients diagnosed with LTBI

Therapy Characteristic	Number(n=189)
Initial LTBI therapy (%)	
Isoniazid	138 (73.0%)
Rifampin	24 (12.7%)
Other	27 (14.3%)
Completion of adequate therapy (%)	
Yes	122 (64.5%)
No	67 (33.5%)
Timing of therapy (%)	
Pre-transplant	142 (75.1%)
Post-transplant	47 (24.9%)
Reason for discontinuation of therapy (%)	
Liver enzyme elevation	18 (9.5%)
Non-hepatic drug toxicity	24 (12.7%)
Death	12 (6.3%)
Non-adherence	6 (3.2%)
Other/unspecified	7 (3.7%)

Table 2. Characteristics of LTBI therapy in 189/200 patients (11 patients refused therapy).

Results: Treatment Outcomes

Factor	Treatment completion 122/189 (64.5%)	Liver enzyme Elevation* 18/189 (9.5%)	Non-hepatic drug toxicity** 24/189 (12.7%)
Treatment initiation post-transplant	0.47 (0.24, 0.92) p = 0.034	3.50 (1.30, 9.44) p = 0.019	0.11 (0.01, 0.86) p = 0.010
Liver transplant candidate or recipient	0.20 (0.10, 0.40) p < 0.001	10.48 (3.50, 31.40) p < 0.001	0.39 (0.11, 1.38) p = 0.205
Isoniazid therapy	0.99 (0.56, 1.94) p = 0.595	0.71 (0.25, 2.02) p = 0.579	2.11 (0.69, 6.47) p = 0.192

Odds ratios for factors associated with LTBI treatment outcomes (95% confidence interval).
*leading to premature discontinuation of therapy
**includes gastrointestinal intolerance (9/24; 37.5%), rash (4/24; 16.7%), peripheral neuropathy (4/24; 16.7%), gout (1/24; 4.2%) or not otherwise specified (6/24; 25.0%).

- Patients followed for minimum 1 year post-transplant; 599.4 patient-years (median 5.1 years/patient)
  - **No cases of active TB identified**

Conclusions

- LTBI treatment in SOT more likely to be successful when initiated pre-transplant
- Liver candidates and recipients more likely to have liver enzyme elevation, discontinue therapy prematurely with conventional treatments
  - Alternative regimens should be explored further; Fluoroquinolones, 12-week isoniazid + rifapentine
- A centralized referral and management program is effective for LTBI treament in SOT candidates and recipients
  - No cases of active TB in contrast to previous reports in settings with low endemic rate (0.5-6.4%)

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Clin Infect Dis 2009; 48: 1666