**High Discordance Rate in Lung Transplant Rejection Grading: A Review of 414 Transbronchial Surveillance Biopsies**

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**INTRODUCTION**

Transbronchial biopsies are routinely performed in lung transplant recipients to assess for rejection, and are graded according to a standardized schema established by The International Society for Heart and Lung Transplantation (ISHLT) in 1996 (1). Acute rejection is characterized by lymphocytic perivascular inflammation, and is graded according to severity from Grade A0 (no rejection) to A4 (severe rejection). Airway rejection, or lymphocytic bronchitis/bronchiolitis, is manifested by inflammatory infiltration of the small airways, and is similarly graded from Grade B0 to B4. The few studies that have evaluated the reliability of the formulation have reported a wide range of interreader agreement (2,3). However, the presence and severity of acute rejection and lymphocytic bronchitis/bronchiolitis are important predictors for bronchiolitis obliterans syndrome and chronic allograft rejection, and thus of graft failure. We assessed the concordance rates between independent pathologists’ readings of transbronchial biopsies obtained from patients enrolled in a large multicenter randomized trial.

**MATERIALS & METHODS**

Transbronchial biopsies were obtained at 6 weeks, 3, 6, and 12 months after transplantation from 181 patients enrolled in 7 U.S. transplant centers in the AIRSAC study. A total of 414 surveillance biopsies were obtained. The biopsies were read at each center by various pathologists using the ISHLT 1996 grading criteria. The biopsies were then re-graded by one central pathologist blinded to the original reading and compared to the original reading to determine interreader agreement. Specimens deemed inadequate by any pathologist were excluded from the study as well as specimens demonstrating evidence of infection. Interreader agreement was analyzed using the kappa statistic. Because the diagnosis of Grade 1 rejection on surveillance biopsy usually does not alter treatment, the data was dichotomized into two clinically relevant categories for each type of rejection: Grade ≤ 1 and Grade ≥ 2.

**RESULTS**

Of the 310 biopsies considered sufficient for Grade A rejection, 60% (186) were graded similarly by two independent pathologists with an overall weighted kappa of 0.26 (95% confidence interval [CI] 0.18 – 0.34). Of those graded differently, 69% (87) differed by one grade and 31% (39) differed by two grades. 76% of 87 (87%) and 57 of 39 (90%) were downgraded by the central pathologist, respectively. When the dichotomized system was applied, the concordance rate was 80% with a kappa of 0.18 (95% CI 0.00 to 0.36).

**CONCLUSION**

In this study, there was a high discordance rate among pathologists’ interpretations of lung transplant biopsies. These results suggest that consistency and experience may be enhanced by designating a single pathologist to interpret lung transplant biopsies in each center. The study also emphasizes the importance of recognizing bronchus-associated lymphoid tissue (BALT), which is often hyperplastic. Failure to recognize BALT can lead to an over-diagnosis of acute rejection.

**REFERENCES**