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From the authors:

We appreciate the comments of H.R. Collard and T.E. King Jr and agree that surgical lung biopsy should continue to play a significant role in the assessment of patients with diffuse interstitial lung disease, particularly those without "classic" radiographic features of usual interstitial pneumonia (UIP) on high-resolution computed tomography (HRCT). We anticipated that our report would generate controversy, given the surprisingly high 30-day surgical mortality rate in patients with idiopathic UIP (idiopathic pulmonary fibrosis (IPF)) [1].

H.R. Collard and T.E. King Jr indicate that the implication of this study is that there is a high short-term mortality following surgical lung biopsy if UIP is present, and that "conclusions that might be drawn from this article are concerning as they risk discouraging the use of surgical lung biopsy in the very patients who benefit from it the most (*i.e.* patients with atypical features…)". These conclusions are far broader and stronger than any we expressed in our manuscript. Our data do not support such a conclusion; rather, they only raise the possibility that increased risk may be present in selected patients with UIP. We stressed that our patients, who were found to have UIP by surgical lung biopsy, were highly selected and represented a small proportion of the patients with IPF or connective tissue disease-associated UIP at our institution. These patients were subjected to biopsy because of their atypical features, and may have had more advanced or rapidly progressive disease than other patients with UIP. We indicated that these patients "may be at higher risk" for death following surgical lung biopsy than patients presenting with more typical features or patients with other interstitial lung diseases. This distinction is more than arbitrary, it is important. Additionally, we recognized that our findings may have been the result of small patient numbers and selection bias. However, we also felt that these data were compelling enough to suggest that others should look carefully at their surgical mortality in this group of patients (biopsy demonstrating UIP with presenting clinical features, which are atypical or nondiagnostic) in order to determine whether our findings were based on chance or a true reflection of previously under-appreciated risk in this specific patient group. Understanding the risk of surgical lung biopsy in this group is important when one considers that the recent American Thoracic Society and European Respiratory Society consensus statement recommended performing surgical lung biopsy in patients demonstrating atypical clinical or radiographical features of IPF [2]. This recommendation has also been emphasized by H.R. Collard and T.E. King Jr and is in agreement with our own view and practice.

Surgical mortality rates at our institution are historically low, as indicated in our manuscript [1]. In fact, the mortality rate in 771 cases of video-assisted thoracic surgery reported by Allen *et al.* [3] from our institution was 1.9%. There was a higher mortality rate in patients with diffuse lung disease in this series. The relatively high death rate in patients with IPF/UIP presenting with atypical or nondiagnostic features suggests that these patients may be at higher risk for death following surgical lung biopsy than patients presenting with more typical features or patients with other interstitial lung diseases. However, these data do not establish this as a universal fact.

H.R. Collard and T.E. King Jr may be correct in their assertion that our experience may have been a statistical "fluke" related to peculiar features of the patients biopsied, but we do not believe that the multiple reports of low "short-term mortality in surgical lung biopsy" outlined in table 1 by H.R. Collard and T.E. King Jr prove their point. Many of these reports are from time periods when IPF encompassed a broader spectrum of disorders, not in keeping with the more limited definition of IPF/UIP now accepted [2, 4]. Even if we accept, by leap of faith, that patients in these prior reports had what we now understand to be UIP (many of whom were described as showing "pulmonary fibrosis", "interstitial fibrosis", and "usual interstitial pneumonia"), these patients may not have been comparable to the patients in our series (severity of disease at the time of biopsy, the proportion with an "accelerated course" prior to biopsy, and the degree to which they demonstrated "atypical" clinical or HRCT findings). Indeed, many of the prior cases are not from the HRCT era and are unlikely to be precisely relevant to the discussion at hand. In addition, a review of the cited references indicates that the actual proportion of patients with UIP in the series reported by Boutin *et al.* [5] Bensard *et al.* [6] Gaensler and Carrington [7], Vansteenkiste *et al.* [8] Rena *et al.* [9] and Krasna *et al.* [10] ranged from only 3–27%. Although 52% of patients in the series of Miller *et al.* [11] were felt to have UIP, this only amounts to 22 patients. The series of Jaklitsch *et al.* [12] and Carnochan *et al.* [13] do not provide histopathological details and the proportion of patients with UIP, if any, is unknown. In the series of Zegdi *et al.* [14], which included 64 patients, the overall mortality rate was 4.7%. On closer review, however, two of the three deaths probably occurred in the 19 patients with IPF, suggesting that the actual surgical mortality in patients with IPF was 11% (two of 19). Only 20 of the 61 patients in the series of Ayed and Raghunathan [15] had "interstitial fibrosis", one of whom died. In the series of Ferson *et al.* [16], which

included 75 patients, only 35 patients had "interstitial fibrosis". There were nine deaths among these 75 patients (12% mortality). One cannot determine from the paper whether the deaths were concentrated in the "interstitial fibrosis" patients (as in our experience). If that were the case, the overall mortality in that group could have been as high as 26%.

Therefore, in our opinion, the references offered by H.R. Collard and T.E. King Jr lend very little information regarding the risk of surgical lung biopsy for patients with idiopathic pulmonary fibrosis/usual interstitial pneumonia presenting with atypical features. As we stated in our paper, we ask that other centres carefully examine their experience in this group of patients to more accurately estimate the risk of surgical lung biopsy in patients with idiopathic pulmonary fibrosis/usual interstitial pneumonia. We still recommend surgical lung biopsy in patients with interstitial lung disease of undetermined nature, when other diagnostic studies have been unrevealing and potential benefits outweigh the risks.

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