

News Release

Title

Mild elevation of pulmonary vascular resistance predicts mortality regardless of mean pulmonary artery pressure in mild interstitial lung disease

Key Points

- Pulmonary hypertension (PH) is defined by elevated mean pulmonary arterial pressure (MPAP), and elevated pulmonary vascular resistance (PVR) reflects pulmonary vascular abnormalities. PH is an important complication that negatively affects mortality in patients with interstitial lung disease (ILD).
- In our analyses of newly diagnosed ILD patients, mild elevation of PVR (> 2 Wood Units) was associated with a higher mortality rate, even in those with $MPAP \leq 20$ mm Hg.

Summary

Pulmonary hypertension (PH) is defined by elevated mean pulmonary arterial pressure (MPAP), and elevated pulmonary vascular resistance (PVR) reflects pulmonary vascular abnormalities. PH is an important complication that negatively affects mortality in patients with interstitial lung disease (ILD). ILD comprises a wide range of lung diseases associated with fibrotic destruction of the lung parenchyma and includes idiopathic pulmonary fibrosis (IPF), which has a higher mortality than many types of cancer. MPAP of > 20 mm Hg at initial evaluation was reported to increase the mortality rate in patients with IPF, but the clinical significance of PVR in patients with various types of ILD has not been fully elucidated.

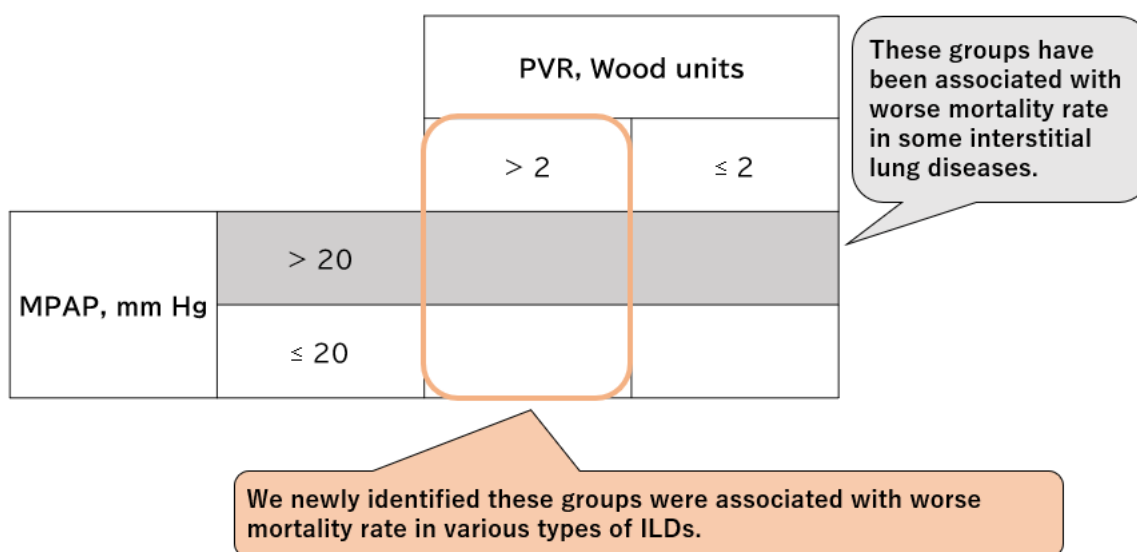
In this study, we retrospectively analysed patients with ILD who underwent right heart catheterisation (RHC) in the initial evaluation of ILD between April 2007 and April 2018.

Our data suggest that PVR was strongly associated with mortality, independent of existing predictors. Furthermore, we found that mild elevation of PVR (> 2 Wood Units) was associated with higher mortality even in those with $MPAP \leq 20$ mm Hg.

We concluded that the simultaneous interpretation of PVR and MPAP is important in patients with ILD.

Research Background

Pulmonary hypertension (PH) is defined by elevated mean pulmonary arterial pressure (MPAP), and elevated pulmonary vascular resistance (PVR) reflects pulmonary vascular abnormalities. PH is an important complication that negatively affects mortality in patients with interstitial lung disease (ILD). Mild elevation of MPAP is associated with mortality in some ILDs, but the clinical significance of mild elevation of PVR has not been clarified. This is because most hospitals in Japan and abroad do not perform right heart catheterisation (RHC) at the time of ILD diagnosis.

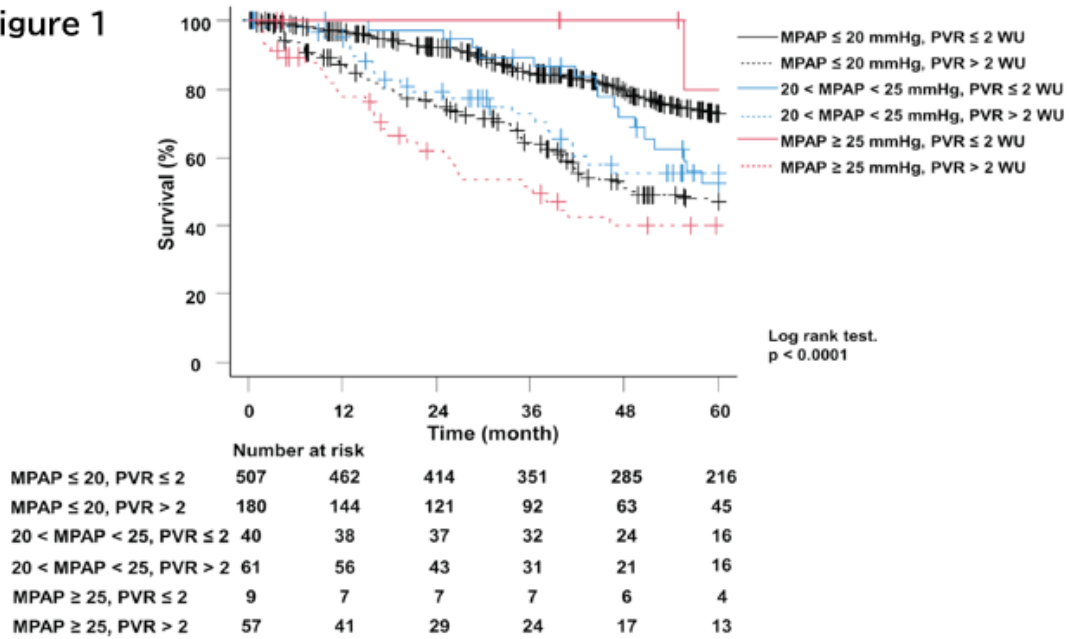


Research Results

In this study, we retrospectively analysed patients with ILD who underwent right heart catheterisation (RHC) in the initial evaluation of ILD between April 2007 and April 2018.

These patients were classified by MPAP (20 mm Hg, 25 mm Hg) and PVR (2 Wood Units: WU) using the 2022 ESC/ERS guidelines for PH. The clinical significance of MPAP and PVR for mortality was analysed by the log-rank test. We found that a PVR greater than 2 WU was associated with a higher mortality rate regardless of the MPAP value (Figure 1).

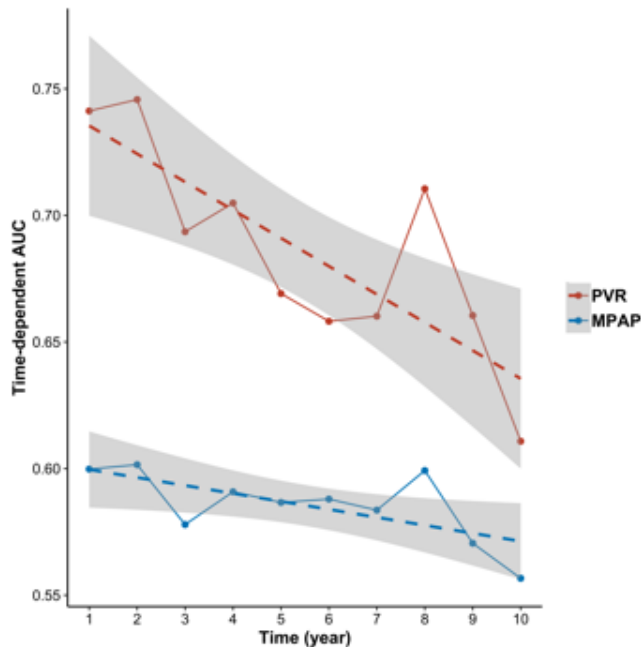
Figure 1



Kaplan-Meier curves for survival of all 854 patients classified by the cut-offs of MPAP 20 and 25 mm Hg and PVR 2 WU. Regardless of MPAP values, patients with PVR>2 WU had a higher mortality rate (median survival time, 48.0 vs 102.7 months; log-rank, p<0.0001). MPAP, mean pulmonary artery pressure; PVR, pulmonary vascular resistance; WU, Wood units.

Furthermore, compared with MPAP, PVR showed better prognostic ability for the mortality rate every year (Figure 2).

Figure 2



Comparison of the time-dependent area under the receiver operating characteristic curves (AUC) for mortality, MPAP and PVR. The horizontal axis shows the years after the initial evaluation and the vertical axis shows the estimated AUC for mortality at the time of interest. PVR had higher predictive performance than MPAP every year. MPAP, mean pulmonary artery pressure; PVR, pulmonary vascular resistance; AUC, area under the curve.

Cox hazard analysis revealed that $PVR > 2$ WU was an independent predictor for mortality from the existing ILD predictors, the ILD-GAP index. Moreover, PVR but not MPAP was associated with a higher mortality rate (Table 1).

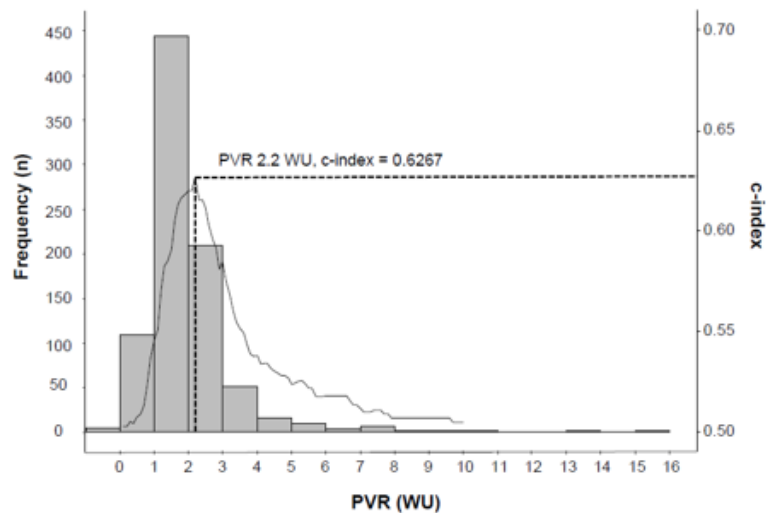
Table 1. Cox proportional hazard models of mortality with adjustment for the ILD-GAP Index

Model	Hazard ratio (95% CI)	p value
MPAP \leq 20 mmHg	Ref	Ref
20 < MPAP < 25 mmHg	0.96 (0.70 to 1.33)	0.8226
MPAP \geq 25 mmHg	1.46 (0.99 to 2.15)	0.0538
PVR > 2WU	1.53 (1.20 to 1.95)	0.0005

ILD-GAP, interstitial lung disease gender, age, physiology model; PVR, pulmonary vascular resistance; MPAP, mean pulmonary arterial pressure; WU, Wood units; CI, confidence interval.

We determined the optimal cut-off value for PVR to be 2.2 WU (Figure 3).

Figure 3



Histogram of PVR and the distribution of concordance index for mortality. The horizontal axis shows the PVR values. The first vertical axis is the number of patients, and the second vertical axis indicates Harrell's c-index for mortality. The line graph shows the c-index of PVR values ranging from 0.1 WU to 10 WU in 0.1 points increments. The optimal cut-off value of PVR for mortality was 2.2 WU. PVR, pulmonary vascular resistance; c-index, concordance index; WU, Wood units.

Research Summary and Future Perspective

We conclude that $PVR > 2$ WU is associated with a higher mortality rate in patients with ILD, regardless of MPAP values. Further studies are needed to reveal the importance of PVR, detect the patients who need right heart catheterisation at the time of ILD diagnosis, elucidate the pathogenesis of ILD, and explore new approaches to managing patients with ILD.

Publication

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