Clinical outcomes and prognostic factors of pemphigus vulgaris and pemphigus foliaceus: A 20-year retrospective study

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To the Editor: Pemphigus, a rare autoimmune disease, causes blistering of the skin and mucous membranes and is classified into pemphigus vulgaris (PV) and pemphigus foliaceus (PF), with lesions forming at different epidermal levels.[1] The disease is associated with immunoglobulin G (IgG) autoantibodies and an elevated mortality risk, exceeding that of the general population by 1.7 to 3.0 times.[2] Despite its chronic nature, studies on long-term outcomes like complete remission off therapy (CROT) and relapse remain limited, often constrained by small cohorts and homogeneous treatments. This study analyzed 621 patients from the Chinese pemphigus cohort, assessing survival outcomes, CROT rates, and prognostic factors to inform better management strategies and improve patient care.

This retrospective cohort study, approved by the Shandong Provincial Institute of Dermatology and Venereology (No. 20230104KYKTKS002), collected data from eligible PV and PF patients diagnosed at the Hospital for Skin Diseases, Shandong First Medical University between January 2003 and January 2023. The patients have given written informed consent to the publication of their case details. The study flowchart is shown in Supplementary Figure 1, http://links.lww.com/CM9/C414, and detailed methods are presented in the Supplementary Methods, http://links.lww.com/CM9/C414.

A total of 621 pemphigus patients were enrolled in the study, with their demographic and clinical features detailed in Supplementary Table 1, http://links.lww.com/CM9/C414. The median follow-up duration was 49 months (range: 2–213 months). By the end of the follow-up period, 546 patients (87.9%) were alive, while 75 (12.1%) had died. The all-cause mortality rates at 1, 3, and 5 years were 2.1%, 6.9%, and 9.2%, respectively [Supplementary Figure 2A, http://links.lww.com/CM9/C414]. Among the deceased, the leading cause of death was infectious diseases (16/75, 21.3%), primarily pneumonia (14/75, 18.7%). Other major causes included cardiovascular diseases (14/75, 18.7%), malignancies (12/75, 16.0%), and cerebrovascular diseases (11/75, 14.7%) [Supplementary Table 2, http://links.lww.com/CM9/C414].

In the analysis of CROT among the 546 surviving patients, 275 (50.4%) achieved CROT, while 168 (30.8%) attained complete remission on minimal therapy (CRMT) during the follow-up period. The CROT rates at 1, 3, and 5 years were 12.8%, 34.3%, and 50.6%, respectively [Supplementary Figure 2B, http://links.lww.com/CM9/C414]. Notably, 61 (22.2%) of the 275 patients who achieved CROT experienced relapse during the study period.

We conducted a subgroup analysis of pemphigus by classifying patients into PV and PF subtypes, including 382 PV and 239 PF patients. The overall mortality rate was 13.1% (50/382) in the PV group and 10.5% (25/239) in the PF group, with annual mortality rates of 2.4%, 7.1%, and 9.1% at 1, 3, and 5 years for PV, compared to 1.7%, 6.8%, and 9.5% for PF [Figure 1A and Supplementary Figure 1, http://links.lww.com/CM9/C414]. Although mortality was slightly higher in PV patients, the difference between the two subtypes was not statistically significant ($P = 0.97$). Mortality risk in PV patients was significantly associated with increased age at onset ($P < 0.001$), comorbidities ($P < 0.001$), and body surface area (BSA) involvement

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≥10% ($P = 0.023$). In PF patients, age at onset ($P < 0.001$) was the only significant risk factor [Supplementary Tables 3 and 4, http://links.lww.com/CM9/C414].

Among the 332 surviving PV patients, 162 (48.8%) achieved CROT with a median time to remission of 35 months. In the 214 surviving PF patients, 113 (52.8%) achieved CROT, with a median time of 24 months (PV vs. PF, $P = 0.002$). The CROT rates at 1, 3, and 5 years were 9.9%, 31.2%, and 45.6% for PV and 17.3%, 39.1%, and 59.0% for PF, respectively [Figure 1B and Supplementary Figure 1, http://links.lww.com/CM9/C414]. In PV patients, BSA involvement ≥10% ($P < 0.001$) and dual positivity for anti-desmoglein (Dsg) 1/3 antibodies ($P = 0.021$) were associated with lower CROT rates [Supplementary Table 5, http://links.lww.com/CM9/C414]. Similarly, in PF patients, BSA involvement ≥10% was also associated with a lower likelihood of achieving CROT ($P < 0.001$) [Supplementary Table 6, http://links.lww.com/CM9/C414].

Among patients who achieved CROT, relapse occurred in 36 of 162 PV patients (22.2%) and 25 of 113 PF patients (22.1%), with no significant difference between the groups ($P = 0.98$). In PV patients, singular positivity for anti-Dsg3 antibody ($P = 0.005$) and for anti-Dsg1 antibody at treatment discontinuation ($P = 0.027$) were significantly associated with relapse [Supplementary Table 7, http://links.lww.com/CM9/C414]. For PF patients, anti-Dsg antibodies measured at treatment discontinuation showed that all relapsed patients (7/7) were antibody-positive, compared to 57.1% (8/14) in non-relapsed patients, although this difference was not statistically significant due to the limited sample size ($P = 0.994$) [Supplementary Table 8, http://links.lww.com/CM9/C414].

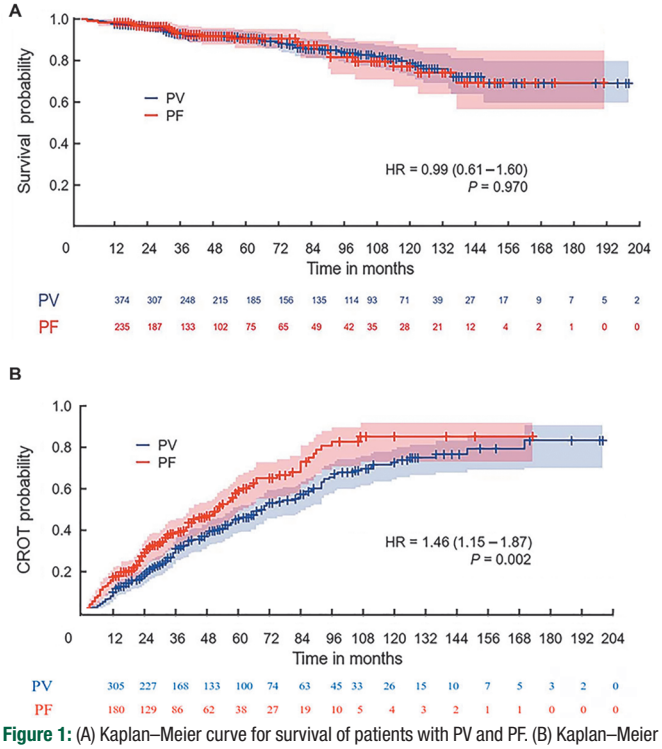

Figure 1: (A) Kaplan–Meier curve for survival of patients with PV and PF. (B) Kaplan–Meier curve of CROT rates in patients with PV and PF. CROT: Complete remission off therapy; HR: Hazard ratio; PF: Pemphigus foliaceus; PV: Pemphigus vulgaris.

We further evaluated the impact of treatment regimens on clinical outcomes. Baseline corticosteroid dosages had no significant effect on mortality, CROT, or relapse outcomes in either PV or PF patients. Similarly, different treatment regimens were not associated with variations in these clinical outcomes. Additional details are provided in Supplementary Tables 9–14, http://links.lww.com/CM9/C414.

This large retrospective cohort study of 621 pemphigus patients over a 20-year period represents a significant contribution to understanding the clinical outcomes and risk factors associated with pemphigus in China. The study revealed a mortality rate of 12.1%, with infections, particularly pneumonia, being the leading cause of death, consistent with global reports.[2,3] The rates of CROT were 50.6% at 5 years, while the relapse rate among those achieving CROT was 22.2%. These findings align with some previous studies[4,5] and highlight the long-term nature of disease management and the need for sustained remission strategies.

Importantly, this study comprehensively analyzes the clinical outcomes and prognostic factors for PV and PF as distinct subtypes. Mortality risk was higher in PV, associated with advanced age, comorbidities, and extensive BSA involvement, whereas age was the primary risk factor for PF. Similarly, BSA involvement ≥10% and dual positivity for anti-Dsg1/3 antibodies were significant predictors of lower CROT in PV, while BSA involvement also impacted PF outcomes. Relapse was associated with anti-Dsg antibodies at treatment discontinuation. These findings underscore the importance of tailored management strategies for PV and PF subtypes. Identifying risk factors can guide clinicians in optimizing treatment and follow-up plans, improving outcomes in this chronic and potentially life-threatening condition.

In conclusion, this study provides critical insights into pemphigus outcomes, identifying subtype-specific risk factors and emphasizing the importance of personalized management to improve long-term survival and remission rates.

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Conflicts of interest

None.

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