Supplementary Appendix

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Clinical outcomes and prognostic factors in bullous pemphigoid patients: A 15-year review in China

Shan Cao,[a,b]* Wenchao Li,[a,b]* Zhenzhen Wang,[a,b] Hongda Li,[a,b] Pengcheng Huai,[a,b] Tongsheng Chu,[a,b] Baoqi Yang,[a,b] Yonghu Sun,[a,b] Peiye Xing,[a,b] Guizhi Zhou,[a,b] Yongxia Liu,[a,b] Shengli Chen,[a,b] Qing Yang,[a,b] Mei Wu,[a,b] Zhongxiang Shi,[a,b] Hong Liu,[a,b,c#] Furen Zhang,[a,b,c,d#]

[a]Hospital for Skin Diseases, Shandong First Medical University, Jinan, Shandong province, China;
[b]Shandong Provincial Institute of Dermatology and Venereology, Shandong Academy of Medical Sciences, Jinan, Shandong province, China;
[c]School of public health, Shandong First Medical University, Jinan, Shandong province, China;
[d]Shandong University of Traditional Chinese Medicine, Jinan, Shandong province, China.

* These two authors contributed equally.
# Corresponding authors: Furen Zhang and Hong Liu.
E-mail: zhangfuren@hotmail.com.
E-mail: hongyue2519@hotmail.com.

Table of contents

Supplementary Tables 2

Supplementary Table S1 Pairwise comparison of three treatment regimens of mortality and complete remission off-therapy outcome in the cohort of patients with bullous pemphigoid 2

Supplementary Table S2 The AUC and C-index of bullous pemphigoid survival predictive model 4

Supplementary Table S3 The AUC and C-index of complete remission off-therapy predictive model with bullous pemphigoid 5

Supplementary Table S4 Multivariate logistic regression analyses of relapse factors associated with patients of bullous pemphigoid 6

Supplementary Table S5 Comparison of stage-specific 1/2/3/5-year mortality in the cohort of patients with bullous pemphigoid 8

References 10

Supplementary Tables

Supplementary Table S1 Pairwise comparison of three treatment regimens of mortality and complete remission off-therapy outcome in the cohort of patients with bullous pemphigoid

Characteristics	Systemic drugs other than corticosteroid (n=191)	Systemic corticosteroid monotherapy (n=335)	Systemic corticosteroid with IS (n=492)	P_{adj1}	P_{adj2}	P_{adj3}
Age at onset, y (mean (SD))	72.7 (13.98)	70.9 (13.40)	67.8 (13.70)	0.46	**< 0.0001**	**0.0043**
Sex						
Male (%)	113 (59.2%)	190 (56.7%)	286 (58.1%)	0.65	0.86	0.72
Female(%)	78 (40.8%)	145 (43.3%)	206 (41.9%)	NA	NA	NA
Delayed diagnosis time, m (mean (SD))	5.7 (10.87)	6.8 (11.86)	8.1 (17.83)	1.0	0.18	0.65
Mucosal involvement						
Yes(%)	29 (15.2%)	82 (24.5%)	149 (30.3%)	**0.014**	**< 0.0001**	0.070
No(%)	162 (84.8%)	253 (75.5%)	343 (69.7%)	NA	NA	NA
Baseline comorbidities						
Yes(%)	136 (71.2%)	273 (81.5%)	412 (83.7%)	**0.0087**	**0.0004**	0.40
No(%)	55 (28.8%)	62 (18.5%)	80 (16.3%)	NA	NA	NA
BSA involvement				**0.0055**	**< 0.0001**	0.066
Mild (<10%)	113 (59.2%)	155 (46.3%)	194 (39.4%)	NA	NA	NA
Moderate (10%-30%)	22 (11.5%)	69 (20.6%)	132 (26.8%)	NA	NA	NA
Severe (>30%)	56 (29.3%)	111 (33.1%)	166 (33.7%)	NA	NA	NA
DIF [a]						
IgG or C3 antibodies						
IgG^+ and $C3^+$	75 (39.3%)	127 (37.9%)	160 (32.5%)	0.78	0.11	0.12
IgG^+ or $C3^+$	116 (61.7%)	208 (62.1%)	332 (67.5%)	NA	NA	NA
IgM or IgA antibodies [b]						
IgM^+ and/or IgA^+	45 (23.6%)	86 (25.7%)	173 (35.2%)	0.60	**0.0034**	**0.0046**
IgM^- and IgA^-	146 (76.4%)	249 (74.3%)	319 (64.8%)	NA	NA	NA
IIF [c]	10 (0-1280)	40 (0-2560)	40 (0-1280)	0.11	0.31	1.0
ELISA antibody						
Anti-BP180 antibody (mean (SD))	108.29 (86.58)	137.20 (78.80)	151.16 (74.12)	**0.0004**	**< 0.0001**	0.065
Anti-BP230 antibody (mean (SD))	54.23 (76.67)	59.87 (77.10)	52.63 (76.27)	1.0	1.0	0.67
Mortality						

Yes (%)	78 (40.8%)	116 (34.6%)	150 (30.5%)	0.16	**0.011**	0.23
No (%)	113 (59.2%)	219 (65.4%)	342 (69.5%)	NA	NA	NA
CROT						
Yes (%)	76 (39.8%)	89 (26.6%)	156 (31.7%)	**0.0024**	**0.048**	0.12
No (%)	115 (60.2%)	246 (73.4%)	336 (68.3%)	NA	NA	NA

$P_{adj1:}$ the adjust *P* value for comparison between systemic drugs other than corticosteroid group and systemic corticosteroid monotherapy group.
$P_{adj2:}$ the adjust *P* value for comparison between systemic drugs other than corticosteroid group and systemic corticosteroid with IS group.
$P_{adj3:}$ the adjust *P* value for comparison between systemic corticosteroid monotherapy group and systemic corticosteroid with IS group.
Abbreviations: IS, immunosuppressants; SD,standard deviation; NA, not applicable; BSA, body surface area; DIF, direct immunofluorescence; IIF, indirect immunofluorescence; ELISA, enzyme linked immunosorbent assay; CROT, complete remission off-therapy.
[a] Antibodies with C3, IgG, IgM and IgA antibodies with DIF.
[b] Positive antibodies with for IgM and/or IgA along with C3 and/or IgG.
[c] Positive for IgG antibody titer with IIF.

Supplementary Table S2 The AUC and C-index of bullous pemphigoid survival predictive model

Characteristics	1st fold	2nd fold	3rd fold	4th fold	5th fold	Average
AUC						
Training data	0.85	0.92	0.92	0.84	0.84	0.88
Test data	0.89	0.87	0.87	0.88	0.88	0.88
C-index						
Training data	0.80	0.79	0.79	0.80	0.80	0.80
Test data	0.79	0.82	0.82	0.79	0.77	0.80

Abbreviations: AUC, area under the curve.

Supplementary Table S3 The AUC and C-index of complete remission off-therapy predictive model with bullous pemphigoid

Characteristics	1st fold	2nd fold	3rd fold	4th fold	5th fold	Average
AUC						
Training data	0.71	0.57	0.54	0.69	0.60	0.62
Test data	0.61	0.63	0.63	0.61	0.63	0.62
C-index						
Training data	0.60	0.61	0.62	0.60	0.62	0.61
Test data	0.62	0.60	0.62	0.68	0.62	0.63

Abbreviations: AUC, area under the curve.

Supplementary Table S4 Multivariate logistic regression analyses of relapse factors associated with patients of bullous pemphigoid

Characteristic, No. (%)	Relapse (n=749)	No relapse (n=269)	Univariate analyses*		Multivariate analyses*	
			RR (95% *CI*)	*P*-value	*RR* (95% *CI*)	*P*-value
Age at onset, mean ± SD, y	68.8 ± 13.9	72.3 ± 13.2	0.99 (0.98-1.01)	0.45	0.99 (0.97-1.00)	0.13
Sex						
Male	440/749 (58.7)	149/269 (55.4)	0.98 (0.66-1.47)	0.94	NA	NA
Female	309/749 (41.3)	120/269 (44.6)	1 [Reference]	NA	NA	NA
Delayed diagnosis time, m	7.1 ± 14.9	7.65 ± 15.0	1.0 (0.98-1.01)	0.41	1.0 (0.99-1.02)	0.95
Baseline comorbidities						
Yes	619/749 (82.6)	202/269 (75.1)	2.67(1.74-4.11)	**<0.0001**	1.81 (1.09-2.96)	**0.020**
No	130/749 (17.4)	67/269 (24.9)	1 [Reference]	NA	1 [Reference]	NA
Mucosal involvement						
Yes	199/749 (26.6)	61/269 (22.7)	1.35 (0.84-2.19)	0.21	NA	NA
No	550/749 (73.4)	208/269 (77.3)	1 [Reference]	NA	NA	NA
BSA involvement						
Mild (<10%)	324/749 (43.3)	138/269 (51.3)	1 [Reference]	NA	1 [Reference]	NA
Moderate (10%-30%)	185/749 (24.7)	38/269 (14.1)	6.09 (2.89-12.87)	**<0.0001**	4.83 (2.17-12.90)	**0.00042**
Severe (> 30%)	240/749 (32.0)	93/269 (34.6)	3.02 (1.82-5.01)	**<0.000**1	2.51 (1.45-4.55)	**0.0015**
DIF [a]						
IgG or C3 antibodies						
IgG^+ and $C3^+$	264/749 (35.2)	98/269 (36.4)	0.95 (0.63-1.43)	0.79	0.98 (0.62-1.57)	0.92
IgG^+ or $C3^+$	485/749 (64.8)	171/269 (63.6)	1 [Reference]	NA	1 [Reference]	NA
IgM or IgA antibodies [b]						
IgM^+ and/or IgA^+	231/749 (30.8)	73/269 (27.1)	1.37 (0.87-2.16)	0.18	0.92 (0.55-1.58)	0.75
IgM^- and IgA^-	518/749 (69.2)	196/269 (72.9)	1 [Reference]	NA	1 [Reference]	NA
IIF-IgG [c]	40.0 (0-2560)	40.0 (0-2560)	1.11 (0.90-1.37) [c,d]	0.33	NA	NA
ELISA positive antibodies						
Anti-BP180 antibody (mean (SD))	146.06 (75.8)	116.27 (85.9)	1.01 (1.0-1.01)	**<0.0001**	1.006 (1.003-1.009)	**<0.0001**
Anti-BP230 antibody (mean (SD))	54.85 (76.5)	57.35 (77.2)	1.0 (0.99-1.0)	0.20	NA	NA
Treatment regimens [g]						
Systemic drugs other than corticosteroid [h]	106/749 (14.2)	85/269 (31.6)	0.41 (0.25-0.68)	**0.00045**	0.60 (0.34-1.05)	0.073
Systemic corticosteroid	240/749 (32.0)	95/269 (35.3)	1 [Reference]	NA	1 [Reference]	NA
Systemic corticosteroid with IS	403/749 (53.8)	89/269 (33.1)	1.98 (1.21-3.24)	**0.0063**	1.38 (0.81-2.38)	0.24

*165 patient could not clearly determine whether they had relapse or not. For data accuracy, univariate and multivariate logistic regression analysis was done on 853 patients only.
Abbreviations: *RR*: risk ratio; *CI*: confidence interval; NA, not applicable; BSA: body surface area; IIF: indirect immunofluorescence; ELISA: enzyme linked immunosorbent assay; IS, immunosuppressant.
[a] Positive for both IgG and C3 antibodies with DIF.
[b] Positive antibodies with for IgM and/or IgA along with C3 and/or IgG.

[c] Positive for IgG antibody titer with IIF.
[d] The unit of IIF is $\log_{10}$ conversion of original value in the regression model.
[e] ELISA BP180 autoantibody values.
[f] ELISA BP230 autoantibody values.
[g] Treatment regimens prior to disease outcome.
[h] Tetracyclines or minocycline with niacinamide.

Supplementary Table S5 Comparison of stage-specific 1/2/3/5-year mortality in the cohort of patients with bullous pemphigoid

Characteristics	Study cohort	Chung, 2022[2]	Kalinska, 2017[3]	Zhang, 2013[4]	Li, 2013[5]	Bardazzi, 2022[6]	Persson, 2021[7]	Joly, 2012[8]	Heng, 2020[9]	Amonchaisakda, 2024[10]	Monshi, 2020[11]	Chen, 2024[12]
Country	China	New Zealand	Poland	China	China	Italian	England	France	Singapore	Thailand	Austria	China
Race	Asia	Various, 70%European	European	Asia	Asia	European	European	European	Asia	Asia	European	Asia
Median age, y	70.2	78.0	78.0	71.0 [a]	67.0	78.0	81.0	82.1	78.0 [a]	80.0/79.0[d]	81	67.3
Study period	January 1, 2009, and December 31, 2023,	2009-2015	2000-2013	2005-2010	1991-2011	2005-2020	1998-2017	2000-2005	2005-2016	2005-2022	2001-2012	2016-2023
Patients, No. [b]	1018	161	205	94	140	572	2658	312	141	217	100	499
Mortality rate, %	33.8	40.0	None	None	None	20.6	None	None	None	None	None	7.4
1y	22.8	20.5	22.4	23.4	12.9	3.2	20.4	38.0	31.0	28.0	25.0	3.7
2y	28.3	None	31.2	None	20.1	None	None	None	None	None	None	4.9
3y	31.2	None	39.5	None	None	18.2	None	None	None	38.0	None	5.3
5y	34.5	None	None	None	33.5	27.4	None	None	None	47.0	None	None
Prognostic factors of mortality	Age at onset, baseline comorbidities, BSA involvement, DIF [c],systemic corticosteroids with immunosuppressants	None	Arterial hypertension, arrhythmia, dementia, Parkinson, epilepsy, prednisone	Age, bedridden condition, cerebrovascular disease, cardiopathy	Sex, neurologic disease, treatment	Age, multimorbidity, BP230, BP180 antibodies	None	None	None	Neurological disease, malignancy, chronic conditions, oral cyclophosphamide	Age,dementia,hospitalization days,BP180 antibodies	Age, male,comorbidities
CROT rate, %.	31.5	None	None	None	None	None	None	None	None	None	None	None
1y	10.9%	None	None	None	None	None	None	None	None	None	None	None
3y	32.9%	None	None	None	None	None	None	None	None	None	None	None

5y	47.5%	None	None	None	None	None	None	None	None	None	None	None	None

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Characteristics	**Cyr, 2022**[13]	**Titou, 2022**[14]	**Shen, 2022**[15]	**Jeon, 2018**[16]	**Gual, 2014**[17]	**Serwin, 2014**[18]	**Banihashemi, 2015**[19]	**Försti, 2021**[20]	**Rozenblat, 2019**[21]
Country	Canada	Moroccan	Thailand	Korea	Spanish	England	Iran	Finland	Israeli
Race	North America	Africa	Asia	Asia	European	European	Asia	European	Asia
Median age, y	79.1	72.0	78.0	76.0	77.8 [a]	74.0 [a]	69.0 [a]	77.5 [a]	79.1
Study period	2010-2020	2008-2017	2007-2017	2016-2013	1990-2010	1999-2012	1995-2010	1985-2012	2009-2016
Patients, No. [b]	166	93	252	103	101	122	140	198	261
Mortality rate, %	47.6	None	54.0	None	None	59.0	1.4	None	None
1y	16.2	25.8	29.0	18.4	12.9	25.0	None	16.7	24.1
2y	27.6	32.3	None	28.2	None	None	None	None	None
3y	None	43	46.0	None	None	None	None	None	None
5y	None	None	52.4	42.0	None	None	None	None	None
Prognostic factors of mortality	Age, male, neurocognitive disorder	Age, comorbidities	Hypertension, corticosteroid, diuretic therapy	Age at diagnose, comorbidities	Age	None	None	Malignancies, polypharmacy	age at diagnosis,dementia, statins use
CROT rate, %.	None	None	None	None	None	None	None	None	None
1y	None	None	None	None	None	None	None	None	None
3y	None	None	None	None	None	None	None	None	None
5y	None	None	None	None	None	None	None	None	None

Abbreviations: CROT, complete remission off-therapy; BSA, body surface area; DIF, direct immunofluorescence.

[a] Average age.

[b] Patients were followed up to analysis mortality.

[c] Positive for IgG and C3 antibodies with DIF.

[d] Median age 80.0 years (outpatient), 79.0 years (inpatient).

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