Survival Analysis of Extramammary Paget’s Disease (EMPD) in Taiwan

Yu-Wei Chang  
Taipei Veterans General Hospital

Hsu Ma  
Taipei Veterans General Hospital

WEN-CHIEH LIAO (liaowenchieh@gmail.com)  
Taipei Veterans General Hospital

Research

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Abstract

**Background:** This study aimed to investigate the survival analysis of extramammary Paget's disease (EMPD) in a Taiwanese population and to provide data for comparison with other studies in various locations and racial populations.

**Methods:** We retrospectively analyzed the medical records of 63 patients with EMPD who were surgically treated from 2002 to 2019 at a single institution. The primary endpoint was the 5-year overall survival rate of EMPD, and the secondary endpoint was recurrence-free 5-year survival. Independent variables included patients' demographic data, concurrent malignancy (i.e., non-EMPD-related cancers), tumor size, distant metastasis, and surgery and/or radiation.

**Results:** Of all the 63 patients, 8 cases were excluded. A total of 43 patients (78.18%) were male, and 12 were female, with a mean age of 72.67 years (range: 44–89 years). The most common affected anatomic site was the penoscrotal region (22 patients, 40.00%), followed by the perianal and perineal regions (17 patients, 30.91%). Among the 55 patients, 41 patients (74.55%) were diagnosed with at least one underlying disease, whereas the most common underlying disease was cardiovascular disease (30 patients, 54.55%). EMPD with deep dermal invasion was a significant poor prognostic factor of overall survival in multivariate Cox regression (hazard ratio(HR): 5.167, \( p = 0.0015 \)). The overall survival rate was 80.00% at 36 months and 65.45% at the end of follow up. The patients 75 years old or older had poorer outcome than those younger than 65 years old (HR: 7.676, \( p = 0.0496 \)). Patients with regional metastasis or distant metastasis had poorer prognosis of 5-year survival (HR: 4.020 and 5.147, \( p = 0.0320 \) and 0.0118, respectively). The limitations of this study include its retrospective nature and sample size.

**Conclusions:** In our series, EMPD with metastasis and deep dermal invasion were the significant harmful factors in both overall 5-year survival and 5-year recurrence-free survival. The surgical excision is not associated with a low risk of local recurrence or overall survival, and long-term follow up is still needed.

**Background**

Extramammary Paget's disease (EMPD) is a rare intraepithelial neoplasm that most commonly affects individuals in their 60s to 80s.\(^1,2\) Given its slow growth and non-specific symptoms, EMPD is easily neglected and results in delayed diagnosis.\(^2-4\) The disease affects sites rich in apocrine glands, including the vulva, scrotum, penis, and perineal and perianal regions and less frequently in the axilla, face, or trunk. High prevalence in Caucasians and predominance in female were reported in Western literature, whereas less frequently occurrence was reported for Asian populations.\(^1-4\)

Previous literatures have identified potential factors related to poor prognosis of EMPD; these factors include the dermis invasion, distant metastasis, concurrent malignancy, male gender, and tumor in the perianal anatomic region.\(^2-6\) Karam et al. conducted a survival analysis of white people-predominant
population with 2001 EMPD patients in 1973–2007 and concluded the high mortality in invasive EMPD patients with old age, advanced stage, and treatment modality.4 Different characteristics and manifestations of EMPD in Asian population, including male predominance and low incidence of concurrent internal malignancy, have been identified.7,8 Nevertheless, given the relative rarity of EMPD in Asian population, limited literature reported findings on Taiwanese population,8–11 whereas a similar comprehensive survival analysis in Taiwan is still lacking.

In this study, we presented our 18-year experience of EMPD cases in a single center in Taiwan. We aimed to analyze the demographic characteristic of the disease and identify potential prognostic factors of overall survival and recurrence-free survival in Taiwanese population.

Methods

Patient Selection And Inclusion Criteria

This retrospective cohort study was conducted by the plastic surgery department of Taipei Veterans General Hospital, Taiwan. The study was approved by the institutional review board of our hospital. Through the electronic patient record system, in January 2002 to January 2019, patients who received biopsy with final diagnosis of EMPD on pathological reports were included. The 5-year survival status was confirmed through electronic patient records. If the survival status cannot be confirmed, phone interview was performed.

Data Extraction And Selection

Patient demographic characteristics, including age of diagnosis, gender, concurrent malignancy, anatomic site of lesion, maximal diameter of lesion, and metastasis status, were extracted and recorded. Dermal invasion of the lesion was divided into upper dermis invasion and deep dermal invasion, and the metastasis status was further classified as regional or distant metastasis. The type of treatment was classified into four groups, including surgical excision alone, surgical excision with adjuvant therapy, nonsurgical treatment alone (radiotherapy, chemotherapy, or phototherapy), and without any treatment. In addition to wide local excision, simple or radical vulvectomy in vulva EMPD were included in the excision. Surgical outcomes, including status of excision margin, recurrence, and recurrence-free interval, were also recorded.

Primary And Secondary Endpoints

The primary endpoint was the 5-year overall survival rate of EMPD, which was defined as the interval between the date of diagnosis on pathology to the date of death of any cause. The poor prognostic factors of 5-year overall survival were identified. The secondary endpoint was recurrence-free 5-year survival, defined as the interval between the date of diagnosis on pathology to the date of recurrence or death of any cause. The related risk factors of recurrence were also analyzed.
Statistical Analysis

All the data were analyzed by SAS® 9.4 software. Discrete variables were presented in percentages, and the continuous variables were presented as mean and standard deviation. Univariate Cox regression was used to evaluate the variables individually to identify the potential factors of poor prognosis in 5-year overall survival and recurrence. The significant variables of poor prognosis or recurrence in univariate Cox regression were further analyzed with multivariate Cox regression and Kaplan–Meier survival curves for the 5-year overall survival and 5-year recurrence-free survival, respectively. Significance was set at $P \leq 0.05$ for each test.

Results

Between January 2002 to January 2019, 63 patients were diagnosed with EMPD in our hospital. To evaluate the 5-year overall survival status, in addition to the electronic medical record, phone interviews were performed to twelve patients, whereas seven patients were lost to follow up and one refused the phone interview (Fig. 1). The Table 1 lists the demographic characteristics of 55 eligible patients. The mean age diagnosis was 72.67 years (range: 44–89 years), with 30 (54.55%) patients diagnosed at 75 years old or older. The majority of the diagnosed patients were male (43 patients, 78.18%), and the most common affected anatomic site was the penoscrotal region (22 patients, 40.00%). The second most affected region was the perianal and perineal region (17 patients, 30.91%). More than half of the patients were diagnosed with a lesion larger than 2 cm (36 patients, 65.45%). Among the 55 patients, 41 (74.55%) were diagnosed with at least one underlying disease, whereas the most common underlying disease was cardiovascular disease (30 patients, 54.55%), followed by metabolic or endocrine diseases (15 patients, 27.27%).
Table 1
Demographics and clinical data of 55 study patients with EMPD

| Variable                              | Patients (N = 55) |
|---------------------------------------|-------------------|
| Gender (Male)                         | 43 (78.18%)       |
| Male                                  | 12 (21.82%)       |
| Female                                |                   |
| Age (year) (Mean = 72.67, Range 44–89)| 14 (25.45%)       |
| Age < 65 years old                    | 11 (20.00%)       |
| Age = 65–74 years old                 | 30 (54.55%)       |
| Age ≥ 75 years old or more            |                   |
| Anatomic site of lesion               | 22 (40.00%)       |
| Scrotum or penis                      | 7 (12.73%)        |
| Vulva or labia                        | 17 (30.91%)       |
| Perianal or perineal region           | 9 (16.36%)        |
| Trunk or others                       |                   |
| Size of lesion (length of maximal diameter) | 19 (34.55%)       |
| 2 cm or less than 2 cm                | 36 (65.45%)       |
| More than 2 cm                        |                   |
| Depth of invasion                     | 38 (69.09%)       |
| Intraepithelial                       | 10 (18.18%)       |
| Micro-invasion of upper dermis        | 7 (12.73%)        |
| Deep invasion                         |                   |
| Metastasis status (N = 7, 12.72%)     | 3 (5.45%)         |
| Unilateral lymph node metastasis      | 1 (1.82%)         |
| Bilateral lymph node metastasis       | 3 (5.45%)         |
| Distant metastasis                    |                   |
| Variable                                      | Patients (N = 55) |
|----------------------------------------------|-------------------|
| Types of treatment                           |                   |
| Surgical excision only                       | 39 (70.91%)       |
| Surgical excision with adjuvant therapy      | 8 (14.55%)        |
| Radiotherapy or chemotherapy only            | 4 (7.27%)         |
| Refused any treatment                        | 4 (7.27%)         |
| Recurrence (N = 51)                          |                   |
| Concurrent malignancy                        | (N = 21, 38.18%)  |
| Adnexal carcinoma                            | 3 (5.45%)         |
| Internal malignancy                          | 18 (32.73%)       |
| Underlying diseases                          |                   |
| Without any underlying diseases              | 14 (25.45%)       |
| Cardiovascular diseases                      | 30 (54.55%)       |
| Respiratory diseases                         | 5 (9.09%)         |
| Metabolic or endocrine diseases              | 15 (27.27%)       |
| Nephrology disease                           | 3 (5.45%)         |
| Gastrointestinal disease                     | 8 (14.55%)        |

Pathological Results And Surgical Outcomes

Based on the pathological results of preoperative biopsy, among the 55 eligible patients, 17 had invasive lesions (30.91%), including 10 lesions with microinvasion of upper dermis (18.18%) and 7 lesions with deep invasion (12.73%). Seven cases indicated metastasis (12.72%), including three unilateral lymph node metastases (5.45%), one bilateral lymph node metastasis (1.82%), and three distant metastases (5.45%). A total of 47 patients (85.46%) received surgical excision of the lesion, including 8 (14.55%) who received surgical treatment with adjuvant therapy. Four patients (7.27%) received radiotherapy or chemotherapy without surgical excision, whereas another four (7.27%) refused any treatment.

Overall Survival Rate And Prognostic Factors

After diagnosis, the overall survival rate declined over the years (Table 2). The overall survival rate was 80.00% at 36 months and 65.45% at the end of follow up. Univariable Cox regression analysis of 5-year all-cause mortality was performed (Table 3) for each variable. Patients with regional metastasis or distant metastasis had poorer prognosis of 5-year survival compared with patients without metastasis (hazard ratio (HR): 4.020, 5.147, $p = 0.0320, 0.0118$ respectively). Furthermore, patients with deep dermal
invasion had worse prognosis compared with those without dermal invasion (HR: 5.167, \( p = 0.0015 \)), whereas no similar harmful effect was noted in the microinvasion of dermis (\( p = 0.6362 \)). Moreover, patients who were 75 years old or older had poorer outcome than those younger than 65 years old (HR: 7.676, \( p = 0.0496 \)). However, among the above significant risk factors, only deep dermal invasion remained as the significant poor prognostic factor in multivariate Cox regression (HR: 3.871, \( p = 0.0338 \)) (Table 4). No other significant prognostic factor was found among the other variables, including anatomic site of lesion, size of lesion, type of treatment, and concurrent malignancy. The 5-year overall survival Kaplan–Meier curves with significant variables revealed that the patients with regional metastasis or distant metastasis EMPD had a significantly poorer prognosis than those without metastasis (log-rank \( p \)-value = 0.0040) (Fig. 2), whereas those with deep dermal invasion had significantly poorer outcome than those with upper dermis microinvasion or intraepithelial lesion (log-rank \( p \)-value = 0.0007) (Fig. 3). Nevertheless, no significant difference was found in Kaplan–Meier survival curves for the 5-year overall survival between the different age groups (\( p = 0.0652 \)) (Fig. 4).

| Years after diagnosis | Number or survival | Rate  |
|-----------------------|-------------------|-------|
| 1st year              | 51                | 92.73%|
| 2nd year              | 47                | 85.45%|
| 3rd year              | 44                | 80.00%|
| 4th year              | 41                | 74.55%|
| 5th year              | 36                | 65.45%|

Table 2
Overall 5-year survival rate (N = 55)
| Variate                               | Mortality rate | Hazard ratio | p-value       |
|---------------------------------------|----------------|--------------|---------------|
| Gender                                |                |              |               |
| Female                                | 16.67%         | Reference    | Reference     |
| Male                                  | 39.53%         | 2.737        | 0.1784        |
| Age                                   |                |              |               |
| Age < 65 years old                    | 7.14%          | Reference    | Reference     |
| Age = 65–74 years old                 | 45.45%         | 7.548        | 0.0653 0.0496 |
| Age = 75 years old or more            | 43.33%         | 7.676        | 0.0496        |
| Lesion site                           |                |              |               |
| Perianal or perineal region           | 52.94%         | Reference    | Reference     |
| Genital region                        | 27.59%         | 0.441        | 0.0925 0.2190 |
| Trunk or others                       |                |              |               |
| Size of lesion                        |                |              |               |
| Lesion = 2 cm or less                 | 26.32%         | Reference    | Reference     |
| Lesion larger than 2 cm               | 38.89%         | 1.624        | 0.3527        |
| Invasion of dermis                    |                |              |               |
| Without dermal invasion               | 28.95%         | Reference    | Reference     |
| Micro-invasion of upper dermis        | 20.00%         | 0.695        | 0.6362        |
| Deep dermal invasion                  | 85.71%         | 5.167        | 0.0015        |
| Metastasis status (N = 7, 12.72%)     |                |              |               |
| Without metastasis                    | 27.08%         | Reference    | Reference     |
| With regional lymph node metastasis   | 75.00%         | 4.020        | 0.0320        |
| With distant metastasis               | 100%           | 5.147        | 0.0118        |
| Recurrence                            |                |              |               |
| Without recurrence                    | 31.82%         | Reference    | Reference     |
| With recurrence                       | 45.45%         | 1.477        | 0.4550        |
| Variate                                      | Mortality rate | Hazard ratio | p-value |
|----------------------------------------------|----------------|--------------|---------|
| Concurrent malignancy                       | 29.41%         | Reference    | Reference |
| No concurrent or subsequent malignancy      | 33.33%         | 1.180        | 0.8744  |
| Concurrent adnexal carcinoma                | 44.44%         | 1.595        | 0.3249  |
| Concurrent internal malignancy              |                |              |         |
| Types of treatment                          |                |              |         |
| With surgical excision                      | 31.91%         | Reference    | Reference |
| Without surgical excision                   | 50.00%         | 1.642        | 0.3787  |
| Excision margin status (N = 47)             | 33.33%         | Reference    | Reference |
| Margin not free                             | 31.03%         | 0.911        | 0.8596  |
| Margin free                                 | 37.50%         | Reference    | Reference |
| Intraepithelial lesion (N = 31)             | 21.74%         | 0.528        | 0.3822  |
| Margin not free                             |                |              |         |
| Margin free                                 |                |              |         |

Table 4
Multivariate Cox regression analysis of 5-year mortality

Recurrence Rate And 5-year Recurrence-Free Survival

During the 5-year follow up, among the fifty-one patients received any type of treatment, eight patients suffered from recurrence (15.69%), with a mean recurrence interval of 15.5 months (range: 1.3–29.6 months). The recurrence-free survival rate declined more rapidly over years than the overall survival rate (Table 5). The recurrence-free survival rate was 70.59% at 36 months and 60.78% at the end of the follow up. Univariable Cox regression analysis (Table 6) of recurrence in the 5-year follow-up interval showed a similar outcome as the overall survival. Distant metastatic disease (HR: 6.440, \( p = 0.0038 \)) and deep dermal invasion (HR: 4.199, \( p = 0.0070 \)) were significant factors leading to poor outcome of recurrence-free survival. No significant association was observed between the margin status and recurrence (\( p = 0.8382 \)). In the subgroup analysis of those with intraepithelial lesion, free-margin status revealed no significant benefit of recurrence-free survival compared with those without free excision margin (\( p = 0.3133 \)). No other significant risk factor of recurrence was found in other variables. Kaplan–
Meier survival curves for the recurrence-free 5-year survival (Fig. 5). While, the significantly poor outcomes in patients with deep dermal invasion (log-rank $p$-value = 0.0032) (Fig. 6) and distant metastasis EMPD (log-rank $p$-value = 0.0014) (Fig. 7) were identified.

Table 5
Recurrence-free survival rate (N = 51)

| Years after diagnosis | Number of recurrence-free survival | recurrence-free survival rate |
|-----------------------|-----------------------------------|-----------------------------|
| 1st year              | 46                                | 90.20%                      |
| 2nd year              | 38                                | 74.51%                      |
| 3rd year              | 36                                | 70.59%                      |
| 4th year              | 34                                | 66.67%                      |
| 5th year              | 31                                | 60.78%                      |
Table 6
Univariate Cox regression analysis of 5-year recurrence-free survival

| Variate                              | Recurrence rate | Hazard ratio | p-value      |
|--------------------------------------|-----------------|--------------|--------------|
| Gender                               |                 |              |              |
| Female                               | 16.67%          | Reference    | Reference    |
| Male                                 | 15.38%          | 1.256        | 0.6836       |
| Age                                  |                 |              |              |
| Age < 65 years old                   | 7.14%           | Reference    | Reference    |
| Age = 65–75 years old or less        | 36.36%          | 4.802        | 0.0550 0.0663|
| Age > 75 years old                   | 11.54%          | 4.067        |              |
| Lesion site                          |                 |              |              |
| Perianal or perineal region          | 13.33%          | Reference    | Reference    |
| Genital region                       | 17.86%          | 0.538        | 0.2017 0.6381|
| Trunk or others                      | 12.50%          | 0.727        |              |
| Size of lesion                       |                 |              |              |
| Lesion = 2 cm or less                | 6.25%           | Reference    | Reference    |
| Lesion larger than 2 cm              | 20.00%          | 2.190        | 0.1613       |
| Invasion of dermis                   |                 |              |              |
| Without dermal invasion              | 14.29%          | Reference    | Reference    |
| Micro-invasion of upper dermis       | 0.00%           | 0.502        | 0.3648 0.0070|
| Deep dermal invasion                 | 50.00%          | 4.199        |              |
| Metastasis                           |                 |              |              |
| Without metastasis                   | 9.09%           | Reference    | Reference    |
| With regional lymph node metastasis  | 75.00%          | 3.504        | 0.0513       |
| With distant metastasis              | 33.33%          | 6.440        | 0.0038       |
| Concurrent or subsequent malignancy  |                 |              |              |
| No concurrent or subsequent malignancy | 12.50%      | Reference    | Reference    |
| Concurrent adnexal carcinoma         | 66.67%          | 3.010        | 0.1546       |
| Concurrent internal malignancy       | 12.50%          | 1.415        | 0.4734       |
Variate | Recurrence rate | Hazard ratio | p-value
---|---|---|---
Type of treatment | | | 
With surgical excision | 17.02% | Reference | Reference 
Without surgical excision | 0.00% | 1.260 | 0.7562 
Excision margin status (N = 47) | | | 
Margin not free | 22.22% | Reference | Reference 
Margin free | 13.79% | 0.906 | 0.8382 
Intraepithelial lesion (N = 31) | | | 
Margin not free | 25.00% | Reference | Reference 
Margin free | 13.04% | 0.531 | 0.3133 

Concurrent Malignancy

Concurrent or subsequent malignancy was noted in 21 patients (38.18%), including 3 patients (5.45%) with adnexal carcinoma and 18 patients (32.73%) with internal malignancy (Table 1). Among the 18 patients with internal malignancy, 10 were diagnosed with gastrointestinal tract malignancy, 4 with genitourinary tract malignancy, 2 with adenocarcinoma with unknown origin, and 2 with parotid cancer. When analyzed with anatomic site of lesion, among 17 patients with perianal EMPD, 8 patients were diagnosed with gastrointestinal tract malignancy (47.06%) compared with 2 gastrointestinal tract malignancy in 38 patients with EMPD (5.26%) in other sites. In the 29 patients with genitourinary EMPD, 3 patients with genitourinary tract malignancy was observed (10.34%), whereas a genitourinary tract malignancy was detected in the other 26 EMPD patients (3.85%). Logistic regression of EMPD anatomic site and internal malignancy revealed the strong association between gastrointestinal malignancy and perianal region EMPD (odds ratio = 16.00, p = 0.0015), whereas no similar association was noted in genital region EMPD and genitourinary malignancy (p = 0.3726) (Table 7).

| Variate | Odds ratio | 95% confidence interval | p-value |
|---|---|---|---|
| Perianal EMPD and gastrointestinal malignancy | 16.000 | 2.885–88.730 | 0.0015 |
| Genital region EMPD and genitourinary malignancy | 2.884 | 0.281–29.609 | 0.3726 |

Discussion
In the present study, the characteristics of EMPD patients in one single-institution were analyzed. As revealed in other Asian population-based studies\(^7,12\) the predominance of male gender in the distribution of EMPD patients was also noted in our cases. The most common affected site was penoscrotal region (40%), similar to the findings of other studies.\(^{13–15}\) The average size of lesion, the mean age of diagnosis, and rate of metastasis (12.72%) were also in compatible range with previous literature.\(^4,5,7,12\)

The overall survival rates in our study were 80.00% (36-month follow up) and 65.45% (60-month follow up) (Table 2), which were compatible with those of previous male-predominant or Asian-predominant study.\(^{12,13}\) Previous studies had identified several potential risk factors of poor prognosis of EMPD, including the level of tumor invasion, lymph node metastases, elevated CEA, perianal lesion, old age, and male gender.\(^5,12,13,16\) In our study, based on the results of univariable Cox regression analysis (Table 3), regional or distant metastasis, age of 75 year-old or above, and deep dermal invasion were identified as significant harmful factors of the overall 5-year survival. Moreover, the Kaplan–Meier curves of overall survival revealed significantly poorer outcome in those with deep dermal invasion (\(p = 0.0007\)) (Fig. 3) and metastasis (\(p = 0.0040\)) (Fig. 4), showing similar outcomes with two population-based studies and previous reviews.\(^6,12,17\) The relationship between survival and microinvasive disease remains controversial, whereas deeply invasive EMPD was linked to poorer prognosis than the non-invasive counterpart.\(^{12,17}\) The association between prognosis and site of lesion had been reported, suggesting that anorectal EMPD has a statistically significantly decreased mean disease-specific survival compared with those without anorectal involvement.\(^4\) However, no significant difference in overall survival was observed between the different groups of lesion site in our study (Table 3).

The 5-year recurrence rate (15.69%) and the mean recurrence interval (15.5 months after diagnosed) in our study (Table 3) were similar to those of other EMPD studies that treated patients with wide local excision.\(^{14,15,18}\) The recurrence-free survival rate was 70.59% at 36-month follow up and 60.78% at 60-month follow up (Table 5), consistent with those of other wide local excision studies.\(^{15,18}\) Based on the results of univariate Cox regression (Table 6), metastasis and dermal invasion were identified as potential risk factors of recurrence; the identical prognostic factors of overall survival had harmful effects on the recurrence, which coincided with that of a previous study,\(^10\) whereas another population-based study reported no relationship between dermal invasion and local recurrence.\(^7\) Previous literature observed a strong association between margin status and recurrence risk,\(^{15}\) whereas in our study (Table 6), no similar significant association was found. In the subgroup analysis of those with intraepithelial lesion, free-margin status revealed no improvement in recurrence-free survival compared with those without free excision margin (\(p = 0.3133\)), which was in conflict with previous literature.\(^{19}\) In our series, the Kaplan–Meier curves of recurrence-free survival revealed deep dermal invasion (Fig. 6) and distant metastasis (Fig. 7) as the factors with harmful effect on recurrence-free survival (\(p = 0.0032, 0.0014\), respectively).

The rates of concurrent malignancy (38.18%), adnexal carcinoma (5.45%), and internal malignancy (32.73%) in our study were in compatible range with previous reviews.\(^2,5,15,21\) Several Asian population-based studies revealed a low concurrent internal malignancy rate in Asian EMPD patients,\(^7,12,14\) which is
in contrast with the result of our study. The potential relationship between the anatomic site of EMPD lesion and internal malignancy was proposed in another study.\textsuperscript{20} We determined the perianal EMPD as a significant risk factor of gastrointestinal malignancy (odds ratio = 16.00, \( p = 0.0015 \)), whereas no similar association was observed between the genital region EMPD and genitourinary malignancy (\( p = 0.3726 \)) (Table 7).

Our study had several limitations. First, all the data were retrospectively extracted from the electronic patient record system, which may lead to potential bias in data extraction or misinterpretation. Inadequate description of pathology reports and outpatient department follow up may also lead to underestimation of the actual rate of dermis invasion and recurrence. In addition, given the long follow-up period of up to 5 years, phone interview was performed as an alternative way of evaluation, in which only limited information can be accessed. Finally, with the rarity of EMPD in Asian population, the present single-center study included 55 illegible patients. A multicenter, larger sample size study in Taiwanese population is still needed for further evaluation.

To the best of our knowledge, this research is the first study in the English language literature about the comprehensive survival analysis of EMPD in Taiwan population. Our report also identified similar disease characteristics and prognostic factors in Taiwan population, similar to other Asian population-based studies, and their differences.

**Conclusion**

EMPD is commonly observed among aged people. The presence of metastatic EMPD and deep dermal invasion are significant harmful factors of the overall 5-year survival and 5-year recurrence-free survival. In most cases, EMPD is not associated with cancer, whereas perianal EMPD is accompanied with a high risk of gastrointestinal malignancy. Regardless of treatment method, long-term follow up is recommended.

**Abbreviations**

EMPD
extramammary Paget’s disease, HR:hazard ratio

**Declarations**

Ethics approval and consent to participate

This study was approved and supervised by the institutional review board of Taipei Veterans General Hospital (Approval number:2020-03-021CC).

Consent for publication
Not applicable.
Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

WL collected the data and assisted with manuscript editing. YC analyzed the data and wrote the manuscript. HM designed and supervised the study. All authors participated in final revision and approved the manuscript.

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