Barw Medical Journal | 2024;2(2):38-46
Journal home page: https://barw.krd/index.php/BMJ

Meta-Analysis

Presentation and Management of Porocarcinoma: A Systematic Review with Meta-Analysis of More Than One Thousand Patients

Aland S. Abdullah[1], Suhaib H. Kakamad[2], Fakher Abdullah[3], Yousif M. Mahmood[4], Gona M. Fatah[5], Imad J. Habibullah[6], Ronak S. Ahmed[7], Rebaz H. Ali[8], Ari M. Abdullah[9], Hiwa O. Abdullah[4], Berun A. Abdalla[5*], Rawezh Q. Salih[10], Abdulwahid M. Salih[1]

1. *College of Medicine, University of Sulaimani, Madam Mitterrand Street, Sulaymaniyah, Kurdistan, Iraq*
2. *Department of Immunology and Hematology, College of Medicine, Kurdistan University of Medical Science, Sanandaj, Iran*
3. *Kscien Organization for Scientific Research (Middle east Office), Azadi Mall, Hamid Street, Sulaymaniyah, Iraq*
4. *Smart Health Tower, Madam Mitterrand Street, Sulaymaniyah, Kurdistan, Iraq*
5. *Department of Biology, College of Education, University of Sulaimani, Sulaymaniyah, Kurdistan, Iraq*
6. *Bakhshin Medical Community Halabja, Halabja, Sulaymaniyah, Kurdistan, Iraq*
7. *Department of Dermatology, Teaching Center for Treating Skin Diseases, Sulaimani Directorate of Health, Sulaymaniyah, Kurdistan, Iraq*
8. *Hiwa Cancer Hospital Centre, Sulaimani Directorate of Health, Sulaymaniyah, Kurdistan, Iraq*
9. *Department of Pathology, Sulaimani Surgical Teaching Hospital, Sulaymaniyah, Kurdistan, Iraq*
10. *Department of Biology, College of Science, University of Sulaimani, Sulaymaniyah, Kurdistan, Iraq*

[*] ***Corresponding author***: *berun.anwer95@gmail.com (B.A. Abdalla). Zargatay Taza, House number 54, Zip code: 46001, Sulaymaniyah, Iraq*

Keywords:
Porocarcinoma
Cutaneous carcinoma
Skin cancer
Aggressive cancer
Infiltrating tumor

Received: January 25, 2024
Revised: February 15, 2024
Accepted: February 28, 2024
First Published: March 7, 2024

Citation: Abdullah AS, Kakamad SH, Abdullah F, Mahmood YM, Fatah GM, Habibullah IJ et al. Presentation and Management of Porocarcinoma: A Systematic Review with Meta-Analysis of More Than One Thousand Patients. Barw Medical Journal. 2024;2(2):38-46. https://doi.org/10.58742/7xjek960

Abstract

Introduction

Porocarcinoma is an aggressive cutaneous carcinoma arising from the intraepidermal component of the sweat glands. Given its uncommon nature, only a limited number of studies have addressed this issue. This study summarizes the different presentations and management of the disease.

Methods

The eligible databases were searched to identify English-language studies published up to January 16th, 2024. The inclusion criteria comprised studies that focused on the presentation and management of eccrine porocarcinoma, with a clear statement of the outcomes of the chosen management. The data collected from the studies included the first author's name, country of study, type of study design, patient demography, the clinical presentation of the tumor and its location, histopathological findings, metastasis status, treatment strategy, and the subsequent prognosis.

Results

The initial search yielded 817 papers, with only 22 meeting the inclusion criteria. The studies comprised 1004 patients with a mean age of 78.7 years. In total, 527 (52.5%) of them were male and 461(45.9%) were female. The most commonly affected regions were the head and neck followed by the lower extremities. The most frequent treatment option was surgical excision in 876 (87.3%) patients. Distant metastasis accounted for about 2%, while lymph node involvement, occurred in 36 cases (3.6%). A good prognosis was reported in 57.3% of the cases. Both the age and tumor size had a significant effect on prognosis ($p < 0.05$).

Conclusion

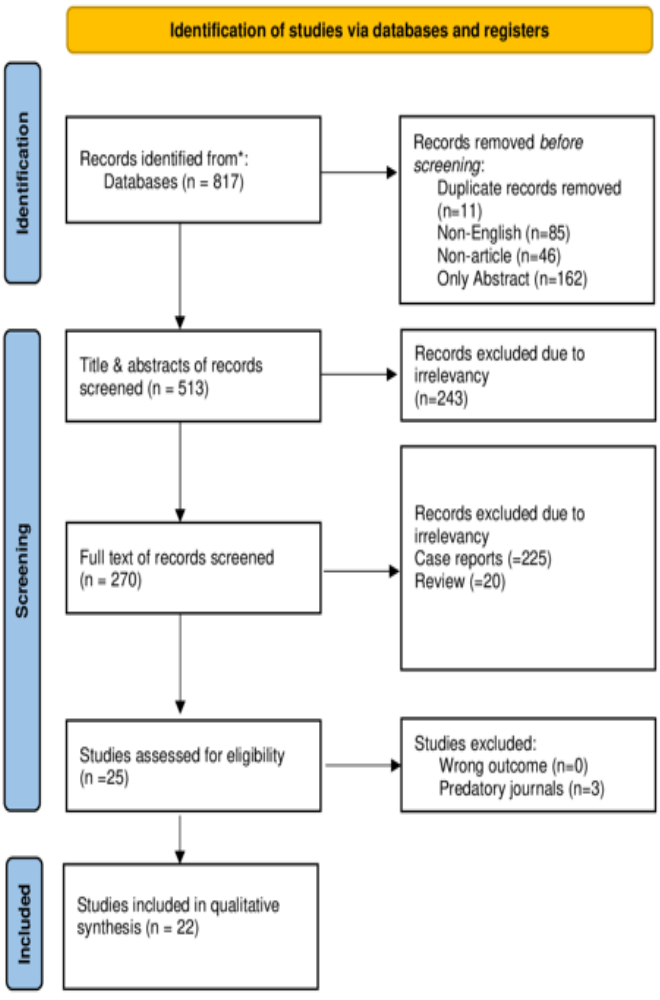
The lesion can develop anywhere on the body, with a survival rate exceeding 50%. Wide-based surgical excision remains the predominant treatment option.

1. Introduction

Porocarcinoma is a rare yet aggressive cutaneous cancer that arises from the intraepidermal portion of the sweat glands [1]. The incidence rate of this malignancy ranges from 0.005 to 0.01%.

The disease used to be known as malignant eccrine poroma and it was first reported in 1963 by Pinkus and Mehregan [2]. The majority of the patients fall within the elderly age range of 50 to over 80 years. The precise etiology of the disease remains unclear; however, identified risk factors encompass immunosuppression, solar damage, and radiation therapy [3]. The lesion may manifest on various body areas, with approximately 50% of the cases observed on the head, neck, trunk, and lower extremities. Regions such as the scalp, ear, and face also exhibit occurrences, albeit to a lesser extent [4]. The disease manifests with various clinical presentations, with a firm nodule or erythematous plaque being the most common [5]. At diagnosis, 10% of cases may exhibit distant metastasis and 20% show lymph node involvement. Given this high level of aggressiveness, different success rates with different treatment regimens have been reported [6,7].

Due to the rarity of the disease, there are a limited number of studies on this issue, with most being observational studies [8-29]. Therefore, this study aims to systematically review the presentation and management strategies of the disease



2. Methods

2.1. Study protocols

The study was conducted in compliance with the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

2.2. Data sources and search strategy

To identify studies published up to January 16th, 2024, a systematic search was performed in the PubMed/MEDLINE, Cochrane Library, Web of Science, CINAHL, and EMBASE databases using keywords such as 'Porocarcinoma,' 'Eccrine Poroma,' or 'Eccrine Porocarcinoma.' The search was restricted to studies published in the English language and involving human subjects

2.3. Eligibility criteria

To be included in this study, eligible studies met the following criteria: 1) Emphasis on the presentation and management of eccrine porocarcinoma. 2) Clear articulation of the outcome resulting from the selected management. 3) The study was valid and not published in predatory journals. The validity of the studies was determined based on the most up-to-date predatory list [30]. Review and case reports have also been excluded

2.4. Study selection process

Two independent researchers initially screened all titles and abstracts to identify studies meeting the eligibility criteria. In cases of disagreement, another author was enlisted to provide the deciding vote and resolve conflicts among the initial researchers.

2.5. Data items

The data collected from the studies included the first author's name, country of study, type of study design, patient demography, the clinical presentation of the tumor and its location, histopathological findings, metastasis status, treatment strategy, and the subsequent prognosis

2.6. Data analysis and synthesis

Microsoft Excel (2019) was used for collecting and organizing the extracted data, while the Statistical Package for Social Sciences (SPSS) software (v.26) was utilized for data analysis. The data are presented in frequency, percentage, mean, and standard deviation. The Chi-squared test was used for quantitative analysis, with a significance level set at a p-value of 0.05 or less

3. Results

3.1. Study selection

Overall, the search identified 817 articles. Before screening, 11 duplicates, 85 non-English articles, 46 non-articles, and 162 abstracts were removed. During the title and abstract screening, 513 studies were assessed, resulting in the exclusion of 243 studies due to irrelevance. The remaining 270 studies underwent full-text screening, with 245 of them excluded due to incompatibility with the inclusion criteria. Of the 25 studies subjected to eligibility assessment, three were excluded for publication in predatory journals. Ultimately, 22 studies remained eligible for inclusion in the review and meta-analysis (Figure 1).

3.2. Characteristics of the included studies

The raw data of the included studies have been summarized in Tables 1 and 2. All included studies were observational. Japan and the United States contributed the most with 5 and 3 studies, respectively, followed by Spain, France, and Finland, each with two studies (Tables 1 and 3).

3.3. Participants

A total of 1004 patients were included in the study, with males (52.5%) being more commonly affected than females (45.9%). The mean age of the patients was 78.7 ± 6.2 years, and the majority were above 65 years old (90.7%) (Table 3).

3.4. Main findings

The clinical appearance of the lesion was unreported in the majority of cases (91%). Among those detailing the clinical characteristics, nodular lesions were most prevalent (4.3%). The primary sites of infection were the head and neck (35%) and lower extremities (34.7%). Histopathological characteristics were mostly undefined (79%), but among those specified, infiltrating tumors (6%) and duct formation (5.4%) were common. Distant metastasis occurred in 20 cases (2%), while lymph node involvement was observed in 36 cases (3.6%) (Table 3). The predominant treatment was surgery in 87.3% of cases, with only 0.5% and 0.4% utilizing radiotherapy or chemotherapy, respectively. Combining chemotherapy and radiotherapy with surgery occurred in two cases (0.2%), and one case was managed with only chemotherapy and radiotherapy (0.1%). Treatment strategy was undefined in 12.6% of patients. Regarding prognosis, 57.3% of cases survived, and 42.7% succumbed. Age over 65 and tumor size exceeding 3 cm were significantly correlated with prognosis ($p < 0.05$) (Table 4).

4. Discussion

Porocarcinoma is a rare cutaneous malignancy originating from the eccrine sweat glands [31]. The exact etiology and pathophysiology of the disease remain unclear [3]. Some studies indicated that the lesion may arise from a pre-existing eccrine poroma [31]. The tumor is exceedingly rare, with an incidence lower than 0.01% [2,32]. This scarcity could account for the limited data available in the literature. According to Joshy et al., the mean age of patients at the time of diagnosis with porocarcinoma is 82 years old [26]. However, the mean age of the reviewed patients in this study was 78.7 years old. The disease is serious, not only due to its high recurrence rate after resection but also because of its aggressiveness and potential to metastasize to vital organs [33]. In this study, among cases with information regarding metastasis, 20 out of 134 patients (14.9%) had distant metastasis, and 36 out of 171 patients (21.1%) showed lymph node metastasis. The mean diameter of the lesion has been reported as 1.46 cm [19]; however, in the present study, the average size was significantly larger, with a mean of 6.74 cm.

Robson et al., in their examination of 69 cases of porocarcinoma, found that the lower extremities (44%) were the most common location for tumor development. This was followed by the trunk (24%), head (18%), and upper limbs (11%) [34]. In contrast, our study revealed the head and neck as the most prevalent site (35%). The lower extremities were the second most common, with 348 cases (34.7%), followed by the trunk (15.6%), the upper extremities (11.8%), and the groin (0.5%). The clinical characteristics of the tumor exhibit a wide range, presenting as a nodule, ulcerative plaque, verrucous plaque, or infiltrating plaque [35]. Among the 90 patients in this study with listed clinical presentations, the nodular appearance was the most common (47.8%). The ulcerative presentation alone was seen in three patients (3.3%), while 10 patients (11.1%) exhibited both ulcerative and nodular features. Papular, verrucous, and other types of clinical presentations were present in six (6.7%), five (5.6%), and 23 (25.6%) patients, respectively. Due to the similarity in appearance and presentation, the clinical differential diagnosis of porocarcinoma includes squamous cell carcinoma of the skin, amelanotic melanoma, extramammary Paget's disease, skin lymphoma, Bowen's disease, and other primary tumors of the skin appendage [35]. Given the differential diagnoses and the diverse clinical presentations, reliance on clinical findings alone for diagnosis is discouraged. Instead, a comprehensive diagnosis should incorporate dermoscopic, immunohistochemical, and histopathological findings [28,35]. Histologically, the lesion may exhibit mature duct formation lined with cuboidal epithelial cells, comedo/diffuse necrosis, and squamous differentiation of the tumor cells [1]. In the current study, the most prevalent histological finding was an infiltrating tumor, observed in 60

Table 1. Basic characteristics of each included study (Part 1).

Author	Country	Type of Study	No. patients	Mean age	Gender		MDP (years)	MTS (cm)
					M	F		
Shiohara et al (8)	Japan	Case series	12	70.9	5	7	6.2	3.7
Luz et al (9)	Brazil	Case series	8	67	3	5	3	4.8
Orella et al (10)	Spain	Case series	9	73	5	4	3	1.9
Mahomed et al (11)	South Africa	Case series	21	61.5	10	11	N/A	4.7
Kurashige et al (12)	Japan	Case series	8	72.6	6	2	2.5	3.9
Gu et al (13)	Japan	Case series	9	64.7	6	3	N/A	2.5
Xu et al (14)	United States	Case series	12	66	8	4	2.9	3.5
Zahn et al (15)	United States	Cohort	16	N/A	N/A	N/A	N/A	N/A
Yamamoto et al (16)	Japan	Case series	5	73.2	4	1	2.7	1.7
Meriläinen et al (17)	Finland	Case series	14	64.5	9	5	N/A	N/A
Kazakov et al (18)	Czech Republic	Case series	11	60.1	5	6	N/A	N/A
Gómez-Zubiaur et al (19)	Spain	Case series	7	69	5	2	N/A	1.46
Villena et al (20)	Philippines	Case series	3	60	0	3	7	1.7
Shope et al (21)	United States	Case series	12	63	6	6	N/A	N/A
Yazar et al (22)	Turkey	Case series	7	62.1	5	2	N/A	2.53
Goto et al (23)	Japan	Case series	22	77.1	12	10	N/A	24.1
Kervarrec et al (24)	France	Case series	14	73	5	9	N/A	12
Puttonen et al (25)	Finland	Cohort	10	69.6	5	5	N/A	5.1
Joshy et al (26)	United Kingdom	Cohort	738	82	396	342	N/A	N/A
Riera-Leal et al (27)	México	Case series	33	74	12	21	2.7	N/A
Belin et al (28)	France	Cross-sectional	24	72.6	15	9	N/A	2.8
Kim et al (29)	Korea	Case series	9	65.9	5	4	N/A	N/A

Barw Medical Journal | 2024;2(2):38-46 | https://doi.org/10.58742/7xiek960

Clinical characteristics of the lesions							Affected site						Histopathological findings					
Nodular	Ulcerative	Papular	Verrucous	Nodular & Ulcerative	Other	N/A	Head & Neck	Trunk	UE	LE	Groin	N/A	Duct Formation	SCD	Infiltrating tumor	Giant cells	Tumor cell	Other	N/A
8	1	0	0	1	2	0	1	0	1	10	0	0	10	2	0	0	0	0	0
0	0	0	0	0	6	2	2	0	2	4	0	0	0	0	0	0	0	0	8
0	0	0	0	0	1	8	4	1	0	4	0	0	0	0	0	0	0	0	9
0	0	0	0	0	0	21	4	4	4	6	1	2	0	0	13	2	0	6	0
0	0	0	0	8	0	0	2	1	2	3	0	0	8	0	0	0	0	0	0
9	0	0	0	0	0	0	4	2	0	3	0	0	0	0	0	9	0	0	0
0	0	0	0	0	0	12	5	3	1	3	0	0	4	0	6	0	0	2	0
0	0	0	0	0	0	16	6	3	2	5	0	0	0	0	0	0	0	0	16
0	0	0	0	0	0	5	0	1	0	4	0	0	0	0	0	0	5	0	0
0	0	0	0	0	0	14	2	3	1	7	0	1	0	0	0	0	14	0	0
7	0	0	0	1	3	0	6	0	1	3	1	0	1	0	0	0	0	10	0
3	0	4	0	0	0	0	1	1	3	2	0	0	0	0	2	0	5	0	0
1	0	2	0	0	0	0	3	0	0	0	0	0	3	0	0	0	0	0	0
0	0	0	0	0	0	12	9	2	0	1	0	0	0	0	0	0	0	0	12
0	0	0	0	0	0	7	4	2	0	0	1	0	0	0	0	0	0	7	0
0	0	0	0	0	0	22	0	0	0	10	0	12	14	7	0	0	0	1	0
0	0	0	0	0	0	14	0	2	1	11	0	0	9	0	0	0	0	5	0
0	0	0	0	0	0	10	3	4	0	0	0	3	0	0	0	0	0	0	10
0	0	0	0	0	0	738	273	109	93	261	2	0	0	0	0	0	0	0	738
15	2	0	5	0	11	0	12	10	5	6	0	0	0	0	29	0	0	4	0
0	0	0	0	0	0	24	8	9	2	5	0	0	0	0	10	0	0	14	0
0	0	0	0	0	0	9	3	0	0	0	0	6	6	0	0	0	0	3	0

** No.: Number, N/A: non-available, F: Female, M: Male, MDP: Mean duration of presentation, MTS: Mean tumor size, UE: Upper extremities, LE: Lower extremities, SCD: Squamous cell differentiation*

cases (28.4%) out of the 211 patients with known histological findings. This was closely followed by duct formation (26.1%). Less frequently identified histological findings included tumor cells in 24 cases (11.4%), giant cells in 11 cases (5.2%), and squamous cell differentiation in nine cases (4.3%).

Immunohistochemical analysis, though not commonly conducted, is considered an additional valuable tool for diagnosing porocarcinoma, particularly in excluding differential diagnoses [1]. Markers such as carcinoembryonic antigen and epithelial membrane antigen are commonly utilized to identify ductal structures, with epithelial membrane antigen being more consistently positive.

Table 2. Metastatic status, management, and outcome of porocarcinoma in the included studies.

Authors	Patient No.	Distant metastasis			Lymph node metastasis			Treatment							Prognosis	
		+ve	-ve	N/A	+ve	-ve	N/A	R	S	C+R	S+C	S+R	S+C+R	N/A	Alive	Died
Shiohara et al (8)	12	4	8	0	6	6	0	0	7	1	2	1	1	0	8	4
Luz et al (9)	8	5	3	0	4	4	0	0	8	0	0	0	0	0	6	2
Orella et al (10)	9	0	9	0	0	9	0	0	9	0	0	0	0	0	9	0
Mahomed et al (11)	21	0	0	21	3	18	0	0	21	0	0	0	0	0	18	3
Kurashige et al (12)	8	0	8	0	0	8	0	0	6	0	0	1	1	0	6	2
Gu et al (13)	9	0	0	9	0	0	9	0	6	0	2	1	0	0	9	0
Xu et al (14)	12	0	12	0	1	11	0	0	3	0	0	0	0	9	9	3
Zahn et al (15)	16	0	0	16	0	0	16	0	0	0	0	0	0	16	16	0
Yamamoto et al (16)	5	0	0	5	4	1	0	0	0	0	0	0	0	5	2	3
Meriläinen et al (17)	14	2	12	0	0	1	13	0	13	0	0	1	0	0	11	3
Kazakov et al (18)	11	0	0	11	0	0	11	0	0	0	0	0	0	11	11	0
Gómez-Zubiaur et al (19)	7	0	7	0	1	6	0	0	5	0	0	1	0	1	6	1
Villena et al (20)	3	0	3	0	0	3	0	0	3	0	0	0	0	0	3	0
Shope et al (21)	12	0	0	12	3	0	9	0	12	0	0	0	0	0	9	3
Yazar et al (22)	7	0	7	0	2	0	5	0	7	0	0	0	0	0	7	0
Goto et al (23)	22	1	0	21	0	0	22	0	0	0	0	0	0	22	22	0
Kervarrec et al (24)	14	5	9	0	0	14	0	0	0	0	0	0	0	14	14	0
Puttonen et al (25)	10	2	8	0	0	0	10	0	10	0	0	0	0	0	10	0
Joshy et al (26)	738	0	0	738	0	0	738	0	725	0	0	0	0	13	340	398
Riera-Leal et al (27)	33	0	0	33	6	27	0	0	0	0	0	0	0	33	33	0
Belin et al (28)	24	1	23	0	6	18	0	0	21	0	0	0	0	3	17	7
Kim et al (29)	9	0	5	4	0	9	0	0	9	0	0	0	0	0	9	0

** No.: Number, N/A: Non-available, +ve: Positive, -ve: Negative, R: Radiotherapy alone, S: Surgery alone, C+R: Chemotherapy + Radiotherapy, S+C: Surgery + Chemotherapy, S+R: Surgery + Radiotherapy, S+C+R: Surgery + Chemotherapy + Radiotherapy*

Table 3. Summary of baseline characteristics of the included study.

Variables	Frequency/percentage
Age (mean ± SD) #	78.7 ± 6.2
Age group	
≤ 65 years old	77 (7.7%)
> 65 years old	911 (90.7%)
N/A	16 (1.6%)
Gender	
Male	527 (52.5%)
Female	461 (45.9%)
N/A	16 (1.6%)
Country of study	
Japan	5 (22.7%)
United States	3 (13.6%)
Spain	2 (9.1%)
France	2 (9.1%)
Finland	2 (9.1%)
Others	8 (36.4%)
Study design	
Case series	18 (81.8%)
Cohort	3 (13.6%)
Cross-sectional	1 (4.6%)
Clinical characteristics of the lesions	
Nodular	43 (4.3%)
Nodular & Ulcerative	10 (1.0%)
Papular	6 (0.6%)
Verrucous	5 (0.5%)
Ulcerative	3 (0.3%)
Other	23 (2.3%)
N/A	914 (91.0%)
Affected site	
Head and Neck	352 (35%)
Lower Extremities	348 (34.7%)
Trunk	157 (15.6%)
Upper Extremities	118 (11.8%)
Groin	5 (0.5%)
N/A	24 (2.4%)
Prognosis	
Alive	575 (57.3%)
Dead	429 (42.7%)
Tumor size (mean ± SD) *	6.74 ± 7.17
≤ 3 cm	64 (6.4%)
> 3 cm	107 (10.6%)
N/A	833 (83.0%)
Histopathological Findings	
Infiltrating tumor	60 (6.0%)
Duct formation	55 (5.4%)
Tumor cells	24 (2.4%)
Giant cells	11 (1.1%)
Squamous cell differentiation	9 (0.9%)
Other	
N/A	52 (5.2%)
	793 (79%)
Distant Metastasis	
Positive	20 (2.0%)
Negative	114 (11.3%)
N/A	870 (86.7%)
Lymph Node Metastasis	
Positive	36 (3.6%)
Negative	135 (13.4%)
N/A	833 (83%)
Treatment	
Surgery	865 (86.2%)
Surgery + Radiotherapy	5 (0.5%)
Surgery + Chemotherapy	4 (0.4%)
Surgery + Chemotherapy + Radiotherapy	2 (0.2%)
Chemotherapy + Radiotherapy	1 (0.1%)
N/A	127 (12.6%)

*No.: number, SD: standard deviation, # Only 988 cases, N/A: non-available, * Only 171 cases.*

While these markers aid in detecting the presence of ducts, they may not conclusively exclude squamous cell carcinoma, as it also presents with ducts, thus potentially lowering the specificity of these markers as a diagnostic tool for porocarcinoma.

Table 4. Association of age group and tumor size with prognosis

Variables	Prognosis ratio (Dead/Alive)									
Age group	0.0	0.17	0.27	0.33	0.41	0.5	1.17	1.5	0.0	0.17
≤ 65 Years	30 (23.6%)	21 (75%)	14 (100%)	12 (30%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	30 (23.6%)	21 (75%)
> 65 Years	97 (76.4%)	7 (25%)	0 (0%)	28 (70%)	24 (100%)	12 (100%)	738 (100%)	5 (100%)	97 (76.4%)	7 (25%)
Total	127 (100%)	28 (100%)	14 (100%)	40 (100%)	24 (100%)	12 (100%)	738 (100%)	5 (100%)	127 (100%)	28 (100%)
P-value	<0.001									
Tumor size	0.0	0.17	0.27	0.33	0.41	0.5	1.17	1.5	0.0	0.17
≤ 3cm	28 (37.8%)	7 (25%)	0 (0%)	0 (0%)	24 (100%)	0 (0%)	0 (0%)	5 (100%)	28 (37.8%)	7 (25%)
> 3cm	46 (62.2%)	21 (75%)	0 (0%)	28 (100%)	0 (0%)	12 (100%)	0 (0%)	0 (0%)	46 (62.2%)	21 (75%)
Total	74 (100%)	28 (100%)	0 (0%)	28 (100%)	24 (100%)	12 (100%)	0 (0%)	5 (100%)	74 (100%)	28 (100%)
P-value	<0.001									

Other markers, such as CD117, can aid in differentiating squamous cell carcinoma from porocarcinoma. According to Goto et al., the marker was positive in all porocarcinoma cases, whereas in cases of squamous cell carcinoma, it was positive in only 19% [23].

Due to the limited number of studies addressing the disease, there is no established standard treatment regimen for porocarcinoma. However, wide surgical excision represents the most prevalent treatment strategy, as adjuvant therapies demonstrate limited benefits [6,7]. The current study yielded similar results, with 876 out of 877 treated patients undergoing surgical excision. Among them, 865 (98.6%) exclusively underwent surgery, while five patients underwent surgery in combination with radiotherapy, four with chemotherapy, and

two with both chemotherapy and radiotherapy. No patients received radiotherapy alone, and one patient received radiotherapy and chemotherapy without undergoing surgery. The prognosis for early-stage porocarcinoma is favorable with surgery alone, but it deteriorates with disease progression [1]. Among the 1004 patients in this study, 575 (57.3%) survived, while 429 (42.7%) succumbed. Age and tumor size were significantly correlated with prognosis.

This study is constrained by the inability to draw a conclusive inference regarding several variables, as the included studies inadequately delineated them.

5. Conclusion

Porocarcinoma, as a rare skin cancer, lacks a standard treatment regimen. Histopathological analysis is required to confirm the diagnosis. Surgical excision, despite some advocating for additional therapies, remains the primary treatment. Both age and tumor size affect the prognosis, and the survival rate reaches over 50%.

Declarations

Conflicts of interest: The author(s) have no conflicts of interest to disclose.

Ethical approval: Not applicable, as systematic reviews do not require ethical approval.

Patient consent (participation and publication)**:** Not applicable.

Funding: The present study received no financial support.

Acknowledgments: None to be declared.

Authors' contributions: BAA was a major contributor to the conception of the study, as well as to the literature search for related studies. ASA, HOA, SHK, and FA were Involved in the literature review, the writing of the manuscript, and data analysis and interpretation. YMM, GMF, and IJH Literature review, final approval of the manuscript, and processing of the tables. RSA, RHA, AMA, RQS, and AMS were involved in the literature review, the design of the study, and the critical revision of the manuscript. BAA and HOA Confirmation of the authenticity of all the raw data. All authors approved the final version of the manuscript.

Use of AI: AI was not used in the drafting of the manuscript, the production of graphical elements, or the collection and analysis of data.

Data availability statement: Not applicable.

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