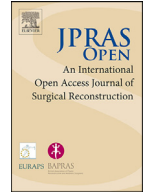




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Review Article

“Basal cell carcinoma of the hand: A systematic review and meta-analysis of incidence of recurrence”

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ABSTRACT

Background: Hand basal cell carcinoma is a rare and complex disorder. Due to the hand's anatomical features, managing hand BCC is challenging. Therefore, we have conducted this systematic review to investigate various clinical characteristics, investigations, and treatment options related to hand BCC. Furthermore, a meta-analysis was used to provide pooled recurrence rates.

Methods: We conducted this review per the International Prospective Register of Systematic Reviews (PROSPERO) guidelines. This study performed a systematic literature review in February 2022 using the following electronic databases: Cochrane, MEDLINE, and EMBASE. Key terms include hand basal cell carcinoma, basal cell carcinoma, management, outcome, and recurrence. We evaluated articles according to predefined quality criteria.

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Results: The study included 9725 patients and 51 published articles. A total of 35 case reports, 2 case series, 1 prospective study, and the remaining retrospective studies were evaluated. An asymptomatic skin lesion was the main complaint. In 10 studies, Moh surgery was the most frequently used treatment method. In the seven studies included in the meta-analysis, the overall incidence rate of recurrence among the included patients was 1.49 cases per year.

Conclusion: The optimal extent of surgical treatment is still controversial, though an early biopsy can help identify lesions at an early stage. It is the first study to provide occurrence rates based on a meta-analysis. Developing treatment guidelines for BCC of the hand will be the focus of future research.

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Introduction

Basal Cell Carcinoma (BCC) is the most common type of skin cancer, and its incidence is increasing worldwide.¹ BCC is usually a slow-growing tumor that hardly ever metastasizes. However, it can lead to significant patient morbidity.² It is well established that sun exposure is the leading risk factor for BCC.² Although patients' cumulative exposure to ultraviolet light is a significant risk factor for BCC, exposure to ultraviolet light alone does not precisely predict the probability of developing BCC at a specific site.² Other factors include lighter skin phototypes, smoking, the number of blistering sunburns, and immunosuppression.^{3,4} The dorsum of the hand is considered a frequently sun-exposed area; the occurrence of BCC in that area is relatively uncommon.⁵ One of the major causes of the rare occurrence of BCC in the dorsum of the hand is the paucity of sebaceous structures in that area.⁶ It is believed that BCC originates from pluripotential epithelial cells in the deep layers of the epidermis and hair follicles, and it tends to occur only in areas where both hair follicles and sebaceous glands are present.^{6,7} The incidence of hand skin cancer is estimated to be around 10–15% of all skin cancers.⁸ Of these, the incidence of hand BCC is approximately 11%.⁸ Moreover, when BCC occurs proximally to the upper extremity, it usually presents as classical BCC. On the other hand, acral BCC presents as erythematous skin plaques with scaling or exophytic tumors with the absence of the classical pearly appearance and telangiectasia. The diagnosis of a suspected BCC is made through either a shave biopsy or a punch biopsy.⁹ There are several histological types of BCC, including superficial and nodular, and types with high recurrence rates, such as micronodular, infiltrative, metatypical, and morpheiform patterns.¹⁰ Nodular BCC is the most commonly documented histological subtype on the dorsum of the hand.¹⁰ Treatment options for BCC of the hand vary; they include both surgical and nonsurgical treatment options. Nonsurgical options include topical immunomodulators (e.g., imiquimod), cryotherapy, radiation, photodynamic therapy, intralesional treatment (e.g., 5-fluorouracil), curettage, and electrodesiccation.^{9,11} Although the tumor management of the hand surgically requires special considerations, surgical excision is the favored treatment method for BCC. Reconstruction of the hand is challenging as the surgeon must consider protecting both the hand's function and appearance. Margins differ depending on the grade and the size of the lesion. The recommended margins for smaller or low-grade lesions are 4 mm, while larger, high-grade lesions require margins of at least 6 mm.⁹ Moreover, Moh surgery is thought to be beneficial in maximizing tissue preservation and lowering the recurrence rate.⁹ The literature lacks comprehensive systematic reviews and meta-analyses of the literature regarding the presentation, optimal management, and outcomes of hand BCC. To the authors' knowledge, this is the first systematic review that assesses a variety of clinical characteristics,

investigations, and treatment options in the literature for hand BCC. We have additionally presented pooled recurrence rates based on a meta-analysis.

Methods & materials

Literature review

We designed this systematic review using Cochrane review methods and utilized preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines.^{12,13}

This study followed the International Prospective Register of Systematic Reviews (PROSPERO) statement (ID: CRD42022313017).¹² The ethical approval was waived due to the type of study, and the review was carried out in compliance with the Helsinki Declaration. In February 2022, a systematic search was conducted in the following databases: MEDLINE, Cochrane, and EMBASE. The keywords used were the following: basal cell carcinoma, BCC, hand, nail, thumb, subungual, treatment, wide excision, local excision, amputation, conservative therapy, recurrence, and outcome. The search results included studies published without time frame limitations.

Study selection

Four reviewers evaluated the titles and abstracts of the gathered articles that were included, and the included studies were selected for a comprehensive review. If the title or abstract did not provide enough information about the article's content, the full text was examined. A fifth independent reviewer reviewed all articles selected by both groups. The inclusion criteria of the study review are as follows: (1) articles published from inception to February 2022; (2) conveyed a randomized controlled trial; prospective or retrospective cohort/comparative, case-control, case series, or case reports; (3) adult and pediatric patients; (4) patients with hand BCC (volar, dorsal, and nail unit); (5) those that reported outcomes of interest for the clinical questions proposed; and (6) all languages were included in the review. The studies that were eliminated for satisfying the exclusion criteria were as follows: (1) improper method (illustrated by a meta-analysis/systematic review, economic analysis, animal study, cadaver study, narrative review, or editorial); (2) conveyed no outcomes of interest; and (3) articles that did not include patients with hand BCC.

Screening and data extraction

Four independent reviewers screened full-text articles using the Rayyan search engine,¹⁴ and data were collected. Any disagreement was resolved by a fifth reviewer. General demographic data were gathered, such as authors' last names, country, study design, sample size, patients' age, sex, race, main presenting symptom, history of skin cancer, immune status, location of lesion, morphology, tumor invasion, treatment modality, follow-up timeframe, diagnosis, and recurrence/cure rates, which were further analyzed for meta-analysis. The level of evidence was assigned to each of the included articles, following the criteria described in the American Society of Plastic Surgeons' rating levels of evidence and grading recommendations.¹⁵

Bias assessment

We used the methodological index for the nonrandomized studies (MINORS) assessment tool. The instrument is a validated 12-item instrument designed to assess the quality of nonrandomized surgical studies.¹⁶ Two reviewers evaluated the risk of bias in all included studies using the MINORS criteria, and a third reviewer reviewed the assessments. The methodological quality and synthesis of case series and case reports were assessed using the methodological quality and synthesis of case series and case report assessment tool.¹⁷ A total of eight questions are divided into four main domains: selection, ascertainment, causality, and reporting. For both reviewers, the final answers were identical.

Statistical analysis

In the data analysis stage, the pooled estimates were calculated based on studies with at least 10 patients and available follow-up periods (years). The overall proportion of patients with BCC was computed according to the meta-analysis of single proportions. The incidence rate of recurrence was collected from each study, and a pooled outcome was estimated using person-time as time (years), the rate of recurrence as an event, and the total number of patients with BCC as the overall number. We calculated the overall incidence rate using log transformation and the inverse variance method, and continuity correction was applied for studies with zero events. Random-effects models were applied for all the analytical approaches. Heterogeneity assessment was carried out using the I^2 test. To assess the sources of heterogeneity, we carried out a subgroup analysis based on the treatment modality and sensitivity analysis.

Results

Characteristics of the included studies

A total of 3081 articles were found in this systematic review, including 924 articles from EM-BASE, 1540 articles from MEDLINE, and 617 articles from the Cochrane library. The number of articles for review remained at 2985 after removing duplicates. Initially, we were able to retrieve 110 full-text publications. However, after applying the previously defined inclusion and exclusion criteria, 51 studies were included in the qualitative synthesis published between 2006 and 2020 (Fig. 1). The following reasons prompted the exclusion of 59 articles: improper methods (systematic review, review article, and letter to editor), $n = 12$, no outcome of interest ($n = 19$), the full text could not be located ($n = 14$), the specific location of BCC was not stated ($n = 12$), included non-hand BCC patients ($n = 2$). Thirty-five studies were case reports,^{18–52} 2 studies were case series,^{53,54} 1 study was a prospective cohort analysis,⁵⁵ and the remaining studies were retrospective cohort studies. Two studies were published in Australia,^{27,40} 6 studies were published in Asia,^{22,23,27,32,47,49} 17 studies were published in Europe,^{8,19,25,34,35,38,39,41,43,45,53,56–61} and the remaining studies were published in North America. A total of 9725 patients were included (760 patients had BCC). More details about the characteristics of studies and patients are provided in Table 1.

Clinical characteristics

The mean patient's age was 62.8 years old (a range between 1.16 to 90 years old). Two studies were reported in the pediatric age groups in 1.16 and 5.56 years old. The main presenting complaint in ten of the articles was an asymptomatic skin lesion, 3 were mass-like, 3 were nail deformities, 4 were nonhealing ulcers, 14 were ulcerated lesions, and 15 did not mention anything. In terms of race, 20 of the articles were Caucasians, and only 1 study reported an Asian patient.²²

The clinical characteristics are listed in Table 2. Nail involvement was reported in 41 studies, of which the nails were involved among the patients in 16 studies (39%),^{20–22,28,31,33,35,36,38,42,43,45,46,48–50} Hand laterality was reported in 37 studies,^{6,18–37,39–53,60} and the lesions were approximately equally distributed (33 and 31 lesions in the right and left hands, respectively). Metastasis was positive in a case report,²³ and bone involvement was positive in another case report.⁴⁰ In-situ lesions were reported in 4 studies,^{22,30,32,39} and invasive lesions in 8 articles.^{20,23,24,29,38,40,41,51} Treatment modalities included Moh surgery in 10 studies,^{6,19–21,24,30,33,36,43} curettage and cryosurgery in 1 study,⁵⁵ amputation in 4 studies,^{35,40,45,48} and surgical excision in the remaining studies.

Results of the meta-analysis

In the meta-analysis, seven studies were included. A total of 2051 patients were included, of whom 652 patients had BCC with an overall pooled proportion of 32.24% (95%CI, 14.37% to 57.44%, Fig. 2). There was a significant heterogeneity among studies ($I^2 = 98.7\%$, $p < 0.0001$).

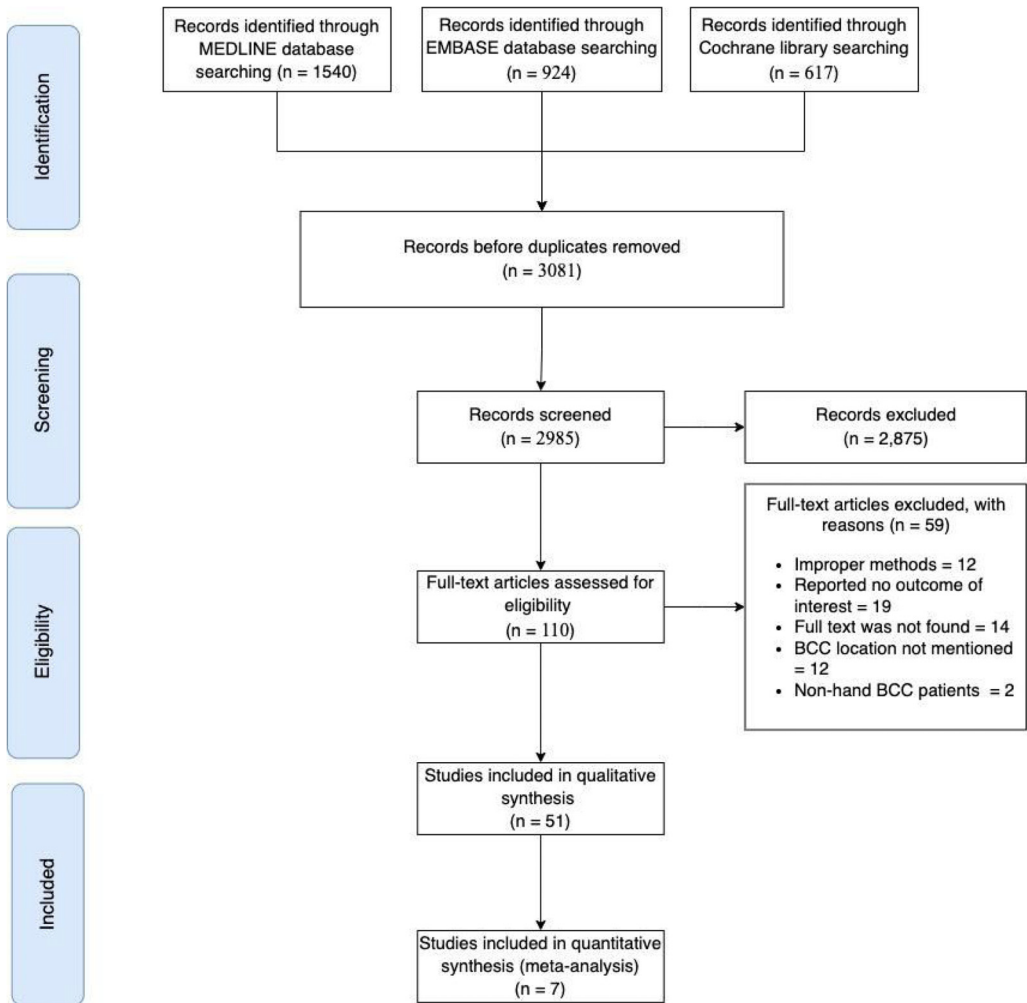


Fig. 1. The PRISMA flowchart for systematic review. The process of selecting the included studies.

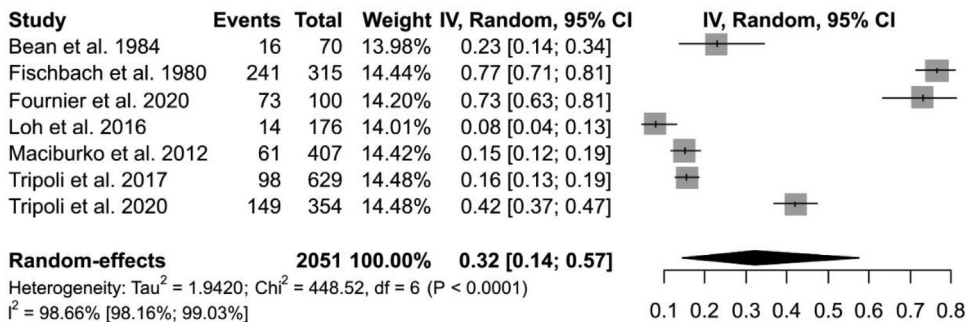


Fig. 2. A forest plot shows the rate of BCC among the included patients.

Table 1
Characteristics of the included studies and the recruited patients.

Author	Design	Country	BCC/N	M/F*	Mean Age	Race	Level of evidence
Abeldaño et al. 2006 ⁵³	CS	USA	01-Mar	0/1	64	NA	Level IV
Bean et al. 1984 ⁶³	R	USA	16/70	NA /NA	NA	White	level II
Chakrabarti et al. 1993 ⁶¹	R	UK	4/275	2/2	68	NA	level II
Clifford et al. 1955 ⁶⁴	R	USA	May-62	NA/NA	NA	NA	Level II
Coulombe et al. 2018 ¹⁸	CR	Canada	01-Jan	0/1	NA	NA	Level II
Dika et al. 2013 ⁴³	CR	Italy	01-Jan	0/1	73	NA	level V
Engel et al. 2008 ¹⁹	CR	Germany	01-Jan	1/0	58	NA	level V
Enna et al. 1978 ⁴⁴	CR	USA	01-Jan	1/0	87	white	Level V
Fischbach et al. 1980 ⁶²	R	USA	241/315	NA/NA	NA	NA	level V
Forman et al. 2007 ²⁰	CR	USA	01-Jan	1/0	70	White	level II
Fournier et al. 2020 ⁵⁵	P	Canada	73/100	53/47	NA	White	Level V
Galeano et al. 2002 ⁴⁵	CR	Italy	01-Jan	1/0	81	NA	Level I
Grine et al. 1997 ²¹	CR	USA	01-Jan	1/0	62	White	level V
Guana et al. 1994 ⁴⁶	CR	USA	01-Jan	1/0	74	white	Level V
Higuchi et al. 1988 ⁴⁷	CR	Japan	01-Jan	1/0	84	white	level V
Hoffman et al. 1973 ⁴⁸	CR	USA	01-Jan	0/1	65	NA	level V
Kendall et al. 1969 ⁹⁵	R	USA	Aug-73	8/0	70	na	Level II
Kim et al. 2000 ²²	CR	Korea	01-Jan	0/1	51	Korean	Level V
Kim et al. 2009 ²³	CR	Korea	01-Jan	0/1	63	NA	Level V
Lam et al. 2019 ²⁴	CR	USA	01-Jan	0/1	71	NA	level V
Lateo et al. 2005 ²⁵	CR	UK	01-Jan	0/1	73	white	level V
Loh et al. 2015 ⁶⁶	R	USA	14/6654	NA /NA	NA	White	level V
Loh et al. 2016 ⁶	R	USA	14/176	12-Feb	65.1	White	Level II
Lopez-Sanchez et al. 2019 ²⁶	CR	Australia	01-Jan	0/1	60	Caucasian	Level II
Machida et al. 2011 ²⁷	CR	Japan	01-Jan	0/1	76	NA	level V
Maciburko et al. 2012 ⁸	R	UK, Australia	61/407	NA/NA	71.8	NA	level V
Martinelli et al. 2006 ²⁸	CR	USA	18/18	NA/NA	NA	NA	level II
Mikhail et al. 1985 ²⁹	CR	USA	02-Feb	1/0	36	NA	Level V
Okuyama et al. 2006 ⁴⁹	CR	Japan	01-Jan	0/1	90	white	Level V
Oriba et al. 1997 ³⁰	CR	USA	01-Jan	0/1	85	NA	level V
Özkan et al. 2017 ⁵⁴	CS	Turkey	03-Jul	3/0	56	NA	Level V
Pollo et al. 2019 ³¹	CR	Brazil	01-Jan	0/1	70	NA	level V
Rallis et al. 2010 ³²	CR	India	01-Jan	0/1	63	NA	Level IV
Riml et al. 2013 ⁵⁶	R	Austria	NA/524	NA/NA	74.7	NA	level V
Robins et al. 1981 ³³	CR	USA	02-May	01-Jan	NA	NA	Level V
Rudolph et al. 1987 ⁵⁰	CR	USA	01-Jan	0/1	59	white	level II
Salomão et al. 1999 ⁵¹	CR	Brazil	01-Jan	0/1	49	fair skinned	Level V
Sarfati et al. 2008 ³⁴	CR	French	01-Jan	1/0	64	NA	level V
Serrano-Ortega et al. 2002 ³⁵	CR	Spain	01-Jan	1/0	63	white	level V
Shimizuz et al. 2013 ³⁶	CR	USA	01-Jan	0/1	68	NA	Level V
Tavares et al. 2018 ³⁷	CR	Brazil	01-Jan	0/1	58	NA	level V
Tehrani et al. 2009 ³⁸	CR	UK	01-Jan	0/1	50	NA	level V
Torrelo et al. 2014 ³⁹	CR	Spain	02-Feb	2/0	5.65	NA	Level V
Tripoli et al. 2017 ⁵⁸	R	Italy	98/629	388/241	NA	NA	Level V
Tripoli et al. 2020 ⁵⁹	R	Italy	149/354	211/143	69.5	NA	Level II
van Zuuren et al. 2000 ⁶⁰	R	Netherlands	11-Nov	09-Feb	63.3	White	Level II
Vandeweyer et al. 2003 ⁵⁷	R	Belgium	07-Jul	06-Jan	71.2	NA	level II
Watson et al. 2019 ⁴⁰	CR	Australia	01-Jan	1/0	52	white	level V
West et al. 1990 ⁵²	CR	USA	01-Jan	1/0	70	white	level V
Yousif et al. 2013 ⁴¹	CR	UK	01-Jan	1/0	45	NA	Level V
Zhu et al. 2014 ⁴²	CR	USA	01-Jan	1/0	43	Caucasian	level V

* Gender distribution was based on the total number of patients with BCC; CR: case report; CS: case series; R: retrospective cohort; P: prospective cohort; M: male; F: female.

The incidence of recurrence

The overall incidence rate of recurrence among the included patients was 1.49 cases per year (95%CI, 0.58 to 3.82, Fig. 2). The heterogeneity among studies was significant ($I^2 = 83.2\%$, $p < 0.0001$). However, studies which recruited patients who underwent surgical excision showed no significant

Table 2
Clinical characteristics of patients.

Author	Location	Morphology	Nail involvement	Diagnosis
Abeldaño et al. 2006 ⁵³	palm	erythematous ulcerated lesion with distinct borders,	No	BCC Unspecified
Bean et al. 1984 ⁶³	dorsum (7) - thumb (1) - fingers (2) - wrist (3) - web (1)	NA	NA	NA
Chakrabarti et al. 1993 ⁶¹	Fingers and dorsum of the hand	NA	No	NA
Clifford et al. 1955 ⁶⁴	dorsum of hand	NA	No	NA
Coulombe et al. 2018 ¹⁸	Palms and lateral fingers	erythematous and edematous, and some were crusted	NA	BCC (Gorlin syndrome)
Dika et al. 2013 ⁴³	The proximal nail fold of the right IV and V fingers	An ulcerated lesion	Yes	Perinugal basal cell carcinoma (BCC)
Engel et al. 2008 ¹⁹	Thumb	Erosive and erythematous	No	BCC Unspecified
Enna et al. 1978 ⁴⁴	dorsal aspect of the middle phalanx of the ring finger	diffusely erythematous	No	variant basal cell carcinoma with an adenomatoid pattern
Fischbach et al. 1980 ⁶²	NA	NA	NA	NA
Forman et al. 2007 ²⁰	Thumb Nail	Eroded plaque	Yes	Nodular BCC
Fournier et al. 2020 ⁵⁵	Hand	NA	NA	Superficial
Galeano et al. 2002 ⁴⁵	dorsal and medial surface of left-hand thumb just distal to MP joint	small flat ulcerated lesion	painful exophytic mass on the dorsal and medial surface of his left thumb just distal to the MP joint, which had infiltrated the first commissura	Bowenoid BCC
Grine et al. 1997 ²¹	Posterior nailfold of the thumb	Ill-defined erythematous scaly lesion	Yes	Nodular BCC
Guana et al. 1994 ⁴⁶	The dorsal distal phalanx of the right thumb involving the proximal and lateral nail fold	Scaly, erythematous nodule with a central ulceration	Yes	Nodulo-ulcerative BCC with minor sclerosing component
Higuchi et al. 1988 ⁴⁷	The lateral surface of the proximal phalanx of the ring finger	A sharply circumscribed ulcer with a dusky red, partially blackish, irregular surface	No	BCC
Hoffman et al. 1973 ⁴⁸	The ulnar side of the thumb	ulceration with surrounding induration and redness and exposure of the distal phalanx	Yes	BCC
Kendall et al. 1969 ⁶⁵	dorsum of hand	NA	No	NA
Kim et al. 2000 ²²	The right fifth fingernail	Linear longitudinal Melanonychia on fingernail	Yes	Superficial BCC
Kim et al. 2009 ²³	Fourth finger	Erythematous plaque	No	Infiltrative

(continued on next page)

Table 2 (continued)

Author	Location	Morphology	Nail involvement	Diagnosis
Lam et al. 2019 ²⁴	Palm	Well-demarcated, erythematous, ulcerated plaque	No	Collusion tumor BCC and SCC in situ
Lateo et al. 2005 ²⁵	Palm	Erythematous, minimally raised, smooth plaque	No	BCC with eccrine-type ductal differentiation.
Loh et al. 2015 ⁶⁶	Dorsum	NA	No	8 BCC unspecified- 4 nodular- 1 ulcerative- 1 infiltrative
Loh et al. 2016 ⁶	Dorsum	NA	NA	Nodular BCC
Lopez-Sanchez et al. 2019 ²⁶	Palm	A well-defined pink plaque slightly elevated, skin-colored plaque with a keratotic, crusted center	No	Nodular
Machida et al. 2011 ²⁷	Palm	Erythematous plaque	No	Superficial
Maciburko et al. 2012 ⁸	Dorsum	Ulcerative lesion	NA	Nodular
Martinelli et al. 2006 ²⁸	Nadorsumil unit	Erythematous, crusted, tender papule	Yes	unspecified bcc
Mikhail et al. 1985 ²⁹	Lateral nail fold to the radial aspect of fifth finger	a well-defined ulcer, pigmented spots and crusty debris over the nail	No	Unspecified
Okuyama et al. 2006 ⁴⁹	The ulnar side of the proximal nail bed of the thumb	Crescent-shaped, eczematous, and pink plaque	Yes	BCC
Oriba et al. 1997 ³⁰	Dorsal aspect of second digit	Rash and swelling	No	Nodular
Özkan et al. 2017 ⁵⁴	Phalanges	Friable lesion with periungual erythema and onychodystrophy	No	NA
Pollo et al. 2019 ³¹	Nail	Fleshy	Yes	infiltrative
Rallis et al. 2010 ³²	Second interdigital space	Scaly erosion	No	Ulcerated
Riml et al. 2013 ⁵⁶	NA	The affected nail is slightly ridged, wide brown streak extending along the entire length of the nail.	NA	Nodular BCC
Robins et al. 1981 ³³	1 nail unit- 1 palm		Yes	NA
Rudolph et al. 1987 ⁵⁰	thumb nail		Yes	BCC
Salomão et al. 1999 ⁵¹	In the palm of the right hand, next to the proximal phalanx of the second digit	A crusty ulcerated lesion	No	BCC Unspecified
Sarfati et al. 2008 ³⁴	Dorsum of Thumb	Irregular periungual ulceration	No	Ulcerated BCC
Serrano-Ortega et al. 2002 ³⁵	The proximal nailfold of the middle finger of the right hand	a painless ulceration with well-defined edges and a necrotic base	Yes	BCC Unspecified

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Table 2 (continued)

Author	Location	Morphology	Nail involvement	Diagnosis
Shimizu et al. 2013 ³⁶	right 5th digit & left thumb	A plaque extended from the distal interphalangeal joint to the fingertip (right), & a pink papule was noted beneath the nail plate(left)	Yes	Superficial BCC (right) & superficial and nodular BCC (left)
Tavares et al. 2018 ³⁷	Periungual region of the left thumb	granulomatous and friable ulcer with infiltrated margins	No	Basosquamous cell carcinoma
Tehrani et al. 2009 ³⁸	Base of thumbnail	NA	Yes	BCC
Torrelo et al. 2014 ³⁹	Dorsum of hand, second finger	Papules	No	Nodular, syndromic
Tripoli et al. 2017 ⁵⁸	Dorsum	Ulcerated lesion	NA	Superficial
Tripoli et al. 2020 ⁵⁹	Dorsum	Ulcerated lesion	NA	Unspecified
van Zuuren et al. 2000 ⁶⁰	Dorsum	NA	No	Nodular BCC
Vandeweyer et al. 2003 ⁵⁷	Dorsum of the hand	ulcerated	No	infiltrative BCC with free margins
Watson et al. 2019 ⁴⁰	Hand	A locally invasive ulcerated lesion of the right upper limb	No	Nodular
West et al. 1990 ⁵²	The dorsum surface of the proximal phalanx of the index finger	An ulcer with a clean, granular base and a raised erythematous border	NA	Sclerosing BCC
Yousif et al. 2013 ⁴¹	Dorsoradial aspect of ring finger	Ulcerative, raised with a rolled edge	No	Nodular
Zhu et al. 2014 ⁴²	dorsal aspect of both hands (transversed joint) & distal tip of the left small finger	large ulcerated	Yes	BCC multilobular

heterogeneity in the incidence rate of recurrence (incidence = 1.48 case-years, 95%CI, 0.86 to 2.55, $I^2 = 0\%$, $p = 0.56$). Additionally, subgroup differences were significant based on the treatment provided ($\text{Chi}^2 = 35.66$, $p < 0.0001$). Heterogeneity analysis for other treatment modalities was not conducted because these treatment approaches were performed in a single study (Fig. 3).

To further investigate the sources of heterogeneity, we implemented an influence analysis (sensitivity analysis) by omitting each included study at once. The study of Fischbach et al. had the largest influence effect size.⁶² Following the exclusion of such a study, the overall heterogeneity dropped to 1.2%, and the overall incidence rate was 1.28 cases per year (95%CI, 0.76 to 2.14, Fig. 4). The exclusion of other studies did not influence the heterogeneity analysis.

Quality assessment and risk of bias

The authors evaluated the case reports and case series included in the study. Bias was evaluated separately and concurrently by two reviewers. We used a methodological quality assessment tool based on 8 components that are divided into 4 domains: selection, ascertainment, causation, and reporting (Table 3).⁶⁰ The findings of both reviewers were the same, regardless of whether the material seemed biased. MINORS were at least 52.84% in all retrospective and prospective studies considered. There was 1 comparative study, and it ranked a total score of 24. Eleven noncomparative studies had an average score of 8.45 (range 12–4). The results are summarized in Tables 4 and 5.

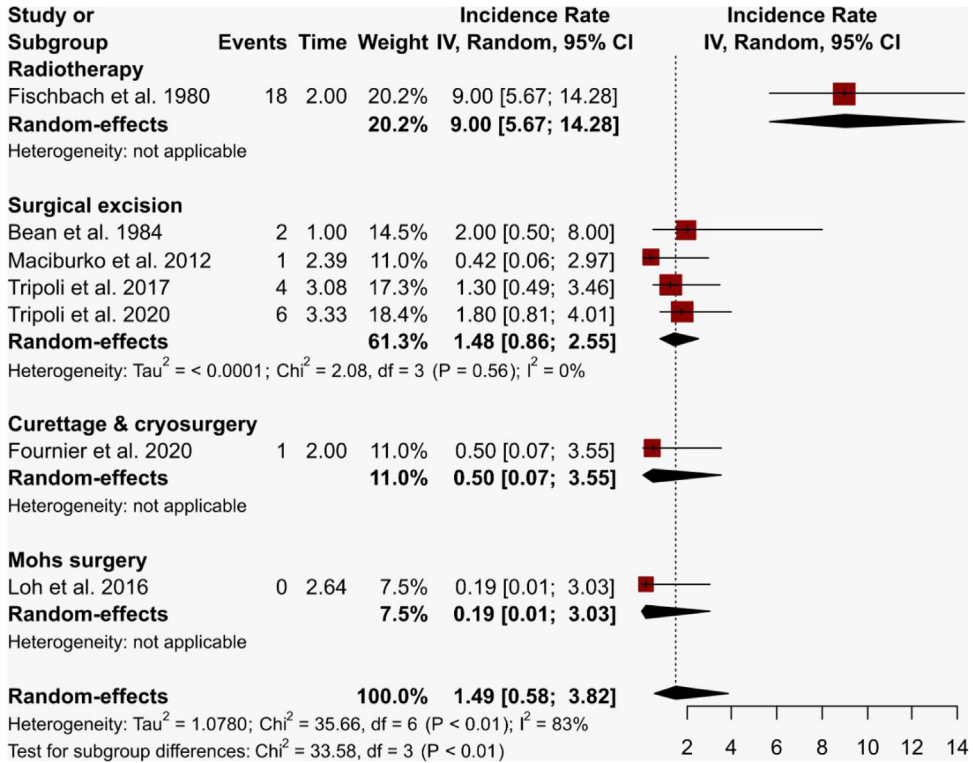


Fig. 3. A forest plot shows the incidence rate of BCC recurrence among patients treated by four modalities.

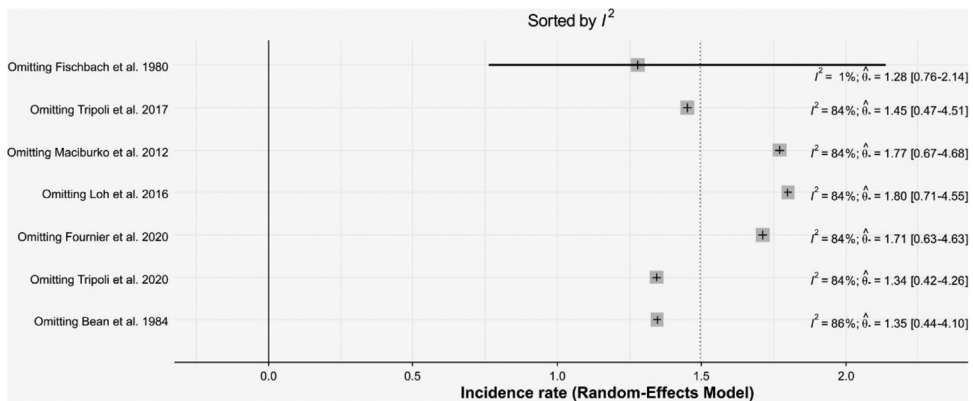


Fig. 4. A forest plot shows the results of the influence analysis.

Discussion

Skin malignancies are considered the most common primary malignancies of the hand.⁹ Although basal cell carcinoma accounts for 80% of all cutaneous malignancies, squamous cell carcinoma occurs more frequently on the hand when compared to basal cell carcinoma.⁹

Table 3
Qualitative assessment of the included studies.

Domain For Evaluating the Methodological Quality of Case Reports and Case Series								
Reference	Selection			Ascertainment		Causality		Reporting
	Leading Explanatory Questions							
	Q. 1	Q. 2	Q. 3	Q. 4	Q. 5	Q. 6	Q. 7	Q. 8
Mikhail, 1985 ²⁹	YES	YES	NO	YES	NO	NO	YES	NO
Rallis, 2010 ³²	YES	YES	YES	YES	NO	NO	YES	YES
Oriba, 1997 ³⁰	YES	YES	YES	YES	NO	NO	NO	YES
Torrelo, 2014 ³⁹	YES	YES	NO	YES	NO	NO	NO	NO
Yousif, 2013 ⁴¹	YES	YES	YES	NO	NO	NO	YES	YES
Tehrani, 2009 ³⁸	YES	YES	YES	NO	NO	NO	YES	YES
Kim, 2009 ²³	YES	YES	NO	YES	NO	NO	NO	NO
Sarfati, 2008 ³⁴	YES	YES	YES	YES	NO	NO	NO	NO
Engel, 2008 ¹⁹	YES	YES	NO	NO	NO	NO	NO	NO
Kim, 2000 ²²	YES	YES	NO	YES	NO	NO	NO	NO
Forman, 2007 ²⁰	YES	YES	YES	NO	NO	NO	NO	YES
Grine, 1997 ²¹	YES	YES	YES	YES	NO	NO	NO	YES
Watson, 2019 ⁴⁰	YES	YES	YES	NO	NO	NO	NO	NO
Lam, 2019 ²⁴	YES	YES	NO	YES	NO	NO	NO	YES
Lateo, 2005 ²⁵	YES	YES	NO	YES	NO	NO	NO	NO
Lopez-Sanchez, . 2019 ²⁶	YES	YES	YES	YES	NO	NO	YES	YES
Machida, 2011 ²⁷	YES	YES	YES	YES	NO	NO	YES	YES
Pollo, 2019 ³¹	YES	YES	YES	NO	NO	NO	YES	YES
Tavares, 2018 ³⁷	YES	YES	YES	YES	NO	NO	NO	YES
Shimizu, 2013 ³⁶	YES	YES	YES	YES	NO	NO	NO	YES
ORTEGA, 2002 ³⁵	YES	YES	NO	YES	NO	NO	NO	NO
Coulombe, 2018 ¹⁸	YES	YES	NO	YES	NO	NO	NO	NO
Zhu, 2014 ⁴²	YES	YES	YES	NO	NO	NO	YES	YES
Higuchi, 1988 ⁴⁷	YES	YES	YES	YES	NO	NO	YES	YES
Enna, 1978 ⁴⁴	YES	YES	YES	YES	NO	NO	NO	YES
Okuyama, 2006 ⁴⁹	YES	YES	NO	YES	NO	NO	NO	YES
Hoffman, 1973 ⁴⁸	YES	YES	YES	YES	NO	NO	NO	YES
Rudolph, 1987 ⁵⁰	YES	YES	YES	YES	NO	NO	NO	YES
Galeano, 2002 ⁴⁵	YES	YES	YES	YES	NO	NO	YES	YES
Guana, 1994 ⁴⁶	YES	YES	YES	YES	NO	NO	NO	YES
West, 1990 ⁵²	YES	YES	YES	YES	NO	NO	NO	YES
Dika, 2013 ⁴³	YES	YES	YES	YES	NO	NO	NO	YES
Salomão, 1999 ⁵¹	YES	YES	YES	YES	NO	NO	YES	YES
Martinelli, 2006 ²⁸	YES	YES	YES	YES	NO	NO	NO	YES
Robins, 1981 ³³	YES	YES	YES	YES	NO	NO	NO	YES
Ozkan, 2017 ⁵⁴	YES	YES	YES	YES	NO	NO	YES	YES
Abeldano, 2006 ⁵³	YES	YES	YES	YES	NO	NO	NO	YES
Zuuren, 2000 ⁶⁰	YES	YES	YES	YES	NO	NO	YES	YES
Maciburko, 2012 ⁸	YES	YES	YES	YES	NO	NO	YES	YES

Selection: [question 1]. Does the patient(s) represent(s) the whole experience of the investigator (center) or is the selection method unclear to the extent that other patients with similar presentations may not have been reported?.

Ascertainment: [question 2]. Was the exposure adequately ascertained? [question 3]. Was the outcome adequately ascertained?.

Causality: [question 4]. Were other alternative causes that may explain the observation ruled out? [question 5]. Was there a challenge/rechallenge phenomenon? [question 6]. Was there a dose-response effect? [question 7]. Was follow-up long enough for outcomes to occur?.

Reporting: [8] Is the case(s) described with sufficient details to allow other investigators to replicate the research or to allow practitioners to make inferences related to their own practice?.

Furthermore, the dorsum of the hand is considered a frequently sun-exposed area. However, hand BCC occurrences are relatively uncommon when compared to the head and neck.⁶ This is mainly attributed to the deficiency of pilosebaceous glands in that area.²¹ Moreover, Zuuren et al. argue that the dorsum of the hand is considered a rare site of BCC occurrence when compared to other body sites.⁶⁰ When taking skin surface into account, BCC of the dorsum of the hand tends to have roughly

Table 4
MINORS assessment tool for nonrandomized comparative studies ($n = 1$).

Item	Fournier, 2020 ⁵⁵
A clearly stated aim	2
Inclusion of consecutive patients	2
Prospective collection of data	2
Endpoints appropriate to the aim of the study	2
Unbiased assessment of the study endpoint	2
Follow-up period appropriate to the aim of the study	2
Loss to follow-up less than 5%	2
Prospective calculation of the study size	2
An adequate control group	2
Contemporary groups	2
Baseline equivalence of groups	2
Adequate statistical analyses	2
<i>Total score</i>	24

the same frequency as other body sites—excluding the face and neck, where BCC is most common.⁶⁰ To the best of the authors' knowledge, this is the first systematic review that examines a variety of clinical characteristics, investigations, and treatment options available in the literature for hand BCC. Furthermore, we have presented pooled recurrence rates based on a meta-analysis. The overall rate of hand BCC recurrence was 1.49 cases per year. However, after excluding cases treated with radiotherapy as a single modality, which accounts for the highest recurrence rate among the included studies,⁶² the overall incidence rate will be 1.28 cases per year, with almost all patients managed surgically. A systematic review published in 2009 investigated the clearance rate of BCC after 5 years of follow-up and found a 99% clearance rate with Mohs micrographic surgery, 91–95% with wide local excision, and radiotherapy associated with a lower clearance rate of 90%. In spite of its higher recurrence rate than surgical excision, radiotherapy still provides better cosmetic outcomes. It must be considered as one of the first nonsurgical choices in patients who cannot survive surgeries.⁶⁷ A recent RCT compared the combination of curettage and cryosurgery versus curettage and electrodesiccation in managing sBCC. At 12 months of follow-up, only one patient experienced a recurrence in the cryosurgery group. Both techniques had good scar results by the end of the study. Nonetheless, the short follow-up period might not reflect reality, and more studies are needed to investigate the combination of different modalities.⁵⁵ However, involvement of the nail unit is much more frequent on the fingernails than on toes.²⁸ In these studies, 34 out of 2051 patients experienced fingernail involvement with variable morphological features including ulcerative, longitudinal plaque, or onychodystrophy.^{20–22,28,31,33,35,36,38,42,43,45,46,48–50} Many of the reported studies found initial difficulties in obtaining the correct diagnosis of BCC due to the wide variety of lesions and malignancies that can arise from the hand with similar morphological features, including glomus tumor,²⁹ melanoma,⁵⁰ and actinic keratosis.²⁰ These findings highlight the importance of performing biopsies in cases with uncertain diagnoses or failure of treatments to detect misdiagnosis. Almost all patients with nail involvement were managed surgically by MSS (43%), simple excision (31%), or amputation (19%). None of the patients experienced recurrence except for a single case reported ten months post-operation. The author suggested a minimal clearance margin of 0.5 mm to be responsible for the recurrence rather than the failure of the modality.³⁸ Mohs micrographic surgery has shown superiority in the clearance rate and the advantages in preserving the adjacent soft tissue with high accuracy. Therefore, the integrity of sophisticated hand function is preserved. The need for soft-tissue coverage post-excision is variable according to the lesion size and site. Several studies reported the successful usage of FTSG with optimum function restoration and good cosmetic outcomes.^{20,32,41,46} In a single case report, a local flap was used successfully, but two months later, a recurrence occurred and ended with amputation of the thumb.³⁸ However, in most cases, where Mohs micrographic surgery has been used, they found no indication for autologous reconstruction and managed the case by dressing and healing subsequently by secondary intention.^{21,29,28,33}

Table 5
MINORS assessment tool for nonrandomized noncomparative studies ($n = 11$).

Item	Tripoli, 2017 ⁵⁸	Loh, 2016 ⁶	CHAKRABARTI, 1993 ⁶¹	Loh, 2015 ⁶⁶	Riml, 201,3 ⁵⁶	Bean, 198,4 ⁶⁴	Fischbach, 1980 ⁶²	Clifford, 1955 ⁶⁴	Kendall, 1969 ⁶⁵	Tripoli, 2020 ⁵⁹	Vandeweyer, 2016 ⁵⁷
A clearly stated aim	2	2	2	2	2	2	2	2	0	2	0
Inclusion of consecutive patients	0	0	0	0	0	0	0	0	0	2	0
Prospective collection of data	0	0	0	0	0	0	0	0	0	0	0
Endpoints appropriate to the aim of the study	2	2	2	2	2	2	2	2	2	2	2
Unbiased assessment of the study endpoint	2	2	2	2	2	2	2	2	2	2	0
Follow-up period appropriate to the aim of the study	2	2	0	2	2	2	2	0	0	2	2
Loss to follow-up less than 5%	1	2	0	2	2	2	2	0	0	2	2
Prospective calculation of the study size	0	0	0	0	0	0	0	0	0	0	0
<i>Total score</i>	9	10	6	10	10	10	10	6	4	12	6

To our knowledge, this systematic review and meta-analysis are the first to investigate the current management options and outcomes of BCC in the hand. The strengths of this systematic review and meta-analysis are that it is noncommercial, has strict inclusion and exclusion criteria, and was reported in line with the PRISMA criteria with no deviations from the protocol. The methodological quality and synthesis of all the studies were assessed for bias, and all had MINORS above 70%. This study analyzed the most recent hand BCC studies at the time of writing, providing the most comprehensive data pool available. Nonetheless, our study has several limitations. First, most of our results were based on case reports, which comprised most of the studies included in this systematic review, with the weakest evidence level. Second, most of the studies included in this study were from North America and Europe; hence, the results may not be generalizable. Third, not all studies included in this systematic review are recent, mainly due to the paucity of published articles discussing this topic. Finally, a long-term follow-up period is needed to measure the accurate prognosis, and not all studies had a sufficient follow-up period. Due to heterogeneity and a lack of data from several studies, prospective randomized studies are needed to shed light on the recurrence rate, management of hand BCC, and health advances. In conclusion, the treatment options for BCC of the hand vary depending on the presentation. Moh surgery was the preferred treatment option for hand BCC with no reported recurrences, whereas radiotherapy alone had the highest recurrence rate and inferior cosmetic results. The overall incidence rate of recurrence among the included patients was 1.28 case years (95%CI, 0.76 to 2.14). Collaboration between different medical practitioners is required to manage hand BCC. In the future, research should focus on developing an appropriate set of criteria for treating BCCs of the hands, especially regarding the recurrence rates of various treatments and the long-term complications of such treatments.

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Declaration of Competing Interests

The authors have no relevant financial or nonfinancial interests to disclose.

Ethics approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was waived due to the nature of the study.

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