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Treatment of retronychia: A systematic review and suggested treatment algorithm

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5 TITLE PAGE
67 Title: Treatment of retronychia: a systematic review and suggested treatment algorithm
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Abstract

Reitronychia is an inflammatory disorder typical of the great toes characterized by arrested nail growth, ingrowth of the nail plate into the proximal nail fold and paronychia. There is no standardized treatment for reitronychia, and its management should be weighed based on the severity stage, treatment modality, and clinical outcome. In this paper, a systematic review of the literature was performed to assess all published data regarding the treatment of reitronychia. A total of 231 patients from 24 studies were included in the analysis. Conservative management was adopted in mild-intermediate forms, consisting of medical (topical or intralesional high-potency corticosteroids) and podiatric treatment (taping, clipping back the onycholytic plate, orthosis), leading to a global cure rate of 41.2%, with no reported side effects. Non-conservative management, i.e. chemical or surgical avulsion of the nail plate, proved resolute in 71.2% of cases. Surgical avulsion of the nail plate produced the highest cure rate (78.2%), but was burdened by 9.6 % of long-term sequelae, mainly nail dystrophies.

A decision-making algorithm was designed to give clinicians treatment indications based on the severity stage of reitronychia, treatment invasiveness, and possible clinical outcomes.

Introduction

Retronychia is an inflammatory process caused by the posterior ingrowth of the nail plate in the proximal nail fold, with consequent inflammation of the periungual tissues (paronychia) and overlap of stacked nail plates one upon the other¹. The incidence of this affection is probably underestimated. However, most of the reports suggest a clear-cut prevalence for the female sex, young adulthood, and toenails. Although bilateral or multifocal presentations have been reported, retronychia usually occurs in a single digit, mostly the big toe².

Clinical manifestations of retronychia encompass a wide spectrum of signs and symptoms. Early findings include a reduced/absent growth of the nail plate and a variable degree of proximal nail fold inflammation³. As the disease progresses, elevation and yellowish discoloration (xanthonychia) of the proximal portion of the nail plate develops as a consequence of the growth of multiple overlapping nails and exerts a push-up force favoring the posterior embedding¹. The pivots of this process are the lateral horns of the matrix adhering strictly to the nail plate, thus avoiding its detachment¹. The growth of the new nail plate beneath the old one that remained attached leads to continuous microtrauma of the proximal nail fold (proximal nail ingrowing) with inflammation. The periungual tissues become swollen and erythematous, with possible formation of granulation tissue. The misalignment of the nail plate facilitates distal onycholysis and raising of the distal pulp due to the nail bed retraction¹. Clinical signs of retronychia are often accompanied by subjective symptoms, including pain and walking troubles⁴.

The pathogenesis of retronychia has been well documented in the literature. A minor traumatic injury to the nail matrix usually triggers the initial step, inducing arrest of the longitudinal nail growth². Retronychia differs from onychomadesis or Beau's lines because the detached plate loses the horizontal alignment, but keeps a connection with the nail structures (lateral matrix horns). As a result, the shedding process cannot be accomplished¹. The matrix produces a new underlying plate, which is unable to push the old plate forward, promoting the embedding of the upper plate within the

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3 proximal nail fold. Moreover, distal onycholysis increases the plate's susceptibility to back and forth
4 movements¹. This leads to the indirect injury of the distal matrix, with interruption of its mitotic
5 activity and generation of a new plate, perpetuating the process. The persistent inflammation of the
6 nail unit gives rise to fibrosis and scarring retraction⁴. This finding is in line with an ultrasonography
7 study, which detected a shorter distance between the matrix and the distal interphalangeal joint⁵.
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12 Several papers have studied the pre-existing conditions which make the first toenail prone to trauma
13 and predispose to the development of retronychia. These include a claw-toe shape of the 2nd-5th
14 digit, or the combination of long hallux and shorter 2nd digit, which causes the reflex compensatory
15 hyperextension of the hallux, while the congenital malalignment of the big toe predisposes to nail
16 ingrowth²⁻³. Besides, the nail matrix is extremely vulnerable to an ischemic injury. Systemic diseases
17 causing a reduced oxygen supply to the matrix have a high probability of damaging it. This is the
18 case with arthritis and thrombophlebitis, as well as compartment or postpartum syndromes^{4,6}.
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32 Retronychia, particularly in the early stage, can mimic several nail disorders, including tumor-like
33 conditions (i.e. mucoid cyst)⁶ and nail cancers (amelanotic melanoma, squamous cell carcinoma,
34 Bowen disease, and keratoacanthoma)⁷⁻⁹ or virtually any inflammatory, infectious and iatrogenic
35 cause of paronychia².
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43 Ultrasound criteria of retronychia have been validated in several papers, although the diagnosis
44 mainly relies on clinical examination and nail avulsion, to detect superimposed nail plates under the
45 proximal nail fold⁵.
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51 There is no standardized treatment for retronychia. Mild forms may regress spontaneously, while
52 others show a good response to topical medications. Surgical avulsion of the nail plate should be
53 performed as a straightforward solution in advanced cases, to remove the ingrown nail layers.
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58 A systematic review of the literature was performed to assess all published data regarding treatment
59 of retronychia.
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Materials and Methods

On August 13, 2020, we performed a systematic review of papers published in MEDLINE, EMBASE, Google Scholar, and Cochrane databases, using the search term “Retronychia”. Information sources of the search were processed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyzes (PRISMA) and are outlined in Figure 1.

All the studies related to the treatment modalities of retronychia published until the search date were included. All included articles clearly described the management, surgical or medical, the number of treated lesions and the outcome of retronychia. Cure was defined as the regrowth of a normal nail plate, with the relief of symptoms and paronychia resolution. Secondly, specific study characteristics (patient demographic data) and article features (accessible full text) were set as inclusion criteria.

Results

A total of 230 non-duplicate studies were identified during the search process. Of these, 27 were considered eligible after their title and abstract had been carefully screened. The full-text assessment led to the exclusion of a further 3 papers because they did not discriminate between the therapeutic modalities or the outcomes of patients treated with surgery and medical treatment. The 24 included studies were divided into groups according to the treatment management. These studies were published between 2008 and 2020. This review included 9 case reports, 10 case series, and 5 retrospective studies (Table 1).

The overall number of retronychia patients was 222. A conservative approach was adopted in 122/222 (54.95%), while surgery was performed in 99/222 (44.59%) of patients. The mean age of patients was 31.34 years in the surgery group and 28.47 years in the medical group. The two groups showed a comparable mean disease duration (6.7 and 5.8 months in the surgical and medical patients respectively), a female preponderance (female to male ratio respectively of 4.7:1 and 2.1:1) and the

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3 prevalent involvement of the first toenail (78.4% and 71.3%). The most commonly reported symptom
4 was localized pain (98.3%), whereas impaired walking occurred only in a minority of cases (6.8%)^{6,10-}
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8 ¹². The main triggers of retronychia reported in the surgical group were, in decreasing order: trauma
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10 (21.6%)^{1-2,5-6,12-17}, sport (18.9%)^{1-2,15,17-19} and tight footwear (13.5%)^{2,13,17,20-21}; vice-versa the same
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12 factors were reported with an increased prevalence and opposite order in the medical group:
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14 trauma (17.3%)^{1,17}, sport (26.7%)^{2,11,17,22-23}, tight footwear (44%)^{2,11,17,22-23} respectively. The most
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16 reported clinical signs of retronychia were: paronychia, periungual discharge^{12,14-15,20,24-25}, yellowish
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18 discoloration of the nail plate (xanthonychia)^{10,12-16,18,21-26}, granulation tissue formation^{1,13-15,19,21-23},
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20 subungual hemorrhage²³, back and forth mobility of the overlying nail plate^{13,15-16,18,21} and distal
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22 onycholysis promoting bed retraction and raising of the distal pulp^{6,12-13,15,22-23,26}.

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27 The review identified 6 subsets of treatment modality. Conservative management included the
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29 administration of local steroids, cycles of intralesional steroid injections, and podological treatment.
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31 The avulsion of the nail plate was performed either by surgery or by topical application of keratolytics
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33 under occlusion followed by mechanical nail debridement. With regards surgical treatment, 12
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35 articles, involving 46 patients, did not specify the type of approach used for avulsion of the nail plate,
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37 whereas 6 articles, involving 51 patients, used the proximal approach; 2 articles based on two patients
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39 performed the distal approach. In detail, Reigneau and Gatica-Torres performed two proximal partial
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41 nail plate avulsions, which falls into the proximal modality: a complete cure was achieved in two
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43 cases, whereas the third case relapsed and underwent total proximal avulsion with complete
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45 resolution^{12,27}. In 17/93 cases, nail avulsion was pursued after the failure of topical therapy, based on
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47 antibiotics or corticosteroids¹. In one case, surgery was advocated after the lack of response to an
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49 intralesional cycle of steroids²⁸. (Table 1). Cure rate was computed as the percentage of completely
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51 resolved cases minus relapse events on the total population.
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57 Among the surgical approaches, the avulsion with sparing of the innermost plate had a 95.2% cure
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59 rate with evidence of only one recurrence at follow-up, whereas the complete surgical removal of all
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3 nail plates had a cure rate of 76%, with recurrence in 6.7% of cases. Medical management induced
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5 cure rates of 62.5% for chemical avulsion and of 96.4% for intralesional steroid injections (with a
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7 recurrence rate of 12.5% and 0%, respectively). As described by Alessandrini et al.²⁸, intralesional
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9 steroid injections induced cure of retronychia as early as after 2 injections. Topical steroids and
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11 podiatric treatment showed a low rate of success (47.3% and 15.4%, respectively) and a 1.7% relapse
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13 rate for topical steroids.
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18 Follow-up results were reported in 17/25 papers and lasted on average 13.5 months for 1 patients and
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20 6 months for medically treated patients, when specified.
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24 During the post-surgery follow-up 1 case developed a pyogenic granuloma associated with lateral
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26 nail ingrowing¹⁹, 8 patients relapsed^{2,6,11,17,19}, and one case had never healed in the first instance²³.
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28 Nine patients healed with residual nail dystrophies, including xantonychia, slowed nail growth,
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30 micromonychia, and Beau's lines^{11,17,21}.
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33 **Discussion**

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35 Recently, a review on the available treatments of retronychia reported complete resolution rates of
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37 96% versus 38.6% for surgical vs. conservative approach²⁹. Partial resolution was documented in
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39 2.8% versus 22.8% of treated cases, respectively. In our study, we did not consider partially resolved
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41 cases, which sooner or later relapse, and we also excluded recurrences at follow-up. We also included
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43 the recently published intralesional route of steroid administration, which could prove effective for
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45 intermediate-severity cases. Due to rapidly evolving knowledge concerning retronychia, older papers
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47 reported a higher number of misdiagnoses leading to ineffective treatments, including antibiotics and
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49 antimycotics, none of which led to a resolution (Table 2).
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55 Our study provides further evidence to confirm the higher cure rate of non-conservative management
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57 for retronychia, as compared to medical treatment (76.9% vs. 42.1%). However, the conservative
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59 management is virtually lacking in any adverse events and is able to relieve pain rapidly and
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3 effectively. Moreover, the combination of several different treatments may play a synergistic effect,
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5 increasing the cure rate in the early stages. On the other hand, the non-conservative treatment is
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7 burdened by a 9.6% rate of residual onychodystrophy, including micronychchia, pincer nail and
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9 lateral/distal ingrowing, which impact patients' satisfaction. The highest rate of residual
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11 onychodystrophy was reported in an adolescent/young adult group treated with proximal nail
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13 avulsion. Although the reported cases are limited to only a single article, we believe that children and
14
15 adolescents may be more prone to develop side effects for different reasons, such as the greater
16
17 vulnerability of the matrix, poor compliance of recovery times, inadequate use of footwear, etc.
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22 Among non-conservative treatments, chemical avulsion compared with surgery led to a lower cure
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24 rate (62.5% versus 76%) but had a better safety profile, since no complications were reported after 6
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26 months¹⁰. Chemical avulsion consists of a first phase of keratolytic dressing, followed by nail
27
28 debridement. It proved a viable option for treating intermediate to severe stage retronychia (all
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30 patients presented granulation tissue and oozing from the proximal nail fold) in a single-monocentric
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32 study. The keratolytics used were based on 50% urea, 10% salicylic acid conveyed in white petroleum
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34 ointment, and applied under occlusion for one week¹⁰.
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40 When surgery is adopted, the proximal approach and the removal of the superimposed nail plates
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42 with sparing of the innermost plate should be recommended, whenever possible. This leads to a higher
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44 rate of success, with a lower incidence of sequelae and recurrences. The rationale of leaving the newer
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46 proximal nail plate in place is to prevent distal pulp uprise with consequent anterior embedding.
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48 According to Fouilloux, this technique works only if the plate is whitish, bright, and well-attached to
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50 the nail bed¹⁹. The detection of yellowish dyschromia is a red flag that signals poor matrix vitality
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52 and poor adhesion of the plate to the bed. This leads to higher chances of further recurrence, nail
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54 ingrowing and residual dystrophy¹⁹. Partial proximal avulsion can be considered as a viable option
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56 when the distal nail is not excessively damaged and onycholysis is not present. This allows the distal
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58 nail bed to remain covered and prevents elevation of the distal pulp^{12,27}.
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3 Among the conservative treatments, matrix intralesional injection of triamcinolone resulted in a cure
4 rate of 96.43% in a single monocentric prospective study²⁸. This approach can be advocated in
5 intermediate or early stages, when surgery can still be spared. There is no evidence to support the use
6 of triamcinolone in severe cases. The majority of responses are achieved within the 2nd session, with
7 an 85.7% complete response and a further 10.7% of partial improvements. As suggested by the study
8 by Alessandrini et al. the action of intralesional steroids can improve slowed nail growth, exerting a
9 beneficial effect on the matrix²⁸.

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12 The use of high potency topical steroids led to a cure rate of 41.60%. However, this could possibly
13 be higher if limited to early stages, where inflammation of the proximal nail fold could be reduced
14 with good efficacy.

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17 Podological treatment was based on orthosis, orthopedic footwear, clipping back the onycholytic
18 plates and taping techniques, relieving tissue pressure on the nail plate, and preventing distal
19 keratinization and consequent embedding. Even though a moderate benefit was achieved in managing
20 acute initial stage retronychia (25%), the prevention of back and forth movements by correct taping
21 and microtrauma by proper insoles may facilitate nail growth. Moreover, the application of an acrylic
22 nail orthosis on the growing nail may counteract the distal pulp expansion on the nail bed, favored by
23 upward forces during gait.

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26 Co2 laser treatment was reported in a single paper combined with surgical avulsion, and targets the
27 removal of granulation tissue in the severe stage, with minimal or no bleeding, instead of curettage¹.

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30 To summarize all the reviewed data, a flow-chart (Fig. 2) has been designed to provide a therapeutic
31 algorithm that takes into account 3 factors: severity stage, treatment invasiveness, non-
32 response/relapse events.

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3 Early-stage retronychia could be initially treated with high potency corticosteroids (either or not in
4 occlusion) to decrease PNF inflammation. Also, podological treatment is advocated when adhesions
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6 between the nail plate with lateral sulci are found on clinical examination.
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10 Recalcitrant cases could be considered the same as intermediate stage retronychia and managed with
11 intralesional steroids, which provided a higher and faster cure rate. The greater the reduction in soft
12 tissue inflammation, the greater the chance of realigning the overlapping plates favoring their distal
13 shedding. Severe cases, as well as relapsing cases, could be treated either with chemical or surgical
14 avulsion. There are few, but promising evidences concerning chemical avulsion, although only one
15 case series on 8 patients has been published¹⁰. This technique may be considered the first-line
16 treatment for adolescents and teenagers, who are burdened with a higher rate of post-surgery
17 complications, according to Piraccini and coworkers¹¹. A safe alternative is proximal partial avulsion,
18 which prevents the pulp rising on the nail bed. However, it cannot be performed in the case of distal
19 onycholysis, which promotes distal nail fold formation and keratinization^{12,27}. For this reason surgical
20 avulsion should always be pursued by adopting a proximal approach, whenever possible, although
21 many authors of the reviewed articles did not specify the type of approach used. When performing
22 the avulsion of nail plates, it is vital to assess the innermost plate. It may be left in place if no signs
23 of onycholysis (xanthonychia, back and forth mobility) could be detected. In this case, the plate gains
24 a whitish and bright appearance, which suggests a good adhesion to the nail bed and the vitality of
25 the nail matrix. This procedure led to a 100% recovery after the avulsion without any recurrence or
26 side effects in the cases described.
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50 The distal nail fold and the granulation tissue are separate elements that need to be evaluated apart,
51 since there is no direct correlation with the severity stage. Granulation tissue resolves promptly with
52 the topical application of high-potency corticosteroids, mainly under occlusion, or it can be treated
53 effectively with co2 laser, granting minimal bleeding. The distal rising of the pulp favors the
54 ingrowing. This could be prevented with adequate taping and podological treatment, or should it
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3 occur, using urea-based moisturizers applied by adequate massaging. Recalcitrant cases can be treated
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5 with surgical avulsion techniques such as super U or Howard-Dubois^{30,31}.
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8 This study has several limitations. First of all, the data are fragmented concerning follow-up time,
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10 which impacts the possible detection of recrudescence, leading to the overestimation of cure rate in
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12 some cases: in 118 cases the follow-up was not mentioned, while in the remaining part of the cases,
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14 even when mentioned, methods and timing were not often described.
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18 Also, the cure rate takes into account the number of relapses, which in turn depends on the follow-up
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20 period. The mean follow-up time was reported in 17 / 24 studies; it ranged from around one year for
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22 non-medical treatments to about 6 months for medical treatments. Finally, some authors did not
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24 clearly describe the presence or absence of alterations in the regrown nails after treatments. So it is
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26 difficult to draw a definitive conclusion about the exact cure rate, given the high heterogeneity of the
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28 data.
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32 33 **Conclusions**

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36 This review aims to collect and summarize the updated armamentarium for managing retronychia.
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38 Acute and moderately inflamed cases may benefit from conservative therapies, including local or
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40 intralesional steroid therapy, better combined with podological treatment. Chronic, severe, or
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42 recalcitrant cases should be directly addressed to nail avulsion, either chemical or surgical, taking
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44 into account the different risks according to the specific intervention, and with a recovery plan to
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46 avoid possible complications or relapse.
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Figure legends

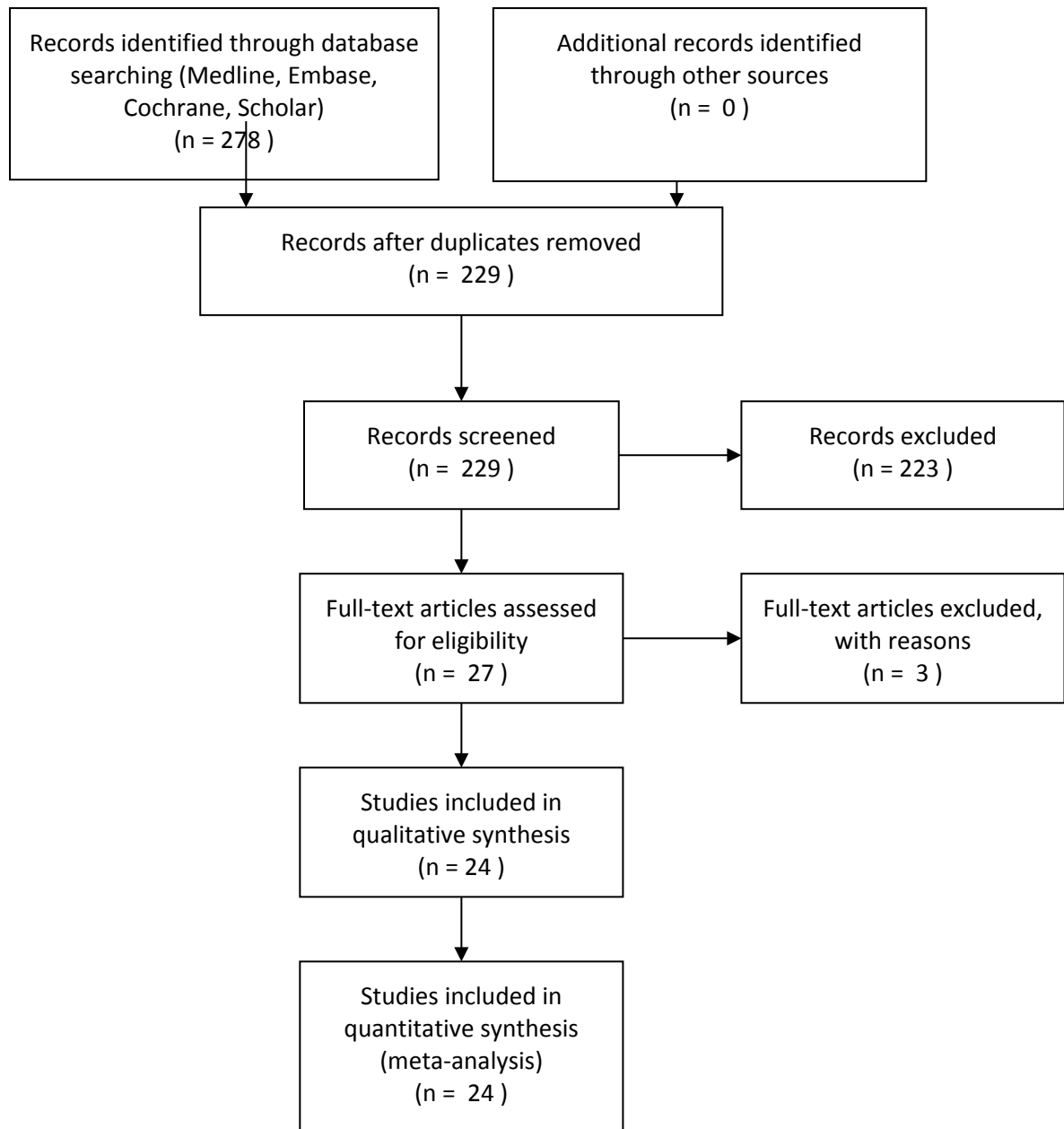


Figure 1: PRISMA flow diagram of the search strategy.

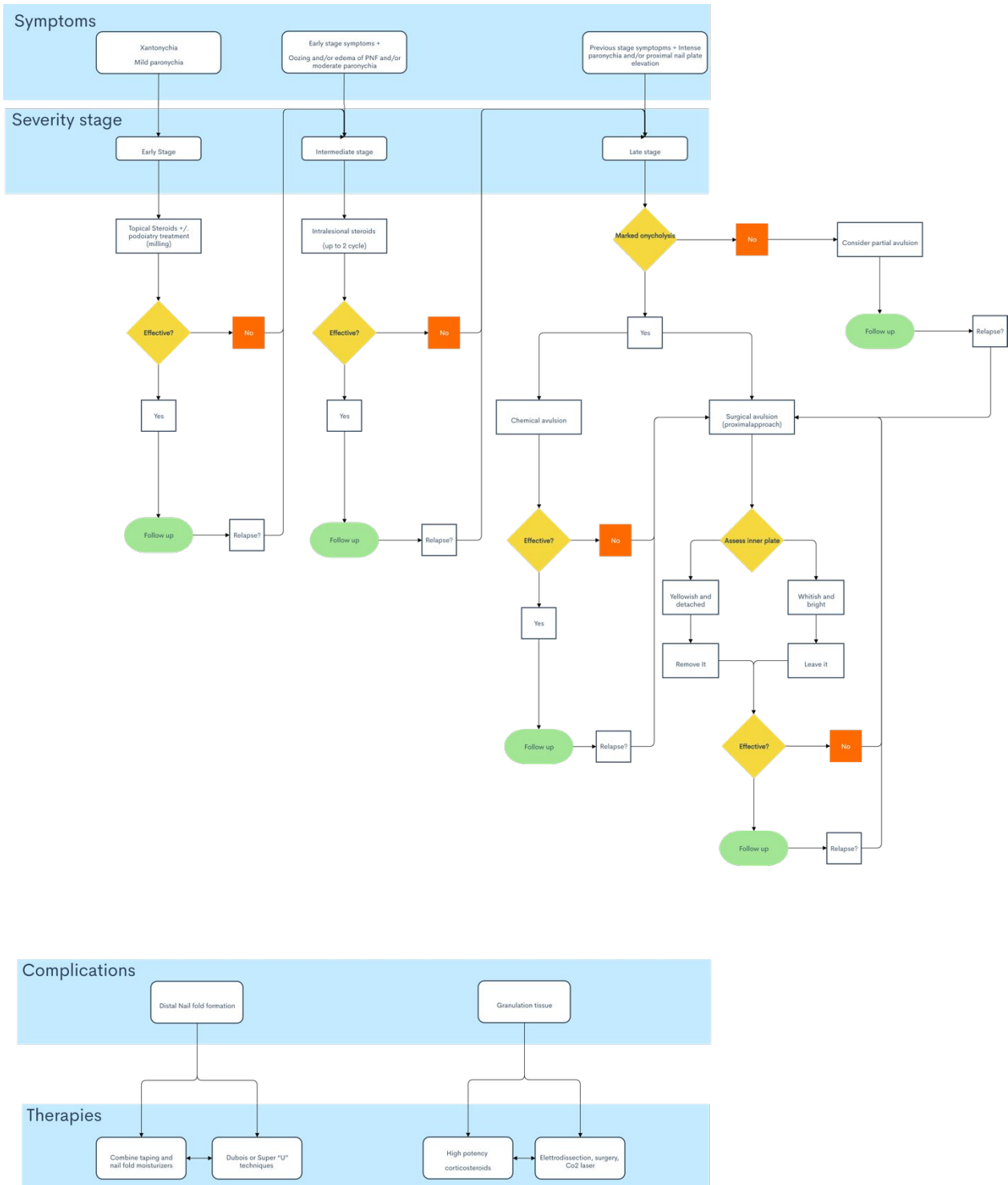


Figure 2: Suggested treatment algorithm aimed to tailor the treatment invasiveness with severity stage and relapse events.

Table legends

First author (year)	Study design	Study type (GRADE) ^a	Patients (n)	Non-conservative management (%)	Conservative management (%)
Alessandrini (2020) ²⁸	RS	P - (2b)	28	0 (1 no-responder was treated with nail avulsion as salvage therapy)	100% Intralesional triamcinolone
Laird (2019) ²³	RS	R - (2b)	25	24% (6/25) Nail avulsion	76% (19/25) Podological treatment (clip back of the onycholytic nail plate) + topical moisturizer
Lencastre (2019) ²²	RS	R - (2b)	56	0	100% Topical steroids with (31/56) or without (25/56) occlusion for an average of 8 weeks.
Nagrani (2019) ¹⁶	CR	4	1	100% Nail avulsion	0
Vastarella (2019) ¹⁰	CS	4	8	0	100% Chemical avulsion
Nakouri (2018) ¹³	CR	4	1	100% Distal nail avulsion with sparing of the innermost plate	0
Poveda-Montoyo (2018) ²⁵	CS	4	2	100% Nail avulsion	0
Campos (2017) ³²	CR	4	1	100% Proximal nail avulsion	0
Robledo (2017) ²⁴	CR	4	1	100% Nail avulsion	0
Alonso-Pacheco (2016) ¹⁸	CR	4	1	100% Distal approach avulsion	0
Gerard (2016) ¹⁷	RS	R - (2b)	18	83.3% (15/18) Proximal nail avulsion	5.6% (1/18) Orthosis, 11.3% (2/18) Topical steroids
Ventura (2016) ²	RS	R - (2b)	20	75% (15/20) Nail avulsion	25% (5/20) Taping

Cabete (2015) ²¹	CS	4	2	50% (1/2) Nail avulsion	50% (1/2) Orthopedic shoes
Gatica-Torres (2015) ²⁷	CS	4	2	50% Proximal avulsion of all superimposed plates, 50% Proximal partial avulsion of 2 nails (1 recurred and 1 healed)	0
Fouilloux (2014) ¹⁹	CS	4	6	100% Proximal nail avulsion	0
Piraccini (2014) ¹¹	CS	4	15	86.6% (13/15) Nail avulsion	13.4% (2/15) Topical steroids
Chang (2013) ¹⁴	CS	4	2	100% Nail avulsion	0
Reigneau (2013) ¹²	CS	4	4	75% (3/4) Proximal nail avulsion, 25% (1/4) Partial proximal avulsion	0
Zaraa (2012) ²⁶	CR	4	1	100% Nail avulsion	0
Wortsman (2011) ⁵	CR	4	1	100% Nail avulsion	0
Chiheb (2010) ²⁰	CR	4	1	100% Nail avulsion	0
Baumgartner (2010) ¹⁵	CS	4	5	100% Proximal avulsion of all superimposed plates	0
Dahdah (2008) ⁶	CS	4	2	100% Nail avulsion with sparing of the innermost plate	0
de Berker (2008) ¹	CS	4	19	89.4% (18/19) Proximal nail avulsion with sparing of the innermost plate (18/18) + CO2 laser (3/18) + topical antibiotics (3/18) + topical corticosteroids (3/18) + steroid injections (1/18) + curettage (1/18)	5.3 % (1/19) Observation

Table 1. Characteristics of the included studies. Abbreviations: ^a: Centre for Evidence-Based Medicine Oxford (1a-5); CS: Case Series; CR: Case Report; RS: Retrospective Study.

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Factor	No. Papers	Surgery	Medical treatment
	24/24	99	122
Sex	22/24	80/99	101/122
-Male		12	34
-Female		78	67
Age (median)	21/24	80/99 31.34	101/122 28.47
Disease duration (months)	19/24	74/99 6.62	65/122 5.89
Follow-up data	17/24		
Affected digit	19/24		
-1		57 (T) 3H	39T 4H
-2		12 T	22T 1H
-3		1 H	1T
-4			
-5			1H
Bilateral digit involvement*	19/24	7	30
Diagnostic criteria	24/24	99	102/122
-Clinical		97	104/104
-Sonographic		2	
-Histological		2	1/104
Symptoms	21/24		104/122
-Pain		86	62
-Impaired walking		14	10
Trigger factors	20/24		93/122
-Trauma		21	1
-Sport		11	20
-Tight footwear		10	25
Predisposing factors	20/24		85/122
-Hallux valgus		8/73	0/85
-Lateral deviation of the digit		2/73	2/85
-Claw-toe			
Misdiagnosis	21/24	10/73	5/85
Misprescription			
-Antibiotics		28	8/75
-Antimycotics		13	4/75
Clinical signs	21/24		75
-Paronychia		73	121

-Other than paronychia		17	
-Xanthonychia		12	79
-Discharge		12	26
-Granulation Tissue		16	18
-Back and forth nail mobility		5	1
-Subungual haemorrhage		3	0
-Keratinized distal nail fold		8	71
Treatment side effects			
-Nail dystrophy		9	
a) Thickening of the nail		5	
b) Micronychia		2	0
-Infection		0	0
-Pincer nail		2	0
-Lateral/distal ingrowing		1	0
-Slower growing		2	
-Pyogenic granuloma		1	

Table 2: Clinical and demographic characteristics of patients and retronychia outcome.

Abbreviations: No=Number.

Treatment	No. pt	No. complete responses	Cured with sequelae	Not cured	Cured with relapses	Fully restored (no relapses or sequelae)	Overall cure rate
Antimycotics	16	0	0	16 (100)	0	0	0%
Antibiotics	30	0	0	30 (100)	0	0	0%
Topical corticosteroids	60	25 (41.7)	0	35 (58.3)	0	25 (41.7)	41.66%
Intralesional steroids	28	27 (96.4)	0	1 (3.6)	0	27 (96.4)	96.42%
Podological treatment	18 ^a	3 (16.7)	1 (5.5)	14 (77.8)	0	3 (16.7)	16.66%
Chemical avulsion + nail debridement	8	6 (75)	0 (0)	2 (25)	1 (12.5)	1 (12.5)	62.5%
Surgical removal	96 ^b	83 (86.4)	10 (10.4)	1 (1.04)	7 (7.3)	80 (80.2)	78.12%
Surgical removal of all nail plates	75	61 (81.3)	10 (13.3)	1 (1.3)	6 (8)	57 (76)	73.3 %
Surgical avulsion with sparing of the innermost plate	21	21 (100)	0	0	1 (4.8)	20 (95.2)	95.2%

Table 3: Summary of results. ^a8 patients were excluded because lost after surgery in ²³; ^b 3 patients were excluded because lost after surgery in ²³.