GENERAL REVIEW

Limb lengthening for deformities in Ollier's disease: a systematic review

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Abstract

Background The management of limb deformity, shortening, and bone defects in treatment of Ollier's disease is a major challenge. This study aims to summarize and compare the different surgical treatments, and to evaluate the outcome and possible prognostic factors of leg lengthening in these patients.

Materials and methods A systematic review of the literature from 1993 to 2017 was performed. Nineteen articles were found including a total of 121 patients with limb deformities because of Ollier's disease. The mean patients' age at the time of first surgery was 12 years. A total of 272 segments were surgically treated (14 segments in the upper limbs) with variable techniques including osteotomies and external fixation, intramedullary nails, as well as epiphysiodesis and lengthening over nail. We studied the bone healing index (BHI), distraction index (DI), distraction time, gained length, total treatment time, and complications.

Results Available implants and techniques allowed correction of patients' deformities (lengthening and correction of angular defects) in most cases. External fixators, circular or monolateral frames were the most commonly used technique. The Ilizarov external fixator was the most commonly used frame (196 segments). The BHI was significantly better when the external fixation was combined with intramedullary nails. Epiphysiodesis was most likely to be more associated with the past than to the present. Joint stiffness, infection, early consolidation, pathological fracture, deformity recurrence, delayed union, non-union, neurapraxia, and overlengthening were the reported complications with an overall rate of 27.9%.

Conclusions There is no consensus for the optimal surgical technique and implants for correction of limbs deformities in patients with Ollier's disease. External fixators most commonly circular are the most commonly used implants; however, complications do occur.

Keywords Ollier's disease · Limb length discrepancy · Deformities · External fixator

Introduction

Ollier's disease, known as multiple enchondromatosis, is a rare non-hereditary benign skeletal disorder, characterized by circumscribed lesions (3 or more) of cartilage arranged in a linear fashion with an asymmetric distribution [1]. Multiple enchondromatosis appears in early childhood. The estimated prevalence is 1:100,000, although the real incidence is unknown because mild phenotypes without skeletal deformities or secondary consequences are often not detected. Ollier's disease is probably attributable to a failure of the normal enchondral ossification resulting from the proliferation of ectopic islands of chondroid tissue, or to the incapacity of the epiphyseal plate to become mature, causing residual chondroid proliferation in the bones [1, 2]. As a consequence, these patients experience bowing of

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the long bones and longitudinal growth anomalies resulting in deformities such as limb length discrepancies (LLD), genu valgus, and broadening of the metaphyses [3–8]. The affected bones show numerous islands of cartilage in close proximity to the physis and the adjacent metaphysis. All bones can be affected in variable degree, with the femur and tibia most often involved. LLD may range up to 10–25 cm by skeletal maturity [1, 2]. Cosmesis is partly a concern; shortening of a lower limb affects the vertebral column and causes stiffness of the ankle joint of the shortened leg and gait disturbances. The presence of weak bone and enchondromas is associated with an increased risk of pathological fractures. Last, patients with Ollier's disease should be monitored for the risk of malignant degeneration to chondrosarcoma ranging from 10 to 30% [2].

Before the development of external fixators and distraction osteogenesis, the correction of the deformities and LLD in patients with Ollier's disease was performed with conventional surgical treatments such as curettage of the cartilaginous lesions, bone grafting, osteotomies, and internal osteosynthesis with plates and screws; however, these options were not feasible in many patients with Ollier's disease because the affected bone was weakened and LLD was usually substantial [3–8]. Internal osteosynthesis implants have been associated with complications, and importantly, they did not allow for lengthening of the involved bone. Therefore, unilateral and circular external fixation frames have become a popular treatment option in the last years [6–18]. The Ilizarov technique is the most common approach used to correct and lengthen LLD, although other types of external fixators have been developed such as the Multi-Axial Correction (MAC) System (Biomet Trauma, Warsaw, Indiana), the Orthofix fixators (Orthofix®, Verona, Italy), and the Taylor Spatial Frame (TSF, Smith and Nephew, Tennessee, USA). Combined techniques including lengthening intramedullary nailing, intramedullary nailing, and circular external fixators have been further described [15–30].

Because of the rarity of Ollier's disease, there is still no standard consensus concerning the optimal surgical technique and implant. Therefore, we performed this study to summarize the current data with regard to surgical techniques used to manage LLD in patients with Ollier's disease, to evaluate the outcomes of the obtained corrections, and to find a possible relationship between the type of correction technique and local recurrence or malignant degeneration in these patients.

Materials and methods

A systematic review was conducted using PubMed and Google Scholar research libraries. Level II to V studies published in the English language from 1993 to March 15 2017

were selected. Studies selection was repeated by a second reviewer for validity, and any discrepancies were resolved by a third reviewer. The search terms used in combination were "Ollier's disease," "bone lengthening," "limb reconstruction," "limb length discrepancy," "distraction osteogenesis," "external fixation," "deformity treatment." Previous articles were not considered as the techniques that were described by those authors are not consistent with current methods.

Inclusion criteria included Ollier's disease patients, surgery in upper and lower limbs, both skeletally mature and immature patients, all lengthening techniques, staged and not surgery, primary and revision cases, and any possible complications. Exclusion criteria included enchondromas of the hands, skull, spine, or any localization not eligible for lengthening, or treated only by curettage. The clinical data extracted from the selected studies included the technique used, clinical results, and complications. The demographic data included age, gender, number and site of operated limbs, and LLD. The clinical results were categorized into objective outcomes including the bone healing index (BHI) or external fixation index (EFI), the distraction index (DI), the distraction time (DT), gained length (GL), and total treatment time (TTT), if reported by the studies' authors. The BHI and EFI are similar; the BHI measures the time until bony union in days in the frame per the amount of lengthening in centimeters, and the EFI measures the time in the external fixator in days per the amount of lengthening in centimeters (days/cm). The DI measures the amount of lengthening per day (mm/day), and the TTT measures the number of days in the external fixator [3]. Complications were defined as any intraoperative or postoperative event that was likely to have a negative influence on the patient's outcome, including pin track infection, non-union, early consolidation, pathological fracture, joint stiffness, nerve injury, and deformity recurrence.

Results

Study selection

The search strategy returned 84 studies; 23 studies were excluded as duplicates, 28 studies were excluded by their title, 10 studies were excluded by their abstract, and 4 studies were excluded by their full text. This left us 19 studies for further analysis [2, 5–7, 9–12, 14–18, 22–26, 30] (Fig. 1). The included studies consisted of case reports and retrospective case series. Because of substantial study heterogeneity and small samples sizes, the data obtained from the selected studies were not adequate to perform a meta-analysis. For these reasons, a descriptive approach to data analysis was performed. Among the 19 studies, 12 were specific on Ollier's disease, while 7 studies described limb corrective
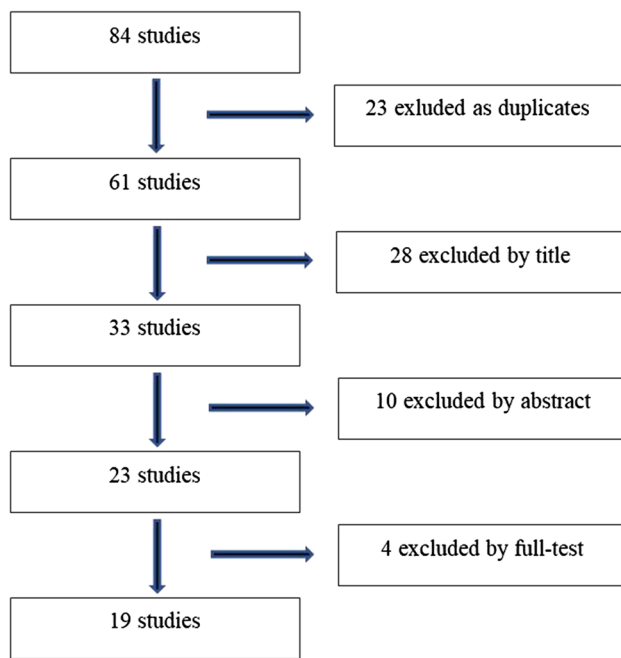
Fig. 1 PRISMA studies selection flowchart

treatments in variable disorders and benign tumors (fibrous dysplasia, fibular hemimelia, hemiatrophy osteomyelitis, giant cell tumor of bone, non-ossifying fibroma, osteochondroma and congenital multiple exostosis, desmoid fibroma, chondromyxoid fibroma, unicameral bone cyst, and Maffucci's syndrome) including Ollier's disease. Of the 198 total patients described in the identified studies, 121 patients had a diagnosis of Ollier's disease and were considered in this analysis; the remaining 77 patients had deformities from the causes mentioned above and were excluded.

Study characteristics

Gender was reported for 57 patients, and age was reported for 112 patients only; there were 34 male and 23 female patients with an age range of 4–37 years at the time of the first surgery. The site of lengthening was consistently reported in all studies; the lower limbs were affected more common by deformities (110 patients), followed by the upper limbs (8 patients) and both upper and lower limbs (3 patients). Overall, 272 segments were lengthened, most commonly in femurs (146 segments, 53.7%), followed by tibias (113 segments, 41.5%), humeri (9 segments, 3.3%), and forearms (4 segments, 1.4%).

Correction techniques

Four techniques of LLD correction were identified: external fixation, external fixation combined with intramedullary

nailing, motorized lengthening nailing, and epiphysiodesis. External fixators alone were used in 252 segments (92.6%). The most commonly used external fixators were circular frames (205 segments, 75.3%); Ilizarov external fixator alone was used in 196 segments (72%), followed by the Taylor Spatial Frame (5 segments), the Sheffield Ring Fixator (2 segments), the Smart External Fixator (1 segment), and the TrueLok ring fixator (1 segment). Unilateral external fixators alone were used in 47 segments (17.2%); the Limb Reconstruction System was used in 22 segments (46.8%), followed by the Orthofix external fixator (10 segments), the Wagner monoaxial external fixator (9 segments), the Heidelberg external fixator (2 segments), the MAC frame (2 segments), and the EBI external fixator (1 segment); in 1 segment, the type of unilateral external fixator was not reported. Combined external fixation and intramedullary nailing was used in 14 segments (5.1%); a circular frame (Ilizarov and TSF in 5 segments each) and elastic stable intramedullary nail were used in 10 segments, and unilateral external fixator and intramedullary nail in 4 segments. Epiphysiodesis was used in 3 segments (1.1%) aiming to shorten the longer limb and correct an angular deformity. Motorized lengthening nails were used in 3 segments (1.1%) in the same patient. Over the years, novel corrections techniques/implants were used, yet external fixators remained the most commonly used techniques/implants, with circular external fixators, most often Ilizarov frames, being used most common.

Outcomes

The BHI was reported in 14 of the 19 studies, and the DI was reported in 13. The BHI changes upon the bone treated (Table 1); the mean BHI for the femur was 33.3 days/cm, for the tibia, it was 34 days/cm, for the humerus, it was 26.4 days/cm, and for the forearm, it was 36.2 days/cm (range, 15.5–83 days/cm). The mean DI was 0.93 mm/day (range, 0.5–1.25). The LLD before treatment was reported in 12 studies, and it ranged from 4.4 to 17.4 cm for the lower limbs and from 4 to 14 cm for the upper limbs. The GL was reported in 15 studies, and it ranged from 2 to 22 cm for the lower limbs and from 4.1 to 14 cm for the upper limbs. The TTT was reported in 13 studies, and it ranged from 90 to 496 days, with a mean of 228.8 days for the upper limbs and 231.1 days for the lower limbs.

Complications related to surgical management

Overall, 76 complications occurred in the 272 lengthening procedures/segments (27.9%) (Table 2). There were 21 cases of joint stiffness (7.7%), especially in patients with simultaneous ipsilateral femoral and tibial lengthening that required long rehabilitation, 14 cases of moderate to severe pin track infection (5.1%) requiring antibiotics and/or

Table 1 Summary of the most important published studies on bone lengthening in patients with Ollier's disease

Study	Patients (n)	Mean age (years)	Implants	Site and number of lengthened segments	Mean BHI (days/cm) and DI (mm/day)	DT (days)	LLD (cm)	GL (cm)	TTT (days)
Maffulli et al. [22]	2	10	Orthofix	Femur and tibia	BHI 28	N.A	6	6	N.A
Pandey et al. [14]	1	8	Circular frame	Femur and tibia	DI 1	N.A	Femur (7), tibia (4)	Femur (9.5), tibia (2)	180
D'Angelo et al. [12]	9	N.A	Ilizarov, Wagner	Femur (13) and tibia (10)	N.A	N.A	N.A	N.A	N.A
Chew et al. [23]	8	4.2*	Epiphysiodesis, Wagner, Monticelli and Ilizarov, Ilizarov	Femur (8)	N.A	N.A	N.A	N.A	N.A
Raimondo et al. [24]	1	10*	Ilizarov	Forearm	BHI 18; DI 1	28	5	4.4	90*
Curran et al. [11]	3	8*	Ilizarov	Femur (2) and tibia (3)	BHI femur 24.7; BHI tibia 30; DI 0.75	N.A	10	14.7	159*
Jesus-Garcia et al. [10]	10	16	Ilizarov	Femur and tibia (4), femur (2), femur tibia (1), femur and humerus (1), femur and humerus (1), femur and forearm (1)	DI 1	48	6.9	4.8	402
Baumgart et al. [2]	1	17	Lengthening nail fitbone	2 femur + tibia	DI 1	136	17.4	13.6	N.A
Aare Martson et al. [16]	1	14	Ilizarov and intramedullary nail	Femur + tibia	BHI femur 22.5; BHI tibia 21; DI 1	N.A	N.A	Femur (22), tibia (10)	496
Kolodziej et al. [5]	3	14	Ilizarov	Humerus (1), humerus and forearm (2)	BHI humerus 26; BHI forearm 54.5; DI humerus 1.5; DI forearm 1	Humerus (130), femur (47)	Humerus (8.4), femur (5)	Humerus (8.8), femur (4.7)	Humerus (228), femur (192 and 366)
Watanabe et al. [7]	4	5.8	Ilizarov, Orthofix, Heidelberg, Taylor spatial frame	Femur and tibia (3), femur (1) (12 total segments lengthened)	BHI 49.2; DI 0.5–1	N.A	4.4	12.2 (4.9 each segment)	157.3 each segment
Tsuchiya et al. [25]	4	9.9*	Ilizarov, Orthofix, Heidelberg, Taylor spatial frame	Femur and tibia (6)	BHI 42.4	N.A	N.A	N.A	168*
Tellisi et al. [9]	1	7	Multi-axial correction frame	Humerus	BHI 18.3; DI 1 to 1.25	N.A	6	9	165

Table 1 (continued)

Study	Patients (n)	Mean age (years)	Implants	Site and number of lengthened segments	Mean BHI (days/cm) and DI (mm/day)	DT (days)	LLD (cm)	GL (cm)	TTT (days)
Van Loon et al. [17]	1	37	Ilizarov	Humerus	BHI 35; DI 0.5	210	14	10	305
Stephens Richards et al. [30]	1	9	Truelock, Epiphysiodesis	Femur	N.A	N.A	N.A	N.A	N.A
Madan et al. [6]	10	10.7	Monolateral limb recon system, Ilizarov, Sheffield Ring Fixator	Femur (18), tibia (12), forearm (1)	BHI 32.5; DI 1	42	N.A	Upper limb (4.1), lower limb (9.9), (3 each segment)	164.8
Popkov et al. [15]	44	13.3	Ilizarov, Ilizarov and elastic stable intramedullary nailing	Group 1: tibia (1), femur (4), femur and tibia (2) Group 2: femur (18), tibia (11), femur and tibia (28)	Group 1: BHI 19.1; Group 2 BHI 29; Overall DI 0.85	N.A	N.A	Group 1 7.4 lower limb 5.8 each segment Group 2 6 each segment	N.A
Eralp et al. [26]	4	9.5*	Ilizarov, Unilateral external fixator, multi-axial correction frame, EBI, Taylor spatial frame, Smart correction computer-assisted	Femur and tibia (2), femur (1), humerus (1)	BHI 31.8; DI 1	N.A	7.85	Upper limb (14), lower limb (5.1)	168*
Groote et al. [18]	13	8*	Ilizarov, Taylor spatial frame, Unilateral external fixator and intramedullary nail, Orthofix	Femur (21), tibia (19)	BHI 36.5; BHI external fixator and intramedullary nail 23.9; BHI femur and tibia 41.8; BHI each bone separately 31.1	N.A	7.1	7.8	178.6*

BHI bone healing index, *DI* distraction index, *DT* distraction time, *GL* gained length, *TTT* total treatment time, *LLD* leg length discrepancy, *N.A* not available

*All diagnoses included

Table 2 Complications in the 272 lengthened segments in patients with Ollier's disease

Complications	Cases (n, %)
Joint stiffness	21/7.8
Infection	14/5.2
Early consolidation	11/4.1
Pathological fracture	9/3.3
Deformity recurrence	8/2.9
Delayed union	5/1.8
Non-union	4/1.4
Neurapraxia	3/1.1
Overlengthening	1/0.3
Total	76/27.9

hospitalization, 11 cases of early consolidation (4%) most of the times because the DI was too low requiring an increase, 9 cases of pathological fracture (3.3%), due to weakened bone and/or early frame removal, 8 cases of deformity recurrence (2.9%), 5 cases of delayed union (1.8%), 4 cases of non-union (1.4%) because of a high DI that required slowing down the distraction rate and/or bone grafting, 2 cases of radial nerve neurapraxia (0.7%), 1 case of common peroneal nerve neurapraxia (0.3%), and 1 case of overlengthening (0.3%). Minor complications including mild pin track infections were identified in more than 40 lengthened segments. With the available information from the selected papers, we did not conclude any correlation between the correction technique/implant used and the incidence of complications. Although a comparison between the techniques/implants used could not be performed because of the variable implants used by a plethora of surgeons and the use of circular external fixators (most commonly Ilizarov frames) in the majority of cases, it seems that circular frames especially combined with an intramedullary nail provide optimal results with few complications.

Discussion

Conventional surgical treatment for skeletal deformities is not feasible in many of patients with Ollier's disease because the affected bone is weakened by the disease and the amount of lengthening necessary for correcting the discrepancy usually is substantial [4–8]. Traditional treatments included curettage of the enchondromas, bone grafting, corrective osteotomies, and internal fixation [9]. However, complete curettage of the enchondromas is realistically impossible as the lesions are extensive [4]. In contrast, lengthening is not more complex compared to other cases of LLD; growth disorder involves bone only, while soft tissues are normal, which explains the relatively straight lengthening procedure

compared to that performed for the management of LLD in patients with congenital anomalies [7, 10, 11].

Concerns regarding limb lengthening in patients with Ollier's disease include the site of corticotomy, biological response of the bone to the lengthening process, structural quality of the regenerated callus, healing response, pathological fractures, and stability of the external fixator to the bone [2, 4–7, 9–16]. D'Angelo et al. advised that the osteosynthesis should be done in radiographically healthy bone and corticotomy should be done at the border between healthy and pathological bone [12]. Watanabe et al. reported seven osteotomies performed intralesionally and five extralesionally; in only one of the seven cases, the regenerated tissue appeared as normal bone [7]. Kolodziej et al. in four of five upper limbs lengthenings observed conversion of abnormal cartilage into normal bone on radiographs [5]. Tellisi et al. performed percutaneous osteotomy just distal to weakened bone from Ollier's disease, but suggested that this can be performed either intra- or extralesionally [9]. Van Loon performed a corticotomy through a small incision at the margin of enchondroma and healthy bone and observed in radiographs regeneration of healthy bone within the region of diseased bone [17]. Groote et al. reported 20 intralesional, 6 transitional, and 14 extralesional corticotomies performed at the apex of the deformity or at a suitable level after the external fixator is anchored to the bone [18]. In their study, the site of corticotomy did not appear to be an important predictor of healing; on radiographs, the regenerated bone looked normal; however, no histological studies confirmed that [18] Madan and Baumgart, using external fixators or intramedullary nails, respectively, performed all osteotomies through enchondromas, and all formed normal bone [2, 6]. Martson and Jesus-Garcia were the only authors that performed a needle biopsy through the regenerated bone and showed that the benign neoplastic tissue was replaced with normal bone [10, 16]. Pandey et al. indicated that osteogenesis under tension occurs by intramembranous rather than by enchondral ossification, which explains the formation of normal regenerated bone [14, 19, 20].

The neo-ossification of regenerated bone at enchondromas is independent from the enchondromatosis because it involves the periosteum and not the physis [21]. Despite the concern of poor quality of the diseased bone, the healing response for fractures and limb lengthening has been remarkably good; healing of pathological and/or iatrogenic fractures was uncomplicated in all cases, either conservative or with adjustment of the implants in situ [4, 6, 7, 9, 10, 15, 18]. Limb lengthening has a similar healing response [5, 6, 9, 15, 18, 22]. The present systematic review showed a wide range of BHI ranging from 15.5 days/cm to 83 days/cm; this can be explained by the variable implants used and sites of lengthening. Additionally, some authors described lengthening in patients affected by variable comorbidities;

this bias does not allow to verify whether there is a statistically significant difference between one technique or another for patients with Ollier's disease only [11, 22–26]. The most commonly used implants were Ilizarov external fixators; this explained by the fact that application of the Ilizarov frames provides enough mechanical strength to perform elongation and axial correction. In contrast, unilateral external fixators are easier to apply and more comfortable for the patients compared to circular frames; however, their use is limited for simple leg lengthening in patients with Ollier's disease [7]. Combined external fixators and intramedullary nails was reported in 5.2% of cases, and has been associated with significantly lower BHI [15].

Early consolidation of bone lengthening is more common in patients with Ollier's disease [27]. Myers et al. noticed a tendency for hypertrophic bone regeneration in patients with achondroplasia and Ollier's disease [13] and recommended a higher rate of distraction. Similarly, Tellisi et al. described early consolidation in a case of humeral lengthening and recommended to accelerate the rate of lengthening of the humerus from 1 to 1.25 mm/day [9], which, however, was not recommended by Van Loon et al. [17]. Madan et al. described three cases of early consolidation in 10 patients that required manipulation under anesthesia and osteoclasis, or cessation of lengthening [6]. Groote et al. reported five cases of early consolidation in 40 femurs and performed repeated corticotomy and closed osteoclasis [18].

Delayed union or non-union may also occur in patients with Ollier's disease [5, 14, 18]. Pandey et al. [5] and Kolodziej et al. [14] decreased the rate of distraction and concluded that DI of 1 mm/day for the forearm is too fast and half speed is advisable [5, 14]. The factors responsible for non-union include traumatic corticotomy, instability of the frame, initial diastasis, too rapid distraction, infection, malnutrition or multiple lengthenings through the same bone, and lengthened bone itself.

Pathological fractures are a concern during lengthening in Ollier's disease because lengthening is performed within or around a tumor [6, 9, 10, 15, 18]. Popkov et al. reported pathological fractures in 3 cases through enchondromas after frame removal in the group with external fixator only [15]. In contrast, the group with combined external fixator and intramedullary nail had no pathological fractures; therefore, intramedullary nailing provides for additional mechanical stability at the lengthened site after frame removal. In general, the regenerate bone appears to be sufficiently strong after lengthening is completed and bone is healed, without long-term sequela. The timing of external fixator removal depends largely on qualitative assessment of the newly formed bone. However, trabeculation in at least three cortices must be visible in the anteroposterior and lateral radiographs for bone healing to be considered complete before frame removal [22].

Joint stiffness or contracture was a common complication in most studies; this is explained by the persistent muscle contracture, duration of adjacent joints immobilization, amount and rate of lengthening, and pressure through the joint surface [6, 10, 14, 16, 18, 22, 24, 26]. Most cases resolved with intense physiotherapy, bracing for soft tissue tension management, and, when possible, minimizing the TTT [11, 15, 18]. Malignant degeneration is another important concern in Ollier's disease [28, 29]. In the studies included in this review, malignant degeneration was not reported in any of the included patients at the site of limb lengthening. Groote et al. reported one patient who developed a low-grade chondrosarcoma of the proximal femur; however, the location of the sarcoma was not in the area of lengthening [18]. Therefore, lengthening in patients with Ollier's disease should be considered safe.

Conclusion

Correction of deformities and LLD in patients with Ollier's disease is challenging. Although there is currently no consensus concerning the optimal surgical technique/implants for lengthening, it seems that circular frames with or without an intramedullary nail provide optimal results with few complications. Nevertheless, the regenerated bone is structurally normal. Early consolidation should be considered, and appropriate adjustment should be made in the rate of lengthening. Non-union is unusual in these patients but can occur. Joint stiffness and contracture can be avoided with intense physiotherapy. Malignant degeneration has not been reported, and the patients should be followed as recommended for their disease.

Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

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