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Review Article

Is the Intramedullary Skeletal Kinetic Distractor a Safe Measure for Bone Lengthening? A Systematic Review
用ISKD髓內骨骼延長釘來進行骨骼延長是一個安全方法嗎？一個系統性回顧

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ABSTRACT

Background: The intramedullary skeletal kinetic distractor (ISKD) is one of the relatively recent methods developed to overcome the complications of conventional bone lengthening methods, such as external fixators. These complications include pain, muscle transfixation, pin-tract infection, reduced joint motion, and prolonged fixation time. However, ISKD-specific complications such as uncontrollable lengthening and hardware failure make the outcomes of ISKD lengthening questionable. In this article, we review published literature on the efficacy and complications of the ISKD device.
Methods: A database search was conducted in PubMed, Ovid Medline, Ovid Full Text, Springer link, EBSCO Medline, Science Direct, ISI Web of Knowledge, and Google Scholar. We included English articles with extractable data about the study population and outcomes, reporting ISKD implantation in the femur or tibia of skeletally mature patients. The included studies were too heterogeneous for a meta-analysis to be performed.
Results: Fifteen of 89 potentially relevant citations were found to match the inclusion criteria. The most common causes of limb-length discrepancy indicating an ISKD implantation were traumatic and congenital. The average lengthening achieved, average patient discharge period, mean follow-up time, average consolidation time and index, average distraction time and index, and number of patients requiring additional operations as well as other outcome measures are discussed in this article. The most common complications were runaway nail, difficulty in achieving lengthening, and poor bone regenerate formation.
Conclusion: Even though the classic complications of external lengthening are virtually diminished, alterations to the current design of the ISKD are needed to avoid the distraction- related complications. Risk of unplanned surgery could be minimized through proper patient selection and proper surgical techniques.

中 文 摘 要

背景：髓內骨骼延長釘（ISKD）是為了克服常規骨骼延長的方法，如外固定支架，的併發症而新近發展的技術。常規骨骼延長方法的併發症包括疼痛，肌肉釘住，針道感染，減少關節運動和長期的固定時間。然而，ISKD　特有的併發症，如無法控制的延長和硬件故障都令人懷疑ISKD的療效。在本文中，我們將回顧已發表關於ISKD療效和併發症的文獻。

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方法：在PubMed，Ovid Medline， Ovid Full Text和Springer link，EBSCO Medline，Science Direct，ISI Web of Knowledge和谷歌Scholar 的數據庫搜索。我們包括那些可以取得研究群組和結果數據，並報告了在骨骼成熟的病人身上把 ISKD植入股骨或脛骨的英語文章。

結果：在89個相關的文章中有15個符合納入標準，當中最常見的手術原因是先天性疾病和創傷。在本文中討論我們討論了平均延長距離，患者平均住院時間，平均隨訪時間，平均骨愈合時間和指數，平均延長的時間和指標，需要接受額外手術的患者的數量等。最常見的併發症是延長釘出位，難以達到延長目標和骨不愈合。

結論：儘管使用ISKD使到外固定支架的典型併發症幾乎消失，目前ISKD的設計仍然需要改動，以避免延長時出現的併發症。無計劃的手術風險可以通過適當的患者選擇和正確的手術方法來最減少。

Introduction

Distraction osteogenesis is the traditional gold standard method for correction of limb-length discrepancy. Circular external fixators (e.g., Ilizarov fixator or Taylor spatial frame) or monolateral fixators (e.g., Orthofix, Orthofix Inc., McKinney, TX, USA or EBI, Dynafix, Parsippany, NJ, USA) provide the traditional means for inducing and utilizing distraction osteogenesis. The most frequently experienced complication is pin-site infection. Minor pin-tract infection rates range from 2% to 80%, and major pin-tract infection rates that reach 23% have been reported.[1,2] Soft-tissue transfixation by wires and pins also can cause muscle contractures, joint stiffness, and pain.[3–5] However, pain is the most common patient complaint during limb lengthening, and may be intense during the 1st postoperative days. Contraction of any muscle transfixed by a pin or wire is particularly painful and often requires medication with narcotics. Night pain and pain during therapy caused by stretching of the muscles and nerves is common and can lead to loss of appetite and even depression.[5,6] The continued presence of an awkward and painful external fixation device, combined with the mental stress and unknown outcome, can lead to variable psychological behaviours. Neurovascular structures are also vulnerable both at the time of screw or wire insertion as well as during distraction.[7,8]

Hip and knee complications, including dislocation and subluxation, are often reported during and after limb lengthening. Also, joint stiffness may occur because of long-standing contractures and increased pressure on the joint surface during lengthening.[4] Pain often diminishes and may inhibit functional loading and movement of the joints during the lengthening process, so loss of range of motion is also common. Lengthening with external fixators can induce secondary axial deformity during or after the lengthening process. After fixator removal, refractures of the regenerated bone can occur. The long period of external fixation delays the patient's return to normal daily activities. Clearly, it is desirable to use some type of implantable device in limb lengthening to eliminate these complications.

Bost and Larsen[9] reported lengthening of the femur using both an external device and an unlocked, first-generation intramedullary nail to eliminate the difficulty of controlling the alignment and avoid the relatively high risk of the incidence of axial deformity that occurs with fixators alone. Paley et al[10] described the technique of lengthening over a locked intra-medullary nail, which allows early removal of the external device after distraction. The locked intramedullary nail provides stability during the consolidation process, which reduces pain, lessens further pin-site problems, and increases patient acceptance of the procedure. Nevertheless, deep osteomyelitis can occur if pin-tract infections spread to the tissue surrounding the intramedullary nail.[11,12]

Another method for safer bone lengthening is lengthening followed by nailing, which minimizes the period of external fixator usage. It uses the application of an Ilizarov external fixator with the principle of distraction osteogenesis to achieve the desired length, and then in another surgery, the external fixator is removed and an interlocking nail is inserted. This allows the patient's bone to consolidate within the interlocking nail alone. This method provides easier and earlier patient rehabilitation because the time of external fixator use is shortened. Nevertheless, complications such as pin-tract infection, muscle and nerve irritation, and joint stiffness are still present at the time of fixator removal. Moreover, if a concurrent infection extends in the presence of the interlocking nail, it often leads to catastrophic deep infection.[13]

The goal of recent advances in the field of limb lengthening is to increase patient acceptance and comfort by avoiding the common complications of the classic external fixators.[14] One important achievement is the use of totally implantable intramedullary, self-distracting lengthening nails.[15–18]

The Albizzia nail (DePuy, Villeurbanne, France) is a mechanically driven device developed in the 1990s. Its lengthening mechanism is activated by rotations of 20° around the horizontal axis. One significant drawback is severe pain that is sometimes associated with the large magnitude of torsion required for lengthening. This resulted in a high incidence of either failed lengthening or the need to return to the operating theatre and closed manipulation of the limb under anaesthesia until distraction could recommence.

The Fitbone (Wittenstein, Igersheim, Germany) is another fully implantable lengthening nail. Its lengthening mechanisms are driven by an internal motor activated by an external transmitter.[12] There have been promising results in the literature, with good return to function and ease of use. However, a significant rate of device failure has been reported, with up to 25% of patients never achieving the desired distraction length.[23]

The intramedullary skeletal kinetic distractor (ISKD, Orthofix Inc., McKinney, TX, USA) is another one of those devices. It is designed to lengthen the bone gradually as a result of small, deliberate rotatory movements between 3° and 9° at the osteotomy site around the longitudinal axis of the nail. Such rotatory movements can be done during normal daily activities such as walking,[19] as has been originally described by Cole et al,[15] and the ISKD is the only intramedullary lengthening device approved by the Food and Drug Administration (FDA).

Although intramedullary lengthening was introduced primarily so that the problems of external fixators can be avoided, significant complications have been reported with this procedure, of which uncontrolled lengthening and nondistractible nail are the most important.[19–21] Reports of nondistracting or runaway ISKD nails are now present, with an incidence of up to 45%.

In this systematic review, our goal is to review and discuss the published literature that describes and criticizes the ISKD as a method for bone lengthening in different groups of patients, to reach a conclusion about the efficacy of ISKD, help surgeons to carefully select the appropriate indicated patients for that procedure, and reduce the risk of unplanned surgery by avoiding the most common surgical pitfalls that reportedly cause complications.

Methods

We carried out a systematic review of published studies reporting the use of ISKD in limb lengthening. We searched eight databases (Pub Med, Springer, EBSCO Medline, Journal Ovid Full Text, OVID Medline Search, Science Direct, ISI Web of Knowledge, and Google Scholar) for relevant publications. We also searched the bibliographies of included articles to identify additional relevant articles. References of included articles and previous reviews and meta-analyses were reviewed to identify additional relevant articles. Between August 2012 and November 2012, routine searches were performed with the following keywords in various combinations: ISKD; intramedullary; skeletal; kinetic; distractor; distraction; lengthening. Two reviewers (M. Abdelmohsen and M. Amgad) independently reviewed the title and abstracts to identify potentially relevant studies for full-text assessment. Any disagreements on which studies to include were resolved by consensus.

Inclusion criteria

We included original peer-reviewed research articles regardless of the study design (prospective, retrospective, cross-sectional, or interventional). Our search was limited to studies published in the English language in a human, skeletally mature patient population.

Exclusion criteria

Exclusion criteria included studies in languages other than English; studies performed on animals; studies describing lengthening techniques using devices other than ISKDs; and unpublished data and abstracts for which full reports were not available.

The following data were extracted from each of the included studies: demographic characteristics of the study population, various prognostic parameters, and complications resulting from the procedure. The included studies were also judged with a checklist of potential sources of bias, as can be seen in Table 1.[15,17,18,20–30]

Results

Studies that met the inclusion criteria were compiled, read, and tabulated. Two studies by Hankemeier et al[14,17] referred to the same patient cohorts, so only one of them was included in the results tables. Table 1 outlines the quality assessment of the included studies in our systematic review. Table 2 lists the demographic parameters of the patients included in each study. Many of the studies we found reported the results of ISKD lengthening in femora only, although the studies by Cole et al,[15] Hankemeier et al,[14,17] Wang and Edwards,[23] Schiedel et al,[27] and Kenawey et al[29] reported tibial lengthening as well regardless of the complications. The most common causes of limb-length discrepancy necessitating ISKD implantation were trauma, congenital causes, and cosmetic surgical procedures. All of the patients in the included studies were adults, with a mean age ranging from 24 years to 40 years. Table 3 compared the different complications encountered in femoral and tibial ISKDs, wherever mentioned. Although five studies mentioned the use of ISKD in the tibia and femora, yet only three of them mentioned the rate of complications encountered specifically for each.[23,27,29] Table 4 summarizes the prognostic parameters of each of the studies, where mentioned. The parameters include the mean time to full weight bearing, mean lengthening achieved, mean lengthening rate, mean time to patient discharge, mean follow-up time, number and percentage of limbs in which satisfactory lengthening was achieved, mean consolidation time and index, mean distraction index, mean intraoperative blood loss, and the number and percentage of patients in whom additional surgical procedures were performed.

Regarding complications, two studies reported no complications in any of the cases treated with ISKD.[17,30] Of the studies that did mention complications, runaway nails and nondistracting nails were most commonly reported. A study by Burghardt et al[28] also found a rather large number of cases that had hardware malfunction. Other reported complications include infection (superficial and deep), insufficient bone regenerate (IBR; causing nonunion), compartment syndrome, premature consolidation, angular deformity, and joint contracture. Detailed numbers of the mentioned ISKD complications and reported complications are summarized in Table 5.

Discussion

Six of the 14 included studies explicitly stated their inclusion and exclusion criteria of the study population and only eight reported the consolidation and distraction indices of included cases. Thus, in about half of the articles that met the inclusion criteria, it was not possible for us to discern whether any cases were excluded based on the outcomes or whether unfavourable outcomes were underreported. As with most research on surgical procedures, it was not possible to blind participants and personnel to the intervention, nor was there any allocation concealment in any of the studies. These factors, among others, present potential sources of bias that need to be taken into consideration when evaluating the evidence presented in this review.

There are many reported advantages of using the ISKD over conventional methods for bone lengthening. There is increased patient comfort and an improved satisfaction with the higher mobility that the ISKD grants. Moreover, the fact that the ISKD is completely intramedullary means that there is virtually no risk of pin-track infections (which may reach up to 80%), as is the case with the Ilizarov frame. Of course, this comes with its own price, as the intramedullary nature of the device makes it impossible to modify or “reset” throughout the lengthening procedure. It should not be surprising that the ability to control lengthening is compromised in a mechanical patient-centred lengthening model. The patient's level of activity and compliance may not be homogenous, and may be responsible for the variability in daily lengthening. To account for this problem, the ISKD implant is coupled with an external sensor that makes the patient aware of daily changes in the nail's length.

Despite this, uncontrolled rapid lengthening of > 1.5 mm per day (or runaway nail as it came to be known) has been repeatedly reported in the literature as an ISKD-specific complication.[20–29] This runaway nail complication was reported by most of the included studies that did mention complications.

One possible explanation is that the patients were not acquainted with the sensor or the device. Also, the patient's level of activity may not be homogeneous, and may be responsible for the variability in daily lengthening. That is why it has been argued by Thonse et al[31] that incompetent patients and patients who are not fully capable of grasping the mechanical lengthening mechanism should be excluded from ISKD procedures and scheduled for one of the more conventional methods such as the Ilizarov frame. Another possibility is that the problem is in the device itself, in which case the design would need to be revised, as has been argued by Kenawey et al[29] and Papanna et al.[22] This finding was supported by Reynders,[24] who claimed that the cause may be because a (too sensitive) distal clutch can be activated by muscle contractions. Indeed, Simpson et al[11] found that the external ISKD sensor starts to lose sensitivity when thigh circumference exceeds 20 cm in the

Table 1
Quality assessment of included studies

Study/potential source of bias and rationale for inclusion	Inclusion and exclusion criteria clearly stated	Reporting of important prognostic factors (consolidation and distraction indices, in particular)	Blinding of participants and personnel*	Allocation concealment*	Risk of incomplete outcome data addressed (attrition and exclusion)	Number of cases in which the desired lengthening was achieved is explicitly mentioned
	Rationale: to avoid exclusion of patients based on the outcomes	Rationale: to avoid underreporting of unfavourable outcomes	Rationale: to avoid placebo and personal factors from affecting the outcome assessment	Rationale: to avoid biased allocation of patients to intervention depending on expected outcome and/or demographic characteristics	Rationale: dropouts and excluded cases might affect the overall outcome of the study	Rationale: to avoid underreporting of unfavourable outcomes
Cole et al[15,†]	No	No	No	No	Low	No
Hankemeier et al[17]	Yes	Yes	No	No	Low	Yes
Simpson et al[18]	No	No	No	No	Low	Yes
Kenawey et al[20]	Yes	Yes	No	No	Low	No
Kubiac et al[21]	Yes	No	No	No	Low	No
Pappanna et al[22]	Yes	Yes	No	No	Low	Yes
Wang and Edwards[23]	Yes	Yes	No	No	Low	Yes
Reynders[24]	N/A	No	N/A	N/A	N/A	N/A
Kucukkaya et al[25]	No	Yes	No	No	Unclear	Yes
Mahboubian et al[26]	No	Yes	No	No	Low	Yes
Schiedel et al[27]	No	Yes	No	No	Low	Yes
Burghardt et al[28]	Yes	No	No	No	Low	Yes
Kenawey et al[29]	No	Yes	No	No	Low	Yes
Vitale et al[30]	N/A	No	N/A	N/A	N/A	No

* Note that these potential sources of bias are very difficult to avoid in a surgery such as intramedullary skeletal kinetic distractor implantation.
† First author is the same person who developed the intramedullary skeletal kinetic distractor, so bias toward proving its efficacy and safety should be considered.

Table 2
Demographic characteristics of patients in each of the included studies

Study	No. of patients	No. of operated limbs	Sex		Age (y)	Operated limbs		Causes of limb-length discrepancy							
			M	F		Femora	Tibiae	Infection	Burn	Trauma	Polio	Knee arthrodesis	Cosmetic	Tumour	Congenital	Other
Cole et al[15]	18	20	14	4	40 (18–65)	6	14	10	1	6	1					
Hankemeier et al[17]	4	4	3	1	29 (18–36)	3	1			3					1	
Simpson et al[18]	30	33	17	13	35 (14.5–81)	33	0			23		1			6	
Kenawey et al[20]	35	37			33 ± 11 (16–61)	37	0			22			1	1	11	
Kubiac et al[21]	9	11	6	3	24 (16–33)	11	0			4					5	
Pappanna et al[22]	3	3	2	1	39 (25–53)	3	0			3						
Wang and Edwards[23]	16	16	13	3	33 (20–54)	11	5			15					1	
Reynders[24]	1	1	1	0		1	0									
Kucukkaya et al[25]	9	9			27.2 (14–40)										3	
Mahboubian et al[26]	11	12	8	3	36 (25–47)	12	0			8					30	
Schiedel et al[27]	69	69			24 (12–51)	58	11	4		17				7		11
Burghardt et al[28]	180	210	109	71	9–60					50			27		84	19
Kenawey et al[29]	53	57			29.1 (14–61)	45	12			33			1	1	20	1
Vitale et al[30]	2	2	0	2	28.5 (22–35)	2	0			1					1	

Data are presented as *n* or *n* (%).

Table 3
Studies reporting femoral and tibial elongation using the intramedullary skeletal kinetic distractor

	Wang and Edwards[23]		Schiedel et al[27]		Kenawey et al[29]	
	Femora	Tibiae	Femora	Tibiae	Femora	Tibiae
N	11	5	58	11	45	12
Runaway nail	4 (36)	1 (20)			9 (20)	
Difficult-to-distract nail	2 (18)	1 (20)	5 (9)	2 (18)	2 (4.4)	
Poor regenerate formation	3 (27)	3 (60)			10 (22.2)	1 (8.3)
Secondary failure of ISKD (broken or removed before consolidation)			1 (2)	4 (36)		
Premature consolidation					4 (8.9)	
Equinus contracture						2 (16.66)
Compartment syndrome						1 (8.3)

Data are presented as *n* (%).
ISKD = intramedullary skeletal kinetic distractor.

case of femoral ISKD, probably because the magnetic fields are too deep for the sensor to detect pole changes. Statistical analysis by Wang and Edwards[23] showed that when the length of the outer nail portion in the distal fragment is < 100 mm, runaway nail is more likely to occur. This is consistent with the findings by Simpson et al,[18] who had seven runaway nails in 33 femoral lengthening procedures using an ISKD nail (21%), and stated that a length of < 80 mm was associated with runaway nail complication. Although Kenawey et al[29] had nine runaway nails in 45 femoral lengthening cases (20%) and none in the patients in the tibial lengthening group, they could not support this relation. Simpson et al[18] mentioned that previous intramedullary nailing was also found to predispose to uncontrolled lengthening.

Difficult-to-distract nails is another common complication of ISKD. Nondistracting nails were defined as nails that fail to distract *in situ* despite increasing the activity level and manually rotating the lower extremities by the patients themselves or with assistance from family members. Kubiak et al[21] first addressed why some nails had difficulty distracting. After having three nondistracting nails in 11 femoral lengthening procedures, they explained that the use of a straight nail such as the ISKD in a curved femur predisposes to binding of the anterior cortices at the osteotomy site and failure to lengthen. Simpson et al[18] reported eight non-distracting nails in their 33 femoral ISKD lengthening procedures, and subsequently developed the previous argument by suggesting that the ease of nail advancement is related to the length of the outer portion of the nail situated in the distal bone fragment. The likelihood of non-distracting nail is increased when there is a longer segment of bone in contact with the thick segment of the nail. They found that a length of > 125 mm is associated with difficult-to-distract nails and < 80 mm is associated with runaway nails, respectively. As mentioned, Wang et al[23] in their study demonstrated that patients with runaway nails had a significantly shorter segment of the thick portion of the nail in the distal fragment than normally distracting or difficult-to-distract nails. However, perhaps because of smaller numbers (difficult-to distract nails = 3), they were unable to confirm that having a longer length of the thick portion of the nail in the distal fragment is associated with difficult-to-distract nails. Difficult-to-distract nails also might be related to the design of the ISKD.[23] However, Schiedel et al[27] argued, rather convincingly, that this may not necessarily be true, given the fact that the manufacturer prohibits full weight bearing until there is radiological

Table 4
Prognostic parameters reported by each of the included studies (where mentioned)

Study	Mean time to full weight bearing (wk)	Mean lengthening (mm)	Mean lengthening rate (mm/d)	Mean time to patient discharge (d)	Mean follow-up time (mo)	Limbs in which target lengthening achieved	Mean consolidation time (d)	Mean consolidation index (d/mm)	Mean distraction index (mm/d)	Mean intraoperative blood loss	Patients in which additional operations were performed (%)
Cole et al[15]	1	49 (29–110)	0.82 (0.4–1.7)		28 (12–48)						
Hankemeier et al[17]	10 (7–14)	31 (26–40)		10 (8–11)	14.2 (14.0–14.5)	4 (100)	80 (51–111)	2.9 (1.8–4.1)	1.2 (0.9–1.8)	230 (100–320)	3 (75)
Simpson et al[18]		46 (15–80)				32 (97)					
Kenawey et al[20]		42.8 ± 12.9 (25–70)	1.2 ± 0.4 (0.7–2.8)		27 ± 9 (12–55)	37 (100)		3.6 ± 0.9 (1.8–6.3)*	1.1 ± 0.3* 1.7 ± 0.6†		
Kubiac et al[21]					16 (12–26)						7 (78)
Pappanna et al[22]		31 (0–60)	0.62	7 (5–9)	20.3 (8–36)	2 (66)		12.66	0.63 (0–1.25)		3 (100)
Wang and Edwards[23]		35 (21–75)				16 (100)	152 (77–365)	4.87 (2.78-11.2)	0.2–2.5		6 (38)
Kucukkaya et al[25]	20.5	38 (20–52)				8 (89)		2.2 (1.2–3.5)			2 (22)
Mahboubian et al[26]			In 10 patients: 1.9 (1.43–2.56) In 2 patients: 0.84 (0.75–0.93)		76 (62–93)	88 (53–100)		9.09 (1.26–51.6)			
Schiedel et al[27]		40.8 (10–80)			16 (6-49)	63 (91)	135 (56–477)	3.39 (2.37–9.54)	1.0 (0.1–2.5)		30 (43)
Burghardt et al[28]						168 (93)					
Kenawey et al[29]		43 ± 16 (2–10)	1		23 ± 12	57 (100)		3.6 ± 0.96			
Vitale et al[30]				8.5 (8–9)							

Data are presented as *n* (%), *n* (range), or mean ± SD.
* In normal regenerate patients (*n* = 29).
† In insufficient regenerate group (*n* = 8).

Table 5
Complications reported by each of the included studies (where mentioned)

Study	No. of patients	No. of inserted ISKDs	Deep infection	Superficial infection	Insufficient bone regenerate (causing delayed union)	Compartment syndrome	Runaway nail	Jammed nail	Difficult to distract nails	Premature consolidation	Non-union	Angular deformity	Joint contracture	Hardware malfunction	Had to abandon technique
Cole et al[15]	18	20												2 (10)*	
Hankemeier et al[17]	4	4													
Simpson et al[18]	30	33			3 (9)		7 (21.2)		8 (24.2)					2 (6.06)	
Kenawey et al[20]	35	37			8 (21.6)		7 (18.9)		1 (2.7)						
Kubiac et al[21]	9	11					1 (9.09)	3 (27.2)		4 (36.3)					
Pappanna et al[22]	3	3		1	1 (33.3)		1	1	1	1	1			1	1
Wang and Edwards[23]	16	16			6 (37.5)		5 (31.2)		3 (18.7)			2 (12.5)		1 (6.2)	
Reynders[24]	1	1					1								
Kucukkaya et al[25]	9	9					4 (44.4)			1 (11.1)	1				
Mahboubian et al[26]	11	12	1		1		1 (8.33)			1	1			1	4 (33.3)
Schiedel et al[27]	69	69							7 (10.1)					6 (8.69)	7 (10.1)
Burghardt et al[28]	180	242†						1 (0.7)	4 (1.65)		3 (1.23)			15 (6.2)	
Kenawey et al[29]	53	57		1 (1.75)	12 (21)	1	9 (15.78)		1 (1.75)	4 (7.01)			2 (3.5)		
Vitale et al[30]	2	2							1 (50)						
Thonse et al[31]	41‡	41					4 (10)		8 (20)						

Data are presented as *n* (%).
ISKD = intramedullary skeletal kinetic distractor.
* Percentages are either quoted or calculated in relative to the total number of operated limbs (inserted ISKDs) per each subsequent study.
† In the study by Burghardt et al,[28] the total number of inserted ISKDs was 242 in 210 patients.
‡ Thonse et al[31] mentioned the complications in only 41 of 91 surgically treated patients.

evidence of consolidation. It may be true that the compressive forces related to premature weight bearing opposed full distraction of the ISKD nails. In order to avoid the aforementioned complications, Wang et al[23] recommended an osteotomy location between 100 mm and 120 mm from the distal end of the thick segment of the nail. Further, Kubiac et al[21] recommended removal of a wedge of bone and ensuring no cortical contact at the osteotomy site to avoid this complication. Also, they recommended prophylactic release of the iliotibial tract in cases in which the distraction is planned for > 4 cm, to avoid the possible effect of the soft-tissue tension on the nail lengthening mechanism. Simpson et al[18] supposed that a tight medullary canal interferes with nail distraction; that is why they advised overreaming by 2.5–3.0 mm to facilitate nail distraction, unless an intramedullary nail had been used previously in the femur, in which case the overreaming should be less: perhaps 2–2.5 mm.

Another common complication with ISKD is IBR. Patients with IBR are those who require additional surgeries to achieve union. Regenerate failure was classified as partial failure of regenerate formation causing partial bony defect (type I) or complete failure of regenerate formation causing complete segmental bony defect (type II), which is subdivided according to the length, < 3 cm (type IIa) or > 3 cm (type IIb).[29]

Of 57 lengthening procedures, Kenawey et al[29] reported 12 cases (21%) of IBR formation resulting in nonunion (11 femoral and 1 tibial), and Wang and Edwards[23] reported six cases of delayed union (37.5%). In another study by Kenawey et al,[29] they reported eight cases of 37 cases (21%).[20] Simpson et al[18] also reported three patients of 33 femoral lengthening procedures with IBR.

IBR formation depends on many factors; the most critical of them being distraction rate and rhythm. Kenawey et al[20] stated that age > 30 years, smoking, length gain > 4 cm, osteotomy at the same site of previous trauma or surgery, and acute correction of associated deformities are other important risk factors for IBR.[20]

The distraction rate predisposing to insufficient regenerate formation has been reported to be 1.5 mm/day by Kenawey et al[20,29] and Wang et al,[23] whereas Kubiac et al[21] reported it to be 3 mm/day. When Kenawey et al[29] compared the femoral and tibial lengthening groups to factors that may affect formation and healing of bone regenerate, they found the rate of poor bony regenerate to be less with tibial lengthening cases compared to femoral cases. Their explanation was attributed to the fact that the femoral group had significantly higher distraction rates than the tibial group. Six of nine patients with runaway nails had IBR in their study. No statistically significant differences were found between both groups regarding age, percentages of smokers, number of concomitant corrections of associated deformities, performing osteotomies at the same level of a previous trauma or surgery, or the magnitude of length gain. Furthermore, no significant difference could be attributed to the etiology of shortening.

Wang and Edwards[23] found no statistically significant difference between femoral and tibial lengthening in terms of length gained, proportion of runaway nails, and proportion of difficult-to-distract nails. Nevertheless, they found a greater proportion of poor regenerate formation in the tibiae in comparison with the femora. They claimed that the number of previous surgical procedures on the lengthened bone was significantly associated with an increased likelihood of poor bone regenerate formation. This, they proposed, may be caused by poor bone quality and blood supply to the surrounding tissues, in addition to extensive scarring. That is why Wang and Edwards[23] advocate the use of traditional lengthening with Ilizarov fixation when dealing with patients who have had multiple prior open procedures.

The designer of the ISKD nail, Cole et al,[15] included in their article a description of 14 cases of tibial distraction using the device. However, consolidation index, rates of poor regeneration, and other complications were not mentioned.

Regarding frank device failure, which is defined as breakage of the nail or absolute failure of the mechanism to lengthen despite a complete osteotomy, it can result from either a manufacturing defect of the nail or a biologically related situation. A study by Burghardt et al[28] specifically studied the hardware failure complication in a large number of surgically treated limbs (210 limbs, 242 ISKDs) and found a rather large number of cases that had hardware malfunction. They reported 15 cases of hardware malfunction in 12 of 180 patients representing an overall failure rate of 6.2%, with fracture of the device occurring in 10 of the 15 failures; subsequent nonunion developed in three of these 10 nails, which presumably caused an overloading of the nail and resulted in breakage. A total of 14 lengthening procedures were performed in the femur (8 of which received femoral nails and 6 received tibial nails) and one was performed in the tibia. Details of the 15 reported failures were as follows: in four cases, a disengaged key ring was noted upon device removal; in four cases lengthening failed because of an error in the manufacturer's assembly; in two cases there were mirror-image nail fractures of the female component resulting in torsion overload; in two cases the key ring and female part broke after nonunion; in two cases there was nonunion caused by torsion overload; in one nail, the lengthening mechanism jammed as a result of being forcefully implanted when it deviated from the prereamed canal into an unreamed portion of the distal metaphysis. This was recognized during the surgical procedure, and the ISKD was immediately exchanged for another nail that functioned correctly. This damage demonstrates that a mechanically complex nail requires more delicate handling than a standard intramedullary nail.

When breakage occurred before the bone was fully consolidated, it is possible that the nail was damaged through an overload during the vulnerable period of the lengthening process. If this is the case, it may be prudent to extend the period before allowing full weight bearing. Additionally, patients should be advised to restrict weight bearing to < 50 lb (22.7 kg) until sufficient consolidation has taken place. To avoid these complications, patients with delayed consolidation need special attention. Burghardt et al[28] believe full weight bearing should be avoided until solid radiological healing has been achieved. In the event of nonunion, consideration should be given to bone grafting and nail exchange earlier than in those with normal trauma.

Because most failures in this study were recognized radiologically at follow-up visits or during removal of the nail, special attention should be paid to the early recognition of implant fractures on radiography. Retrieved nails should undergo a careful inspection by the surgeon for visible defects and to ensure that no broken pieces remain in the limb after surgery.

Despite these failures, Burghardt et al[28] stated that the ISKD is well constructed and is acceptably reliable. Although 15 failures were observed, only three patients required an additional surgical procedure to gain the desired length. Furthermore, none of the failures resulted in catastrophic complications or led to loss of length.

It is worth mentioning that despite the large number of patients included in the study of Burghardt et al,[28] the study discusses only the hardware malfunction complication in 15 patients. No other complications regarding distraction or union were mentioned. That is why the interpretation of the study by Burghardt et al[28] in our review tables was confined only to specific few parts in our tables.

Among the important publications we found was a study by Thonse et al,[31] reporting their experience with 116 ISKD implant cases that were treated over the course of 4 years. An early review of follow-up of the first 41 patients showed that 70% of these

patients experienced distraction that progressed normally. Twenty percent (8 of 41 patients) had a difficult time inducing distraction, and 10% (4 of 41 patients) experienced distraction that progressed too rapidly. Even though they did not report demographic characteristics or prognostic parameters of their patient cohort, they reported a valuable set of general inclusion and exclusion criteria of patients regarding ISKD lengthening. Important classic exclusion criteria include skeletal immaturity, limb-length discrepancy < 20 mm or > 80 mm, active infection, unstable hip/knee joints, metabolic diseases, systemic disease, and smoking. Furthermore, it has to ascertained that bones are of adequate length and that the medullary canals have the appropriate diameter needed to accommodate the ISKD implant. With the femur, the nail is 255 mm long and has a diameter of 12.5 mm (reamed to 14.5 mm). With the tibia, the nail is 215 mm long and has a diameter of 10.8 mm (reamed to 12.5 mm).

Although the ISKD has been approved by the FDA, the UK National Institute for Health and Clinical Excellence (NICE) did not recommend the use of intramedullary lengthening devices after examining the published literature.[32] Schiedel et al[27] concluded, in contrast to the NICE recommendations, that the overall reliability of the ISKD in the femur was good, with 52 of 58 lengthening procedures (98%) being successful. They stated that ISKD can be recommended with good patient selection and in pure lengthening up to 5 cm without associated correction of axial deformity. In the tibia, although the implant functioned in nine of 11 cases, successful treatment was obtained in only five. The tibia results detracted from the overall success of this implant, with 57 of 69 patients (83%) reaching their goal, but it is still comparable with other experiences with this implant.

We agree with the NICE recommendations for the current ISKD design, but we believe that proper patient selection, surgical technique, strict follow-up, and patient compliance along with some technical modification of the current design will help to easily overcome the aforementioned complications.

For tibial ISKD, patients who underwent multiple surgical intervention and patients with unfavorable soft tissue conditions and extensive scarring in whom the healing power and local blood supply are questionable should be excluded from the procedure. For femoral ISKD, patients with excessively curved femora should be excluded from the procedure and shifted to one of the conventional methods.

Regarding the technical modifications related to the implant itself, revisions of the current ISKD design are recommended so that the risk of unplanned surgery could be minimized. These revisions may include slight curvature of the femoral ISKD components to withstand the femoral bowing without intervening with the lengthening mechanism. Also, as previously mentioned that the risk of runaway nail is directly proportionate to the length of the outer portion of the nail inside the distal fragment, the outer portion of the nail could be lengthened more, providing a wide longitudinal opening on both sides to accommodate the two distal screws of the inner portion freely and allow its distraction and the 3–9° of rotation without or with minimal impingement. Also, revision of manufacturing of the sensor should be done to overcome the loss of sensor sensitivity in patients with thigh circumference < 20 cm. Another possible modification is the revision of the distal clutch–rod relationship, so that the too-sensitive distal clutch could be sensitive only to the physiologic movements rather than any muscle contractions. In addition, revision of assembly of the junction between the nail telescopic mechanisms, which is the weakest portion of the nail where most cases of nail fracture occur, should be considered. After reviewing the literature we believe that these modifications, in addition to patient selection and follow-up, will solve most of the ISKD related complications.

Conclusion

The ISKD offers the advantages of early rehabilitation, early full weight bearing, and excellent functional results**.** It also provides stable intramedullary fixation and avoids the inevitable disadvantages of external fixators, such as pin-track infection, painful scars, and discomfort caused by long-term use of the device.

Disadvantages of the ISKD include difficulties in controlling the distraction, especially during femoral lengthening. Distraction rates > 1.5 mm/day are a risk factor for runaway nail and IBR formation with subsequent delayed union. In addition, difficult-to-distract nails and poor bone regenerate formation are other complications that occur with inappropriate patient selection and poor surgical technique. That is why, after analysing the previous studies, surgical technique, patient education, and strict follow-up along with some technical modifications of the current design of ISKD will help to avoid the related complications, and subsequently provide the surgeon another reliable option for bone lengthening with good efficacy and improved patient comfort.

Conflicts of interest

The authors declare that they have no financial or non-financial conflicts of interest related to the subject matter or materials discussed in the manuscript.

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References

1. Eldridge JC, Bell DF. Problems with substantial limb lengthening. *Orthop Clin North Am* 1991;**22**:625–31.
2. Green SA. Complications of external skeletal fixation. *Clin Orthop Relat Res* 1983;**180**:109–16.
3. Herzenberg JE, Scheufele LL, Paley D, et al. Knee range of motion in isolated femoral lengthening. *Clin Orthop Relat Res* 1994;**301**:49–54.
4. Paley D. Problems, obstacles, and complications of limb lengthening by the Ilizarov technique. *Clin Orthop Relat Res* 1990;**250**:81–104.
5. García-Cimbrelo E, Olsen B, Ruiz-Yagüe M, et al. Ilizarov technique. Results and difficulties. *Clin Orthop Relat Res* 1992;**283**:116–23.
6. Young N, Bell DF, Anthony A. Pediatric pain patterns during Ilizarov treatment of limb length discrepancy and angular deformity. *J Pediatr Orthop* 1994;**14**:352–7.
7. Pettine KA, Chao EY, Kelly PJ. Analysis of the external fixator pin-bone interface. *Clin Orthop Relat Res* 1993;**293**:18–27.
8. Young NL, Davis RJ, Bell DF, et al. Electromyographic and nerve conduction changes after tibial lengthening by the Ilizarov method. *J Pediatr Orthop* 1993;**13**:473–7.
9. Bost FC, Larsen J. Experiences with lengthening of the femur over an intramedullary rod. *J Bone Joint Surg* 1956;**38-A**:567–84.
10. Paley D, Herzenberg JE, Paremain G, et al. Femoral lengthening over an intramedullary nail. A matched-case comparison with Ilizarov femoral lengthening. *J Bone Joint Surg Am* 1997;**79**:1464–80.
11. Simpson AH, Cole AS, Kenwright J. Leg lengthening over an intramedullary nail. *J Bone Joint Surg Br* 1999;**81**:1041–5.
12. Baumgart R, Betz A, Schweiberer L. A fully implantable motorized intramedullary nail for limb lengthening and bone transport. *Clin Orthop Relat Res* 1997;**343**:135–43.
13. Emara K, Farouk A, Diab R. Ilizarov technique of lengthening and then nailing for height increase. *J Orthop Surg (Hong Kong)* 2011;**19**:204–8.
14. Hankemeier S, Gösling T, Pape H-C, et al. Limb lengthening with the Intramedullary Skeletal Kinetic Distractor (ISKD). *Oper Orthop Traumatol* 2005;**17**:79–101.
15. Cole JD, Justin D, Kasparis T, et al. The intramedullary skeletal kinetic distractor (ISKD): first clinical results of a new intramedullary nail for lengthening of the femur and tibia. *Injury* 2001;**32**:SD129–39.
16. Guichet JM, Casar RS. Mechanical characterization of a totally intramedullary gradual elongation nail. *Clin Orthop Relat Res* 1997;**337**:281–90.

17. Hankemeier S, Pape H-C, Gosling T, et al. Improved comfort in lower limb lengthening with the intramedullary skeletal kinetic distractor. Principles and preliminary clinical experiences. *Arch Orthop Trauma Surg* 2004;**124**:129–33.
18. Simpson AH, Shalaby H, Keenan G. Femoral lengthening with the Intramedullary Skeletal Kinetic Distractor. *J Bone Joint Surg Br* 2009;**91**:955–61.
19. Catagni MA, Lovisetti L, Guerreschi F, et al. Cosmetic bilateral leg lengthening: experience of 54 cases. *J Bone Joint Surg Br* 2005;**87**:1402–5.
20. Kenawey M, Krettek C, Liodakis E, et al. Insufficient bone regenerate after intramedullary femoral lengthening: risk factors and classification system. *Clin Orthop Relat Res* 2011;**469**:264–73.
21. Kubiak EN, Strauss E, Grant A, et al. Early complications encountered using a self-lengthening intramedullary nail for the correction of limb length inequality. *Joint Dis Relat Surg* 2007;**18**:52–7.
22. Papanna MC, Monga P, Al-Hadithy N, et al. Promises and difficulties with the use of femoral intra-medullary lengthening nails to treat limb length discrepancies. *Acta Orthop Belg* 2011;**77**:788–94.
23. Wang K, Edwards E. Intramedullary skeletal kinetic distractor in the treatment of leg length discrepancy—a review of 16 cases and analysis of complications. *J Orthop Trauma* 2012;**26**:e138–44.
24. Reynders P. The runaway nail: unusual complications of using a self-lengthening intramedullary nail for aesthetic reasons. *Injury Extra* 2009;**40**:165–7.
25. Kucukkaya M, Karakoyun O, Gul M, et al. Results of ISKD procedures. *Injury Int J Care Injured* 2011;**42**(S3):S1–24.
26. Mahboubian S, Seah M, Fragomen AT, et al. Femoral lengthening with lengthening over a nail has fewer complications than intramedullary skeletal kinetic distraction. *Clin Orthop Relat Res* 2012;**470**:1221–31.
27. Schiedel FM, Pip S, Wacker S, et al. Intramedullary limb lengthening with the Intramedullary Skeletal Kinetic Distractor in the lower limb. *J Bone Joint Surg Br* 2011;**93**:788–92.
28. Burghardt RD, Herzenberg JE, Specht SC, et al. Mechanical failure of the Intramedullary Skeletal Kinetic Distractor in limb lengthening. *J Bone Joint Surg Br* 2011;**93**:639–43.
29. Kenawey M, Krettek C, Liodakis E, et al. Leg lengthening using intramedullary skeletal kinetic distractor: results of 57 consecutive applications. *Injury* 2011;**42**:150–5.
30. Vitale K, Miller T, Jimenez AC. Rehabilitation after intramedullary skeletal kinetic distractor implantation. *Am J Phys Med Rehabil* 2006;**85**:176–80.
31. Thonse R, Herzenberg JE, Standard SC, et al. Limb lengthening with a fully implantable, telescopic, intramedullary nail. *Operative Techniques in Orthopedics* 2005;**15**:355–62.
32. National Institute for Health and Clinical Excellence (NICE). Intramedullary distraction for lower limb lengthening, IPG 197. London, NICE. Available from: http://guidance.nice.org.uk/IPG197. [accessed 25.11.12].