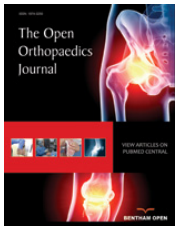

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REVIEW ARTICLE

# Total Knee Arthroplasty in Patients with Juvenile Idiopathic Arthritis

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**Abstract:**

Medical and surgical management of knee pain in juvenile idiopathic arthritis (JIA) is rapidly evolving. It is important for the orthopaedic surgeon to remain informed. In this review, we discuss the recent trends in the surgical management of JIA in light of recent medical advances for the disease. The purpose of this article is to summarize current recommendations for TKA in patients with JIA.

**Keywords:** Juvenile idiopathic arthritis, Arthroplasy, Arthritis, Knee replacement, Patients, Joint pain.

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## 1. INTRODUCTION

Knee pain affects patients of all ages. Up to 15% of the healthy pediatric population has presented to a physician complaining of musculoskeletal pain [1], and 1% of all children are evaluated for joint pain yearly [2]. Orthopaedic surgeons are often the first specialists to evaluate these patients, with one study revealing that up to 62% of children with juvenile idiopathic arthritis (JIA) were referred to an orthopaedist prior to a rheumatologist [3]. Therefore, although the etiology of pediatric joint pain is most commonly benign, orthopaedic surgeons should nevertheless have a thorough familiarity with the broad differential diagnosis for the complaint of knee pain.

The remainder of this article presupposes that a combination of clinical findings, laboratory tests, and advanced imaging has led to the diagnosis of JIA in a patient presenting with knee pain. The purpose of this article is to provide orthopaedic surgeons with an in-depth understanding of contemporary practices for total knee arthroplasty (TKA) in patients with JIA. As more long-term follow-up of TKA in JIA emerges, and as the recommendations for medical management of JIA evolve, so, too, have operative and perioperative recommendations been adjusted [4].

### 1.1. JIA Overview

The classification system for JIA has undergone three iterations of change since the 1970s. The International League of Associations of Rheumatologists most recently proposed that the term "juvenile rheumatoid arthritis" be made obsolete and replaced with the term "juvenile idiopathic arthritis," or JIA [5]. JIA refers to persistent arthritis of unclear etiology lasting >6 weeks in patients <16 years old [6, 7]. The incidence and prevalence of juvenile arthritis are 10-20 patients per 100,000 individuals and 56-113 patients per 100,000 individuals, respectively [8]. The condition is most common in Caucasian females [9]. Over the course of 10 years, 50% of children with systemic or polyarticular disease and 40% with periarticular disease will experience active arthritis; 17% of all affected children will eventually need a walker [10].

Treatment is aimed at pain relief, disease control, and the prevention of damage and disability [9]. Medical management includes a combination of nonsteroidal anti-inflammatory medications [11], intra-articular steroid injections [12 - 14], steroid-sparing immunosuppressive disease-modifying antirheumatic drugs [DMARDs] (methotrexate [15 - 17], sulfasalazine [11, 15, 18], leflunomide [19], azathioprine, cyclosporine, and hydroxychloroquine), and biologic agents. Biologics are a relatively new category of medications and are mostly used off-label for the treatment of JIA. They include TNF-α inhibitors (etanercept [4], adalimumab, and infliximab [11]), interleukin antagonists [20], and other chimeric monoclonal antibodies [21, 22]. Systemic corticosteroids are rarely used in the treatment of JIA due to their many toxicities [12, 13], but they can be used in low doses as a bridging therapy while more slowly-acting DMARDs or biologics take effect.

The sequelae of untreated or poorly-controlled JIA include synovitis and joint contracture [23], bone overgrowth [24], leg-

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length discrepancy [25], growth retardation [26], muscular atrophy [9], atlanto-axial subluxation [27], and micrognathia [28]. For patients in whom medications have proven unsuccessful and the aforementioned complications have occurred, orthopaedic intervention is warranted. Possible operations include total joint arthroplasty, synovectomy, arthrodesis, and soft-tissue releases. For the knee joint in particular, TKA is recommended when persistent joint inflammation has led to joint damage, functional impairment, and constant pain [1, 29].

On a somewhat surprising note, a recent study exploring the incidence of operative intervention for JIA over time has revealed that the number of TKAs performed each year has remained relatively constant [30], despite the advent of newer biologic medications and non-biologic DMARDs. The authors postulated that the TKA rate may be falsely elevated due to increasing referrals to their study institutions. However, the authors also noted that orthopedists have trended towards earlier surgical intervention, no longer waiting for the patient to become non-ambulatory or severely impaired before proceeding with surgery [30]. Therefore, it may be the case that overall rates of TKA for JIA have not changed over the past few decades.

## 2. TKA IN JIA PATIENTS

### 2.1. Surgical Timing

The ideal surgical candidate for TKA is a patient who has reached skeletal maturity [31] in whom all attempts at conservative management have failed, and has monoarticular JIA of the knee; however, this more commonly occurs in osteoarthritis than JIA. In the event that a child has concurrent hip and knee pathology necessitating surgical intervention, it has been recommended to perform total hip arthroplasty before TKA [29, 32, 33]; the rationale for this is that, in fact, some knee pain may originate from the hip. Additionally, one can exercise a hip above an arthritic knee, but it is nearly impossible to exercise a knee below an arthritic hip.

Absolute contraindications to TKA include severe hyperextension deformity, Charcot neuropathic arthropathy, or systemic or local knee infection. A relative contraindication is a skeletal immaturity, as physeal disturbance can precipitate growth arrest or progressive angular deformity [32]. It has, therefore, been recommended to delay TKA in children with marked growth potential [29]. However, it is important to consider that children may have open epiphyseal plates that exhibit irregularity and narrowing; these children likely do not have significant growth remaining and may be candidates for TKA [29]. Some authors even contend that TKA may be indicated regardless of patient age since prolonged preoperative morbidity portends worse outcomes and postoperative function [34, 35].

### 2.2. Perioperative Management

Patients with JIA can be difficult to manage in the perioperative period. The protean extraarticular manifestations of JIA, and the potent systemic effects of the medications used in these patients, pose challenges for medical management [36, 37].

### 2.3. Preoperative Evaluation

Radiographs of both hips and knees should be taken in the anteroposterior and lateral views preoperatively. Dedicated patellofemoral radiographs and standing films should also be obtained to assess overall limb alignment. It is crucial to obtain several views of the operative knee, as flexion contractures can cause the knee to appear artificially large at some angles [32].

Radiographs in JIA may reveal soft-tissue swelling, osteopenia with thin cortices, loss of joint space and severe cartilage destruction without osteophytes, erosions, epiphyseal overgrowth, and an increased metaphyseal diameter with decreased diaphyseal and intramedullary canal width [32, 38]. It is important to template the choice of prosthesis preoperatively with the goal of preserving as much native bone stock as possible.

Though not discussed in this article, it is imperative for these patients to undergo comprehensive cardiac, renal, and cervical spine evaluations. Thorough evaluation of the upper extremities is also warranted, particularly if walking aids will be required postoperatively.

### 2.4. Medication Management

Compared to the general population, patients with JIA have higher rates of infection [39] since most of these patients are treated with immunosuppressive agents, which increase the risk of infection and delayed wound healing. However, complete cessation of immunosuppressive agents in the perioperative period could precipitate disease flare and necessitate the administration of corticosteroids [37]. Therefore, careful consideration and interdisciplinary care must be employed to optimize the use of immunosuppressants in the perioperative period.

### 2.5. Non-biologic DMARDs

#### *2.5.1. Methotrexate*

Methotrexate is the most rigorously studied DMARD used in JIA. Several retrospective studies have found no difference in rates of postoperative infection or delayed wound healing in JIA patients who discontinued methotrexate preoperatively *versus* those who did not [40 - 43]. One study further subdivided the cohorts, looking at whether there was a difference in postoperative complications when discontinuing low-dose methotrexate more than one month before surgery, discontinuing within four weeks of surgery, or continuing through the operative period; no differences were found [40]. Another retrospective study by Murata *et al* reproduced these findings but also showed that there was no difference in the incidence of disease flareups whether methotrexate was discontinued or not [44].

While a number of prospective studies have also shown no difference in infection or wound healing complications whether methotrexate was discontinued or not [45 - 47], other studies have yielded different results. One small prospective study of 32 patients demonstrated increased infection risk in patients who continued methotrexate, with no difference in the rate of disease flareups [48]. Paradoxically, another prospective study

showed decreased postoperative infection rates in patients who continued methotrexate through the perioperative period; there was also a decreased rate of flareups in this group [49]. Of note, these patients were on 7.5-10 mg of methotrexate weekly, a lower dose than is currently recommended for JIA [50].

The American College of Rheumatology/American Association of Hip and Knee Surgeons' (ACR/AAHKS) official 2017 guidelines recommend the continuation of methotrexate throughout the perioperative period (Goodman *et al*., 2017, 2011).

#### *2.5.2. Leflunomide*

The data for continued use of leflunomide in the perioperative period are conflicting. One randomized controlled trial demonstrated no increased risk of infection when holding leflunomide [51], while another prospective study showed a higher risk of postoperative wound complication when leflunomide was continued [46].

The ACR/AAHKS official 2017 guidelines recommend continuing leflunomide though the time of surgery [52]. However, some physicians still prefer to hold leflunomide two days prior to surgery [36]. In the event of a leflunomide-related adverse event, cholestyramine may be administered to facilitate leflunomide clearance [53].

#### *2.5.3. Hydroxychloroquine*

Data for perioperative hydroxychloroquine administration is also lacking, with just one prospective study illustrating no difference in postoperative infection rates [45]. Current ACR/AAHKS guidelines recommend continuing hydroxychloroquine through the perioperative period [36, 52, 54, 55].

#### *2.5.4. Azathioprine and Sulfasalazine*

Recommendations for azathioprine or sulfasalazine administration have not been officially agreed upon in the literature. One retrospective study demonstrated an association between azathioprine use and postoperative infection when univariate analysis was done, but there was no association using multivariate analysis [41]. Another retrospective study paradoxically demonstrated a lower risk of postoperative infection with the continuation of sulfasalazine perioperatively [41]. Therefore, some physicians prefer discontinuing azathioprine and sulfasalazine two days before surgery [36], while others choose to continue or only hold them on the day of surgery [37, 54, 55]. The ACR/AAHKS guidelines recommend continuing these medications through surgery [52].

#### *2.5.5. Tacrolimus*

Tacrolimus is a macrolide calcineurin inhibitor initially developed and used to prevent organ transplant rejection reactions [56]. However, tacrolimus has since proven effective in the management of inflammatory arthridities via three distinct mechanisms: (1) decreases inflammation by inhibiting synovial cell prostaglandin E2 production [57]; (2) regulates matrix metalloproteinase 13 synthesis in rheumatoid synovium [58]; (3) increases systemic levels of corticosteroids by competitively inhibiting P-glycoprotein binding sites on lymphocytes, of which corticosteroids are the substrate [59, 60].

Though few investigators have studied the use of tacrolimus in JIA specifically, one rigorous prospective study by Wang *et al.* examined patients with JIA treated with prednisolone *versus* prednisolone plus tacrolimus for a minimum of 12 months. Following 12 months of treatment, the tacrolimus group displayed decreased erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), white blood cell (WBC) levels when compared to the prednisolone-only group. Additionally, the dose of prednisolone required for symptom abatement was lower for the tacrolimus group compared to the prednisolone-only group [61].

While there is no consensus on the perioperative timing of tacrolimus dosing in JIA, the ACR/AAHKS have based their recommendations off of the transplant surgery literature [62, 63]. In mild/moderate disease severity, the recommendation is to hold tacrolimus for one week preoperatively and resume 3-5 days postoperatively. In severe disease, the medication can be continued at the current dose [52].

#### *2.5.6. Cyclosporine A*

Similar to tacrolimus, cyclosporin A has increasingly been used as an adjunctive treatment for patients who fail methotrexate monotherapy [64]. Multiple studies have reported the safety and efficacy of cyclosporin A and methotrexate or prednisone coadministration [65 - 67]. Ravelli *et al.* followed 17 patients with JIA for at least six months following methotrexate and cyclosporin A treatment, and 47% of patients demonstrated improvement in at least three of six core disease severity outcome variables as defined by Giannini *et al* [68]: 1) physician global assessment of disease activity; 2) parent/patient assessment of overall well-being; 3) functional ability; 4) number of joints with active arthritis; 5) number of joints with limited range of motion; and 6) ESR. In this study, 41% of patients experienced side effects, though none severe enough to warrant cyclosporin A discontinuation [65].

In another investigation, Ruperto *et al.* conducted an open-ended phase IV post-marketing surveillance study on patients with polyarticular JIA who had received cyclosporin A in addition to methotrexate or prednisone. These authors found that 61% of patients continued to rate their symptoms as moderate to severe and elected to discontinue cyclosporin A due to lack of efficacy. About 17% of patients additionally chose to discontinue the medication due to severe side effect profile [67]. Therefore, evidence supporting the use of cyclosporin A in JIA is variable; a controlled clinical trial is needed for more robust information.

While there is, again, no consensus on the perioperative timing of cyclosporin A dosing in JIA, ACR/AAHKS recommendations are drawn from transplant surgery literature [62, 63]. In mild/moderate disease severity, the recommendation is to hold cyclosporin A for one week preoperatively and resume 3-5 days postoperatively. In severe diseases, the medication can be continued at the current dose [52].

### 2.6. Biologic Agents

#### *2.6.1. TNF-α Inhibitors*

TNF-α inhibitors are relatively new agents and are still undergoing investigation for on-label use in JIA. One retrospective multivariate analysis of patients undergoing an orthopaedic surgery for arthritic joints showed an association between severe postoperative infection (deep wound infection, septic arthritis, osteomyelitis) and TNF-α inhibitor use (odds ratio [OR] 5.3) [69]. Johnson *et al.* looked specifically at the effect of TNF-α inhibitor use in 248 patients undergoing 268 TKAs; these authors found no statistically significant difference in infection rates in the anti-TNF group *versus* the group without anti-TNF [70]. Of note, the one deep joint infection requiring implant removal was a patient in the anti-TNF group.

However, when comparing postoperative complications in patients taking these biologics *versus* those taking DMARDs, there are mixed results. Retrospective multivariate logistic regression analyses have revealed independent associations between postoperative wound complications in patients taking DMARDs (OR 5.9) or TNF-α inhibitors (OR 9.8) [71]. The question, then, is whether TNF-α inhibitors pose more of a postoperative risk to than do DMARDs. One prospective study showed reduced rates of postoperative infectious and wound complications in patients taking TNF-α inhibitors rather than DMARDs [72], while another illustrated no difference between the two [73]. Still another retrospective study showed that patients taking TNF-α inhibitors had an increased risk of surgical site infection and deep vein thrombosis (DVT) relative to those taking DMARDs [74]. Larger prospective studies are necessary to better understand the risk of perioperative complications in patients being treated with TNF-α inhibitors for JIA.

A number of retrospective studies have been done to investigate the need to discontinue TNF-α inhibitor administration perioperatively. Five such studies showed no increased risk of surgical site infection regardless of TNF-α inhibitor discontinuation [41, 70, 75 - 77]. Another study confirmed these findings but also reported an increased risk of JIA flare in the discontinuation group [78]. One retrospective series of 52 patients showed no association between the last TNF-α inhibitor dose and surgical site infection risk [79].

The guidelines for preoperative TNF-α inhibitor management are variable [80, 81]. Some practitioners have argued against overarching recommendations, instead urging surgeons to weigh the risk of postoperative wound complications against the risk of disease flareup upon medication discontinuation [82]. Specific guidelines from the American College of Rheumatology/American Association of Hip and Knee Surgeons are to stop all biologic agents prior to surgery and to schedule the surgery at the end of the dosing cycle. Medications should be resumed no sooner than two weeks after the date of the surgery, and only in the absence of impaired wound healing, surgical site infection, or systemic infection [52]. Because data from studies on other biologic medications are sparse [83 - 86], these guidelines have been applied to all biologics.

### 2.7. Operative Management

#### *2.7.1. Review of the Orthopedic Literature*

Twelve studies with a total of 407 patients and 632 TKAs for JIA were identified and reviewed; a summary of the findings can be seen in Table **1**. Consistent over the decades is the observation that TKA for JIA yields notable improvements in ambulation status and range of motion, significant pain relief, and enhanced quality of life.

Studies published prior to 2000, which is when widespread utilization of DMARDs for JIA took hold, do generally report high levels of patient satisfaction. This is likely because functional disability rather than the pain was the primary indication for TKA, and uncontrolled disease precipitates functional decline; furthermore, this surgical intervention tends to restore function quite drastically. While overall survival rates in most of these studies exceeded 95% at five years, they were not entirely devoid of complications. Most complications and revisions were due to component loosening or the need for arthroscopic manipulation under anesthesia (MUA) for stiffness/arthrofibrosis.

**Table 1. Summary of literature on TKA in JIA patients.**

| Ref/Year | # Knees (pts) | CR / PS | % Cemented | Ave Age (yr) | Ave F/U (yr) | % Survival | % Pain-free | XR Result | Complications |
|---|---|---|---|---|---|---|---|---|---|
| Heyse *et al*., 2014 [30] | 349 (219) | Both | 99 | 29 | 12 | 10 yr: 95%<br>20 yr: 82% | n/r | n/r | 18 revisions for loosening, 4 infections, 1 patellar revision, 2 periprosthetic fractures, 3 MUA, 2 vascular complications requiring amputations |
| Malviya *et al*., 2010 [97] | 34 (20) | Both | n/r | 35 M | 16 | 58.5 (20-yr estimate) | n/r | n/r | 3 periprosthetic fractures, 1 delayed wound healing (on MTX + etanercept), 1 revision for infection, 6 revisions for loosening |
| Jolles *et al*., 2008 [98] | 22 (14) | PS | 80 | 33 | 8 | 100 | 100 | 5 knees, >2 mm lucency | 1 MUA |
| Thomas *et al*., 2005 [99] | 17 (10) | PS | 100 | 22 | 6 | 100 | n/r | n/r | 2 transient regional pain syndromes, 1 revision for malalignment |

*(Table 1) contd.....*

| Ref/Year | # Knees (pts) | CR / PS | % Cemented | Ave Age (yr) | Ave F/U (yr) | % Survival | % Pain-free | XR Result | Complications |
|---|---|---|---|---|---|---|---|---|---|
| Palmer *et al*., 2005 [100] | 15 (8) | PR | 80 | 17 | 15.5 | 80 | 100 | 2 knees, valgus deformity | 3 revisions for component loosening, 2 intraoperative fractures, 1 periprosthetic fracture, 1 transient peroneal palsy |
| Parvizi *et al*., 2003 [101] | 25 (13) | Both | 84 | 17 | 10.7 | 92 | 92 | 6 knees, incomplete lucency; 1 knee, >2 mm lucency | 2 revisions for loosening, 1 LOA, 2 MUA, 1 revision for malalignment, 1 component exchange |
| Lybick *et al*., 2000 [91] | 77 (52) | CR | 5 | 33 | 3-13 | 99 | n/r | 14 tibias, <1.5 mm lucency | 1 revision for loosening |
| Boublik *et al*., 1993 [90] | 22 (14) | CR | 45 | 26 | 10.5 | 100* | 95 | 2 knees, 1 mm lucency | 1 patella revision |
| Carmichael *et al*., 1986 [94] | 25 (13) | Both | 100 | 20 | 5 | 100 | 8 | 10 knees, <1 mm lucency | 1 revision for loosening, 11 MUA |
| Rydholm *et al*., 1985 [102] | 17 (11) | n/a | 100 | 25 | 5 | 65 | 82 | 11 knees with lucencies | 1 patella revision, 4 revisions for loosening, 1 revision for malalignment; 2 skin necroses, 1 dehiscence, 4 peroneal palsies, 2 patella subluxations, 1 patella dislocation |
| Sarokhan *et al*., 1983 [29] | 29 (17) | Both | 100 | 23 | 5 | 97 | 97 | 9 knees, <1 mm lucency | 4 patella revisions; 1 infection, 1 tibial subluxation, 1 peroneal palsy, 21 MUA |
| Ranawat *et al*., 1983 [103] | 29 (16) | PS | 100 | 23 | 3 | 97 | 90 | 13 knees, partial lucency; 3 knees, 2 mm lucency | 1 deep infection, 2 transient peroneal palsies |

**Abbreviations:** Ref = reference. pts = patients. CR = cruciate-retaining. PS = PCL-substituting. Ave = average. yr = years. XR = X-ray. n/r = not reported. MUA = manipulation under anesthesia. MTX = methotrexate. LOA = lysis of adhesions.

When analyzing results published after the year 2000, outcomes again appear excellent. This is despite the fact that surgeons opted for earlier surgical intervention, as surgeons no longer waited for patients to become non-ambulatory or severely impaired before proceeding with surgery [30]. Therefore, it can be reasonably inferred that the quality of life has improved for nonoperatively managed patients with JIA due to advancements in medical management and that outcomes of surgery have likewise improved as the preoperative quality of life baseline has been elevated. A difference is noted, however, in the distribution of complications. The primary complication in this cohort of patients was an infection, possibly due to the immunosuppressive effects of methotrexate and other DMARDs. Component loosening, thought to be due to a high activity level in these patients, was the second most common complication [30]. Again, the high activity level in patients with JIA seems to be a new phenomenon attributable to medication advancements. In the early 2000s, Rojer *et al.* specifically discussed that JIA most often affects multiple joints and is severely debilitating, so there is little absolute gain, but significant relative functional gain, following TKA. The supposition that component loosening can be attributed to increased activity would indicate that there is now significant functional gain in patients undergoing concomitant medical and surgical management for JIA.

### 2.8. Cemented *versus* Cementless

One of the primary concerns for young patients with JIA undergoing TKA is their relatively poor bone quality [87, 88]. For this reason, one important goal for orthopedists is to preserve as much bone stock as possible during TKA [30]. Some surgeons have advocated the use of press-fit components rather than cement, as the former operative technique obviates the need for excessive reaming. Not only does this preserve bone, but it also affords shorter operative times, protection from the generation of cement debris, and the potential to achieve biologic fixation [89]. Indeed, both Lybick *et al.* and Boublik *et al.* reported over 99% survival and significant patient satisfaction at four-year follow-up after cementless TKA for JIA [90, 91]. Prudhon *et al.* compared 11-year outcomes of cemented *versus* cementless TKA in an elderly population with a combination of diagnoses (osteoarthritis, rheumatoid arthritis, and posttraumatic arthritis), and the authors found no difference in survivorship between cemented and cementless groups [89]. However, the literature is lacking in decades-long follow-up for cementless TKA in JIA patients. One potential concern is that the severe osteopenia in JIA may sometimes not allow for press-fit cementless components [30, 90]. Therefore, cemented TKA remains the gold standard in these patients [30].

### 2.9. Posterior Cruciate Ligament-Substituting *versus* Posterior Cruciate Ligament-Retaining

There are opposing opinions for PCL-substituting (PS) TKA *versus* Cruciate retaining (CR) TKA, though literature specific to JIA patients is lacking. The remainder of this section will cite articles in which PS *versus* CR was compared in patients with RA, with a small contingent being JIA patients. Those who support using PS argue that this technique allows for more congruency of articular surfaces and better deformity correction, owing to the excellent outcomes observed at 10-year follow-up [92]. PS also minimizes polyethylene wear, which may contribute to TKA survivorship in these patients

[93]. Carmichael *et al.* suggested that the PS technique aids in the correction of severe flexion contracture, therefore advocating its use in patients for whom flexion contractures prove debilitating [94]. In 1996, Laskin *et al.* published a six-year follow-up series of patients who underwent PS *versus* CR, and they ultimately advocated that PS should uniformly be done. The authors found a significantly increased incidence of posterior instability and recurvatum deformity in the CR group, necessitating revision. At the time of revisions, these authors saw a grossly absent PCL with Grade 1 synovial reaction in a number of patients in the initial CR group [95].

Orthopedists who support the CR technique argue that there are several advantages afforded by retention, including increased joint stability and better absorption of shear forces. Additionally, CR allows for femoral rollback, which helps with patients' postoperative mobility (*i.e.* better ability to climb stairs, climb uphill, cycle) and improves the quality of life [30]. Data on long-term outcomes of the CR technique are promising. In 1999, *Schai et al.* published an 11-year follow-up study on CR TKA in 52 patients (81 knees) with adult RA or JIA. The average postoperative range of motion for the JIA group was 107 degrees, and survivorship was nearly 100% for all components. Contrary to Laskin *et al.'s* findings, Schai *et al.* reported subjective stability and <6 mm of clinical anteroposterior laxity in 98% of patients. The authors concluded that the CR technique is effective for TKA for JIA [96].

## CONCLUSION

TKA in patients with JIA poses challenges unique to this disease. As medical management for JIA rapidly evolves, and as more literature on long-term outcomes of TKA emerges, it is imperative for the orthopaedic surgeon to remain current and informed. Though the field is ever-improving, current results of TKA in JIA can be extremely dramatic and gratifying.

## LIST OF ABBREVIATIONS

| | | |
|---|---|---|
| **JIA** | = | Juvenile Idiopathic Arthritis |
| **TKA** | = | Total Knee Arthroplasty |
| **DMARDs** | = | Disease-Modifying Antirheumatic Drugs |
| **ESR** | = | Erythrocyte Sedimentation Rate |
| **CRP** | = | C-Reactive Protein |
| **WBC** | = | White Blood Cell |
| **MUA** | = | Manipulation Under Anesthesia |
| **PS** | = | PCL-Substituting |
| **CR** | = | Cruciate Retaining |

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