CARTILAGE
2023, Vol. 14(3) 305–311

DOI: 10.1177/19476035231164733
journals.sagepub.com/home/CAR
SAGE

Total Knee Arthroplasty (TKA): When Do the Risks of TKA Overcome the Benefits? Double Risk of Failure in Patients up to 65 Years Old

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Abstract

Objective. The aim of this study was to document the survival rate in the middle-aged patient group up to 65 years old and to compare it with other age groups of patients undergoing total knee arthroplasty (TKA) for knee osteoarthritis (OA). *Design.* The Register of Orthopaedic Prosthetic Implants (RIPO) regional registry was used to analyze the results of patients <80 years old affected by primary OA and treated with TKA from 2000 to 2019. The database was investigated according to the age group: younger than 50 years, 50-65 years, or 66-79 years, with the aim to estimate revision surgeries and implant survivorship. *Results.* A total of 45,488 TKAs for primary OA were included in the analysis (M: 11,388; F: 27,846). The percentage of patients <65 years old increased from 13.5% to 24.8% between 2000 and 2019 ($P < 0.0001$). The survival analysis showed an overall influence of age on the implant revision rate ($P < 0.0001$), with an estimated survival rate of 78.7%, 89.4%, and 94.8% at 15 years in the 3 groups, respectively. Compared with the older-aged group, the relative risk of failure was 3.1 (95% confidence interval [CI] = 2.2-4.3; $P < 0.001$) higher in patients <50 years old and 1.8 (95% CI = 1.6-2.0; $P < 0.001$) higher in patients 50-65 years old. *Conclusions.* TKA use in the middle-aged patient population up to 65 years old increased significantly over time. These patients present a double risk of failure with respect to older patients. This is particularly important considering the increasing life expectancy and the emergence of new joint preserving strategies, which could postpone the need for TKA to an older age.

Keywords

knee, osteoarthritis, total knee arthroplasty, survival rate, failure

Introduction

Osteoarthritis (OA) is the 11th cause of years lived with disability according to the World Health Organization: its chronicity leads over time to walking disability and vascular diseases with a 1.55 higher risk of death than the general population.[1] Total knee arthroplasty (TKA) offers pain relief and function recovery for end-stage OA. The number of TKA has increased worldwide, and a further increase is expected as high as 1.26 million procedures annually by 2030 just in the United States,[2] with a consequent important impact for the entire health care system.[3]

This is a consequence of the aging population, which doubled the prevalence of adult OA, but it is also due to the expansion of indications and the growing tendency of surgeons to perform TKAs in younger patients.[4] Almost a third of primary TKAs are performed in patients younger than 65 years, and patients aged between 45 and 55 years are the fastest increasing age group.[5] However, TKAs in younger patients present lower functional results, with higher risks

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Supplementary material for this article is available on the *Cartilage* website at http://cart.sagepub.com/supplemental.

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of revision and the inherent detrimental consequences.[6] While the lower outcome in young patients is already acknowledged, patients up to 65 years old are currently a common indication for TKA. What are the risks of the increasing use of TKAs in this population, older but not old, and still working, and when do the risks of TKA overcome the benefits?

To better understand the effectiveness and risks of TKA in this age group, we performed an age-related analysis using the Italian Regional Register of Orthopaedic Prosthetic Implants (RIPO). The primary endpoint was to document the overall survival rate in the middle-aged patient group up to 65 years old and to compare it with other age groups of patients undergoing TKA.

Methods

RIPO is a regional registry database, collecting all orthopedic implants performed in 63 public and private hospitals of the Emilia-Romagna region in Italy, an area with 4.5 million inhabitants. Data are available from July 1, 2000, to December 31, 2019, with an approximate 98% capture rate.[7] Data about TKA implants include the clinical history, the original diagnosis, the type of procedure, and the type of implant. For the present analysis, patients affected by primary OA were included, while those ≥80 years old or with secondary OA were excluded, as well as those living outside the Emilia-Romagna region, to minimize the bias due to loss to follow-up.

Patient characteristics were screened for the survival analysis with implant revision (insert and/or femoral component and/or tibial component) as primary endpoint. The RIPO database was investigated about TKA according to the age group: younger than 50 years, between 50 and 65 years, or between 66 and 79 years, with the aim to estimate implant survivorship and the reasons for revision surgery. The results were compared among the 3 age groups. Ethics approval was not necessary, due to the features of the registry collecting data as standard practice on all patients in the region, using an authorized format protecting the identity of the patients.

Statistical Analysis

Patient demographics, mortality rates, and reasons for revision were analyzed using descriptive statistics, such as means, ranges, and percentages. Where appropriate, values were compared using a *t* test or chi-square test ($\alpha = 0.05$). Kaplan-Meier survivorship analysis was performed using revision of any component as the endpoint and survival times of unrevised TKAs taken as the last date of observation (December 31, 2019, or date of death). The log-rank test was used to compare survivorship among the 3 groups. The Cox multiple regression model for analyzing survival data was considered. The proportional hazards assumption was tested by the Schoenfeld residual method; age and gender used for adjustment fulfilled the proportional hazard assumption for all the period. The Wald test was used to calculate the *P* values for data obtained from the Cox multiple regression analyses. Differences between groups were considered statistically significant if the *P* values were less than 0.05. All statistical analyses were performed using JMP, version 12.0.1 (SAS Institute Inc., Cary, NC, 1989-2007).

Results

The final population involved 54,230 primary TKAs. The percentage of patients <65 years old increased from 13.5% to 24.8% between 2000 and 2019 ($P < 0.0001$). After applying the exclusion criteria, 45,488 TKAs were included in the analysis (patients: 11,388 men; 27,846 women). All patients included underwent TKA for primary OA. Female gender was prevalent, with male patients accounting for 42.2% of TKA in the younger age group and then decreasing to 30.9% and 28.4% in the middle and older age groups, respectively. Implant type was represented in the majority of the cases by minimally or posterior stabilized implants, and the use of fixed bearings was prevalent in each age group, as reported in **Table 1**. The mean follow-up was comparable among the 3 groups (6.6, 7.1, and 7.3 years, respectively, n.s.).

Thirty-five of 349 were failures recorded in the younger age group, 569 of 9,342 were failures in the middle-aged group, whereas 1,231 of 35,797 were failures observed in the older age group (10.0%, 6.1%, and 3.4%, respectively). With regard to gender-related failures, 1,293 of 32,464 failures were documented in women, whereas 542 of 13,024 failures were documented in men. In particular, in the <50 years age group, rates of revision were 23 of 204 TKAs in women and 12 of 145 in men; in the 50-65 years age group, rates of revision were 389 of 6,537 in women and 180 of 2,805 in men; and in the 66-79 years age group, they were 881 of 25,723 in women and 350 of 10,074 in men, respectively. Main reason for revision in the 3 groups was aseptic loosening (48.6%, 40.6%, and 39.9% of failures, respectively), with septic loosening being the second cause for failure (14.3%, 21.4%, and 24.8%, respectively). More detailed description of failure causes per age class, including failures based on insert stabilization and prosthesis fixation with or without cement, can be found in Tables 1–3 of Supplementary material.

The survival analysis showed an overall influence of age on the implant revision rate ($P < 0.0001$), with an estimated survival rate of 78.7%, 89.4%, and 94.8% at 15 years in the 3 groups, respectively (**Fig. 1**). Implant survival was influenced by younger age at every follow-up time ($P < 0.005$

Table 1. Patients and Implant Characteristics, and Survival Rates Over Time, According to Age Group.

	Age Class		
Descriptive Statistics	<50	50-65	66-79
No. of implants	349	9,342	35,797
No. of patients	329	8,191	30,714
Men	139 (42.2%)	2,530 (30.9%)	8,719 (28.4%)
Women	190 (57.8%)	5,661 (69.1%)	21,995 (71.6%)
Normal-weight patients (%)	21.3	11.1	15.1
Insert stabilization (%)			
Minimally stabilized	44.5	40.9	40.7
Posterior stabilized	50.0	57.3	57.7
Pivot-hinged	5.5	1.8	1.6
Fixed insert (%)	70.4	70.0	67.8
Hospital setting (%)			
Public	0.6	18.0	81.4
Private	0.9	22.6	76.5
5-year survival, (%)	92.2	95.0	96.9
(CI at 95%)	(88.4-94.8)	(94.5-95.4)	(96.7-97.1)
10-year survival, (%)	86.2	92.1	95.7
(CI at 95%)	(80.6-90.4)	(91.4-92.8)	(95.4-95.9)
15-year survival, (%)	78.7	89.4	94.8
(CI at 95%)	(66.6-87.2)	(88.2-90.4)	(94.5-95.2)

CI = confidence interval.

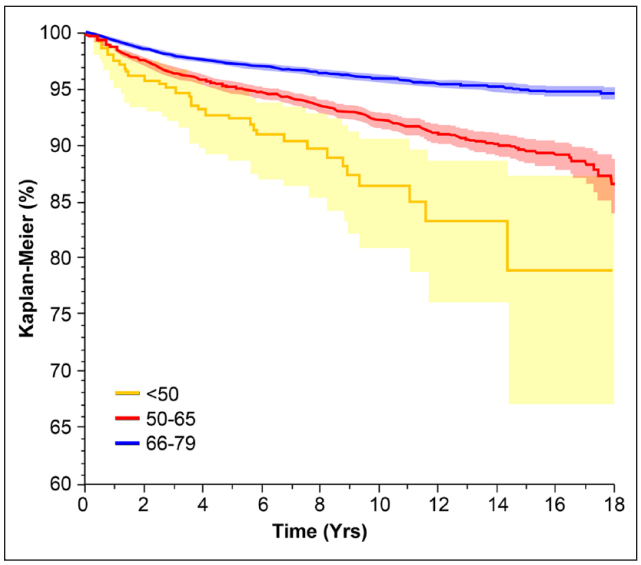

Figure 1. Kaplan-Meier survivorship analysis by age group. Total knee arthroplasties in both the younger age groups presented more failures compared with the older ones.

for all group comparisons) (**Table 1**). Compared with the older age group, the relative risk of failure was 3.1 (95% confidence interval [CI] = 2.2-4.3; $P < 0.001$) higher in patients <50 years old and 1.8 (95% CI = 1.6-2.0; $P < 0.001$) higher in patients 50-65 years old.

Discussion

The main finding of this study is that TKA use in the middle-aged patient population up to 65 years old increased significantly over time, and that these patients present a double risk of failure with respect to older patients.

TKA is increasingly performed not only in elderly patients with end-stage OA but also in younger and more active adults. However, evidence in the available literature is scarcely focused on the specific results of the middle-aged patient category. A recent systematic review and meta-analysis involving 299,291 TKAs showed an overall 82% survival at 25 years.[8] This result may be satisfactory for older patients undergoing TKA for end-stage OA, making them unlikely to face revision surgery during their lifetime. However, no data are provided about the age of these patients, which is an established risk factor for TKA failure, and it would be important to stratify the results according to age, to have a better understanding of the study implications while deciding for treatment indication in the clinical practice. What perspective can be given to middle-aged patients considering this treatment option? How likely are they going to risk a revision in their lifetime? These questions are key, especially because patients younger than 65 years are the fastest increasing patient group and represent the majority of the anticipated primary TKA cases until 2030.[9]

This study, based on the regional registry RIPO, analyzed all patients aged up to 80 years. The registry involves more than 54,000 TKAs performed since year 2000. After applying the exclusion criteria, the final analysis included 45,488 prostheses, which could be analyzed with an age-based stratification. The registry findings confirm the general trend of performing TKAs in the younger population but, more important, an almost double failure rate when patients are younger than 65 years.

This is a clinically relevant and largely neglected aspect in the TKA literature. In fact, an increased risk of failure in patients younger than 50 years undergoing TKA is already known. Castagnini *et al.*[10] focused on patients younger than 40 years, finding a lower survivorship of TKAs compared with the general population. These findings are in line with those of another study of Julin *et al.*,[11] who reported a survivorship lower than 85% at 8 years in a population younger than 44 years. Both these registry findings also reported not to be influenced by the type of implant or fixation, as confirmed by the findings of this study. Conversely, Aujla *et al.* published a systematic review to assess the functional outcomes in TKA patients aged less than 55 years. They found satisfaction and revision rates at 10 years similar to those reported in the literature for other TKA patients. However, this review lacked a meta-analysis, and most of the literature evidence suggests otherwise, with younger age being related to higher failure risks. The Finnish arthroplasty registry data showed patients aged less than 55 years had 8% failure rate at 5 years compared with 3% of those aged more than 65 years.[12] Similarly, the 13th Annual Report of the British National Joint Registry has shown a 13.0% probability of first revision at 12 years after TKA for patients up to 55 years old, compared with 5.2% of all age groups. Vessely *et al.*[13] observed an 82.6% survivorship at 15 years after TKA in patients aged <60 years, concluding that age is the most important factor for implant survivorship.

Being the higher risks of failure acknowledged in the younger age groups, patients up to 50 years old have been evaluated in a separate category, separately documented from the outcome of the middle-aged population, whose specific risk has not been defined before. Thus, this registry was analyzed based on 3 age groups: <50, 50-65, and 66-79 years. The middle-aged group showed a linear increase in prevalence over the study time, although it is questionable if this trend may be justified by clinical effectiveness also in perspective of the life expectancy and of the increasingly high activity level in patients up to 65 years old. These patients perform prosthetic replacement with the expectation to regain functionality and the ability to perform physical activities, both in terms of work, daily life activities, and sport participation. Still, these potential benefits must be weighed against the risks, which are not limited, as previously reported, to the youngest age group only. In fact, besides confirming the risks in the population <50 years old, this study underlines that there is actually a significant increase of revision risk for patients up to 65 years old. In patients 50-65 years old, the fastest growing age group in TKA also in this registry, there is actually a 2-fold revision risk compared with older patients.

Unfortunately, TKA is the preferred option among surgeons for the treatment of the young OA knee, with a massive trend of increasing indication worldwide. W-Dahl *et al.*[14] found the incidence of TKA in patients younger than 44 years increased 5 times compared with unicompartmental knee arthroplasty or osteotomies. This may be due to several factors: first, most of the national health organizations are currently based on a Diagnosis-Related Group (DRG) reimbursement system which favors joint replacement over other options, such as preservative or regenerative procedures. Also, the outcomes after TKA are well documented in the general populations, and in general, these implants show more predictable outcomes, longer survivorship, and lower revision rates compared with nonreplacement options.[14] This may be important for surgeons wanting to provide the most durable and possibly definitive treatment to their patients. Also, short-term results of TKA in middle-aged patients seem to be fairly good, as reported by Niemeläinen *et al.*,[15] who followed-up 232 patients and reported an 85% satisfaction rate 2 years after surgery. However, the registry data analyzed in this study warrant caution, demonstrating a different scenario when taking into consideration long-term results. A double-fold risk of failure was found in patients aged between 50 and 65 years compared with older ones. In light of these findings, TKA remains a valid treatment option, but it should be carefully weighed based on risks and alternative solutions, especially considering the high number of patients who will otherwise face failure. Difficulties, risks, and costs of revision surgeries are known; subsequent revision implies not only reduced activity but also the need for a more invasive surgery at an older age, with increased risks of serious and even potentially life-threatening complications.[16,17]

Effective treatment options for a young OA knee remain limited, but research is showing increasing evidence about the possibility to provide alternative solutions.[18,19] Cartilage restoration procedures have been developed targeting focal cartilage lesions in otherwise healthy joints, showing several limitations when performed in OA joints.[20-22] However, in the last decade, promising results have been shown without the need for metal resurfacing, with different authors treating successfully early OA joints with chondral/osteochondral regenerative procedures, or even mild to moderate stages of unicompartmental OA by addressing the biomechanical and anatomical changes with a combined approach of osteotomy and scaffolds/allografts to restore the damaged cartilage and meniscus tissues, reporting significant clinical improvement at short-term to mid-term follow-up.[23-26] The "biological reconstruction" approach may be

indicated in selected patients with cartilage focal damage in OA joints, with the aim to provide clinical improvement while maintaining an active lifestyle. However, these promising approaches are still far from providing a complete biological restoration of the articular surface.

For more advanced OA, injective biological solutions may be more indicated to target the whole joint environment.[27,28] While not restoring the damaged tissues, these approaches may improve knee homeostasis, thus reducing symptoms and delaying the need for arthroplasty.[29-31] Some findings suggest that the improvement provided by platelet-rich plasma (PRP) can be perceived also beyond 24 months, with a subsequent gradual reduction over time.[32] A recent survival analysis showed that PRP may delay the need for TKA with a median of 4 years and with a survival rate of 85% at 5 years of follow-up.[33] Other researchers also investigated the effectiveness of combined intra-articular and subchondral injections of PRP to address patients with knee OA, supporting their effectiveness in improving functional status and reducing pain, with a relatively low rate of conversion to TKA. More recently, bone marrow aspirate concentrate (BMAC) has been proposed as a promising mini-invasive approach to treat degenerative orthopedic conditions like knee OA.[34] Subchondral BMAC administration showed promising clinical results in preliminary reports on knee OA.[35] In particular, Hernigou *et al.*[36] evaluated 30 young patients with bilateral knee OA secondary to osteonecrosis treated with subchondral BMAC injections on one side and with TKA on the other side. BMAC provided similar clinical outcomes compared with TKA, with a lower complication rate and a quicker recovery. Finally, these authors applied the same approach to 140 patients with bilateral medial knee OA. Subchondral BMAC injections provided an effect on pain that allowed to postpone or avoid TKA up to 15 years of follow-up, with only 25 patients requesting TKA in the knee treated with BMAC.[37] The improvement of these orthobiologic solutions, together with the definition of the patient and disease phases that may benefit more from a biologic approach,[38] could help developing a valid alternative option in younger patients affected by knee OA, especially in lower OA degrees, where TKA showed unfavorable outcomes.

The main limitation of this study is the lack of clinical scores that could fail to detect even more unsatisfied patients not willing to undergo further invasive surgery. Still, these registry data shed new light on this field, where otherwise the perspective is an increase in TKA procedures in younger patients, together with the inherent risks. Unfortunately, there is an increasing pressure toward the use of TKAs, well reimbursed by most of the National Health Care Systems, making it a profitable option to manage the huge volume of OA patients seeking a quick solution for pain and function improvement. Due to the large numbers of TKAs performed worldwide, improving surgical indication in the work-age population will have a significant social impact. It is paramount to find the boundaries of the surgical indications for TKA to offer the best solution to each patient, considering advantages and disadvantages and possibly delaying the need for metal resurfacing. This is particularly important considering the increasing life expectancy and the emergence of new joint preserving strategies, which could postpone the need for TKA to an older age.

Authors' Note

Investigation was performed at the IRCCS Istituto Ortopedico Rizzoli, Bologna, Italy.

Acknowledgments and Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: S.Z. reports nonfinancial support and personal fees from I+SRL and grants from Fidia Farmaceutici S.p.A., CartiHeal, IGEA clinical biophysics, BIOMET, and Kensey Nash, outside the submitted work.

Ethical Approval

Not applicable.

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