SYSTEMATIC REVIEW

Amputation as a Complication after Total Knee Replacement, is it a Real Concern to be Discussed?: A Systematic Review

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Abstract

Total knee replacement (TKR) is a growing attractive treatment for a degenerative knee disease. However, there remain some certain devastating complications to be discussed with patients preoperatively, including limb amputation. This systematic review aimed to determine the rate of amputation following TKR. In this study, the literature was searched up to 2019. The papers were included in which knee amputation was reported following TKR. The primary search concluded the articles from EMBASE, SCOPUS, PubMed, Web of Science, MEDLINE, OvidSP, CINAHL, EBSCO, Web of Science™, and CENTRAL. After screening and excluding case reports, 40 papers were included in the present study. The present review showed that amputation is a real end result of knee replacements either in primary or revision knee arthroplasties, which needs to be discussed with patients for their decision-making. Prevalence of amputation in terms of failure or complications after TKR procedures was estimated between 0.1-10% in different studies , with 5.1% amputation rate in infected TKR and 0.025% amputation. Vascular complications and fractures associated with bone loss and compartment syndrome were other reasons for amputation.

Level of evidence: III

Keywords: Amputation, Arthroplasty, Compartment syndrome, Infection, Total knee replacement

Introduction

O steoarthritis (OA) is the common final result of different kinds of severe knee injuries that can be progressive and carry high rate of morbidity. Since the first report in 1968, knee replacement surgery has gradually become the most efficient predictable and popular procedure addressing end-stage arthritis (1). Today, total knee replacement (TKR) is identified as a highly successful surgery for the treatment of advanced destruction in patients with joint problems, especially primary or secondary osteoarthrosis (2). This procedure can help remarkable pain relief, modification of deformities, as well as enhancement of limb function

Corresponding Author: Mohammad H. Ebrahimzadeh, Orthopedic Research center, Mashhad university of Medical Sciences, Mashhad, Iran Email: ebrahimzadehmh@mums.ac.ir and quality of life (3, 4).

A 90% improvement is reported in the condition of patients who received knee prostheses in long-term clinical evaluations (5-8). Persistent implants with the maintenance of joint proper function are observed in more than 90% after the initial arthroplasty (8, 9). Number of TKR procedures is increasing due to its satisfactory outcome leading to increased life expectancy and quality of life. Due to recent advantages in these procedures, the number of TKRs increased 5% related to previous years in order to grow more rapidly in the next years (10).



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However, arthroplasty may lead to durability and adequate functioning after several years. Revision surgery becomes necessary in patients with failed arthroplasty (11, 12). There are certain minor or major complications regarding this surgery that any knee surgeon discusses with the patient before the operation. Yet, there is a lack of data about the risk of amputation as one of the most devastating end results of knee replacement surgery (13-15). It is possible that the vascular lesions that occur during the operation or infection by severe resistant microorganisms could impose the greatest risk on knee amputation in patients who underwent arthroplasty (16, 17). The present study aimed to determine the rate of amputation as an end result after TKR if it needs to be discussed with the patient.

Materials and Methods

This systematic review was conducted on the papers focused on the presence of amputation after TKR published up to October 2019. Cochrane Handbook guideline stages were used for designing the structure of this study. These seven stages include asking a question, determining the inclusion and exclusion criteria, searching articles, deleting inappropriate studies based on eligibility, evaluating the quality assessment, obtaining the required data, and discussing the topic (18).

Inclusion and exclusion criteria

The Participants-Intervention-Comparison-Outcome-Study design was employed for the determination of eligibility criteria. Publication in English language, selection of human samples, and clear description of the amputation after TKR were considered the inclusion criteria. The articles with insufficient data, review articles, meta-analyses, expert opinions, editorial letters, case reports, case series, consensus statements, and qualitative studies were removed from this study. Due to the observational nature of the study, which was the assessment of the prevalence of amputation in infected TKR, all case-control observational studies, as well as prospective and retrospective articles, were entered in this study. Case series performed on lower than 10 cases were excluded from the present study. All studies were also conducted on human samples. The main inclusion criteria were any outcome study that reported knee disarticulation or above-the-knee amputation as an endpoint in a previous knee replacement.

Literature Search, Study Selection, and Data Extraction

The present study was a systematic review of the relevant peer-reviewed original papers, including case series, case-control studies, and retrospective studies in large national registries. For the purpose of the present study, the data were gathered by two researchers through searching the three electronic databases, including EMBASE, SCOPUS, PubMed Publisher, MEDLINE, Ovid SP, CINAHL, EBSCO, Web of Science[™], and CENTRAL, up to October 2019. The papers were selected with a focus on the presence of amputation in patients with infected TKR. The search terms were "Knee Arthroplasty" or

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"Knee Replacement" in combination with "Amputation".

Risk of bias in individual trials

Cochrane risk of bias guideline was used to assess the risk of bias in the present study (19). The bias due to the selection of participants, bias due to the measurement of intervention, bias due to missing data, free of selective reporting bias, and other sources of bias were the eight main domains, which were assessed in this study. For the calculation of the risk of bias, these eight domains were categorized into low, high, and unknown risks of bias marked as "Yes", "No", and "Unclear", respectively.

Study design

In the first step, the articles reviewing the titles and abstracts were assessed by considering the eligibility criteria. All the articles incompatible with the objectives of this study were excluded from the review. Selection process of the articles is presented in PRISMA flow diagram [Figure 1]. Two investigators (SG, ARM) screened the studies independently for eligibility. They reviewed the titles and abstracts of all the articles separately and were in contact with each other for data extraction. Finally, the remaining full texts were evaluated, and the inclusion/exclusion criteria were determined for the study. References of the included studies, as well as previous reviews, were checked for additional studies. Emails were sent to the corresponding authors of the included studies to seek and confirm any other published or unpublished data. Finally, the required results were recorded in predesigned forms.

Results

A total of 3850 papers were explored in the first search of the databases out of which 450 were potentially eligible based on the titles and abstracts. The articles investigating other complications of knee arthroplasty, except for amputation were removed from the present review. A total of 93 articles were obtained reporting the rate of amputation in patients who underwent TKR out of which 27 papers were removed due to duplicates, and 66 papers remained. The studies with inaccessible full-text versions (n=1) and those published in other languages (n=0) were removed from the study. Moreover, experimental or in vitro articles (n=2), editorial letters (n=1), case reports (n=5), case series with sample sizes lower than 10 (n=5), qualitative and narrative articles (n=9), as well as systematic reviews (n=3), were excluded from this study. Finally, 40 related papers were selected and entered in this review [Figure 1].

The present systematic review was conducted on all papers investigating the rate of amputation due to infection in patients who underwent TKR. Due to the objective of this study, all case-control articles, prospective and retrospective observational studies, and case series with sample sizes higher than 10 were entered in this study. Majority of the articles were retrospective observational reviews. The selected papers in this study were performed in four different regions. In this regard, 18 studies were performed in different regions of Europe (United Kingdom=4, Germany=5, France=2,

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Figure 1. PRISMA flowchart representing the study selection process.

Switzerland=1, Netherlands=1, Finland=1, Sweden=2, Norway=1, and Ireland=1), and 18 articles were carried out in North America (USA=14 and Canada=3). In addition, two studies were conducted in South America (Brazil), and two papers were performed in the Far East (Hong Kong=1 and Korea=1). No articles were observed in Africa and other regions of Asia, except for the Far East.

The above-mentioned studies were carried out on a total of 428,314 patients who underwent TKR with postoperative infection. The age range was reported within 8-94 years. In the majority of studies, the frequency of males was higher than that of females. Most subjects suffered from OA (i.e., primary or secondary). Rheumatoid arthritis, inflammatory arthritis, juvenile idiopathic arthritis, posttraumatic OA, and other arthrosis were other common diseases leading to TKR. Diabetes mellitus was another most common disease resulting in TKR. Tuberculosis, psoriatic arthritis, morbid obesity, splenectomy, giant cell tumor, compound fracture, periprosthetic fracture TKR, liver cirrhosis, apoplexy, arterial hypertonus, hypertension, ischaemic or coronary artery disease, posttraumatic congenital dislocation, chronic obstructive pulmonary disease, history of stroke or transient ischemic attack, osteonecrosis, congenital dislocation of the knee, and haemophilic arthropathy were other diseases leading to TKR. Some studies reported being unable to identify the reasons for primary diagnosis.

Moreover, the rates of the compartment, fracture and bone loss, and vascular complications were evaluated among patients who underwent TKR. No fracture and bone loss were reported in the majority of the included articles. Two studies were performed on the subjects who had infection involving the knee and associated with mild to severe bone loss or osteomyelitis (20, 21). Bone loss was not reported in other studies. One case with bone loss was reported only in one study, which was performed on 32 patients with postoperative infection (22). There were different reports on the rate of fracture

Table 1. Ex	tracted data	i from each in	ciudea stua	у							
Authors (year) References	Country	Type of study	Age	Female/ male ratio	Primary TKR ¹	Infected TK R (sample size) prosthetic joint infection	Combination diseases	Compartment	Fracture and bone loss	Vascular complications	Amputation
Hsieh et al. (2013) (36)	Hong Kong	Retrospective cohort analysis	RA ² : 51 (35-75) NonRA ³ : 63 (32-85)	RA: 34 (74) NonRA: 82 (27)		346	RA: 46 (13.3%)				One patient with amputa- tion to control sepsis
Gardner et al. (2010) (37)	USA	Retrospec- tive cohort study	70 (48-94)	9/35 (79.5%)	12549	44 (44 knees) with culture-positive periprosthetic infection					One above-the-knee amputation
Laffer (2006) (38)	Switzerland	Retrospec- tive cohort study	70 (44-90) median	18/17 (51.4- 48.6%)	534 primary knee arthroplasties	35 patients undergoing surgery for TKR associated infection 13 subjects (2.4%) among whom developed TKR- associated infection	Diabetes mellitus, RA		-		Death of one patient due to sepsis despite upper-leg amputation
Van Rensch et al. (2012) (33)	Netherlands	Retrospective observational study	66	50/50%	22	20: (12 Primary TKR 7: Revision TKR 1: Following unicompart- mental knee arthroplasty	Tuberculosis, advanced primary arthrosis, and RA				Upper-leg amputation in two patients due to persist- ing infection
S Joshy et al. (2007) (39)	United Kingdom	Retrospec- tive	70 (46-92)	16/15	31	31	Osteoarthritis, psoriatic arthritis, RA, diabetes, morbid obesity, and splenectomy			-	Death of one case due to myocardial infarction One case with septicemia Death of eight cases with arthrodesis
Helito et al. (2015) (35)	Brazil	Retrospective	66.3 (42- 84)	50/50%	1596	63 (3.9%)	Primary osteoarthrosis RA, Juvenile RA	-	-		In 10 cases, control of the infection was not achieved. Five cases (50%) underwent amputation. One of the patients who refused amputation developed sepsis and underwent an emergency surgical ampu- tation procedure but died.
Macmull et al. (2010) All patients (20)	United Kingdom	Retrospective review	56 (18-74)	8/11	19	19	Osteoarthritis compound fracture giant cell tumor, RA, periprosthetic fracture TKR	-	All patients with deep infection in- volving the knee and associated with extensive bone loss or osteomyelitis	-	Of the three patients in whom the SMILES spacer did not eliminate infection. Two cases proceeded to an above-the-knee amputation
Pelt et al. (2014) (23)	USA	Retrospective review	63 (35-85)	34/24 (59/41%)	58	58	Osteoarthritis, RA, posttraumatic arthritis and unable to identify the reason for primary diag- nosis	-	Two cement mold fractures and 2 intraop- erative tibia fractures	-	One case with above-the- knee amputation. Three unknown mortalities and one death on postop- erative day Three mortalities due to a myocardial infarction associated with ventricular tachycardia
Rohner et al. (2015) (40)	Germany	Retrospective observational	68		26	26	Osteoarthritis				An above-the-knee amputation in three of the patients

Table 1. Con	tinued										
Sierra RJ et al. (2003) (11)	USA	Retrospective	8.6 (8- 23.6)		18443	18443		-		24 knees with amputation related to peripheral vascular disease	Amputation in 67 (0.36%) cases out of which 22 cases related to TKR, 19 cases for uncontrollable infection, two cases for periprosthetic fracture, two cases for pain, one case for severe bone loss, and one case for vascular complication
Briffa et al. (2012) (24)	UK	Retrospective observational	71.3	20/18	38	38	RĂ	-	One fracture of the modular implant	-	Three patients with an above- the-knee amputation for extensor mechanism failure and failure of suppression treatment Arthrodesis required in 10% and amputation in 6% of the cases
Herold et al. (2011) (31)	Germany	Retrospective chart review	66±14	5/7	25	12	Diabetes, liver cirrhosis, and apoplexy, and arterial hyper- tonus	-		Eight cases out of twelve patients (67%) with pathological vascular status	Amputation performed on one patient due to a multiresistant <i>staphylococcus</i> <i>aureus</i> infection and massive tissue destruction at the time of admission
Klinger et al. (2005) (21)	Germany	Retrospective observational	67 (47- 81)	8/12	20	20	Osteoarthritis, RA, and post- traumatic	-	Mild bone loss in 3 patients, moderate in 12 patients, and severe in 5 patients		An above-the-knee amputation due to infection with methicillin-resistant staphylococcus aureus
Stammers et al. (2014) (25)	United Kingdom	Retrospective observational	72 (23-89)	24/27	430	51	Hypertension, ischemic heart disease, RA, obesity	-	One case with a periprosthetic fracture around the cement spacer with nonhealing wounds due to lymphedema	One case	Seven cases
Parvizi et al. (2008) (32)	USA	Retrospective observational	66 (44-86)	13/3	13517	16	Hypertension, diabetes mellitus, and coronary artery disease	Four compartment fasciotomies performed on 8 of the 16 patients		All cases (n=16)	Above-the-knee amputation performed on one patient with popliteal artery thrombosis with failed bypass
Mahmud et al. (2012) (30)	Canada	Retrospec- tive review	70±10	135/104	239	239	-			One patient with peripheral vascular disease	One patient with peripheral vascular disease and a chronically discharging sinus over the knee with an above knee amputation
Larson et al. (2008) (29)	USA	Retrospective matched case-control	Case: 58 (28-75) Control: 58 (29-75)		26077	19		-	Open fracture in three patients	One peripheral vascular disease	Two cases
Jenny et al. (2012) (34)	France	Retrospective review	72 (45-93)	27/20	47	47					Amputation in one patient for endstage arterial occlusion

Table 1. Cor	ntinued										
Kim et al. (2015) (41)	Korea	Retrospective review	66.3 (40- 90)	147/44	191	191	Osteoarthritis	-			Two patients who underwent above-the-knee amputation
Choi et al. (2012) (42)	USA	Retrospective review	64 (38-85)	24/23	65	65	Osteoarthritis, posttraumatic arthritis, RA, congenital dislocation	-			Two cases Four deaths
Holmberg et al. (2015) (28)	Sweden	Retrospective review	70 (45-91)	62/83	145	145	Osteoarthritis and inflammatory arthritis	-	Four cases with osteoarthritis secondary to the fracture		Two above-the-knee amputation Four deaths
Jämsen et al. (2010) (26)	Finland		70 (35-97)	70/30%	2647	24	Primary or secondary osteoarthritis, RA, and other arthritis	-	1.2% osteo- synthesis for fracture	-	No lower limb amputations or deaths due to infection
Kuchinad et al. (2014) (43)	Canada	Retrospective cohort analysis	66.9	11/10	21	21					Two cases
Jämsen et al. (2006) (22)	Finland	Retrospective cohort analysis	68 (39-85)	21/11	34	32	Osteoarthritis and inflamma- tory arthritis	-	bone loss in one case	-	One case
Abularrage et al. (2008) (16)	USA	Prospectively collected	64.9	4/96% 1605/ 40028	24029	24029	Diabetes mellitus, chronic obstructive pulmonary disease, history of stroke or transient ischemic attack			2% cere- brovascular accident	Two patients undergoing lower extremity amputation
Heyse et al. (2014) (27)	Germany	Retrospective review	28.9 (11- 58)		219	31: Four revisions for infection (1.2% of all cases)	Juvenile idio- pathic arthritis		Two peripros- thetic fractures	Two vascular reasons	Two bilateral amputation for vascular reasons
Choi MD et al. (2011) (44)	USA	Retrospective review	66.6 (38- 87)	31/29	75 (79 knees)	75	Osteoarthritis, RA, posttraumatic osteoarthritis, osteonecrosis, and congenital dislocation of the knee	-	-	-	Five cases with amputation
Westberg et al. (2014) (45)	Norway	Retrospective review	41 (20-82)	4/70	74 (107 knees)	74	Hemophilic arthropathy	-	Four patients with an osteo- synthesis due to a periprosthetic fracture without removing TKR		One patient with an above- knee amputation

Table 1. Cor	ntinued										
Son et al. (2017) (46)	USA	Retrospective review	74±7	48/52%	44466	44466	-				1864 amputations (4.1%)
George J et al. (2016) (47)	USA	Retrospective review	50-80		341954	341954	-				9733 amputations (2.8%)
Amouyel et al. (2015) (48)	France	Retrospective review	68	27/39	109	72					Six cases (8%) undergoing amputation
Bengston and Knutson (1991) (49)	Sweden	Retrospective review	69 (17-91)	87/34%	12118	357	-				23 cases
Isiklar et al. (1994) (50)	USA	Retrospective review	72	50/50%	5045			-			9 cases
de Paula Mozellaa et al. (2012) (2)	Brazil	Retrospective	67.1 53-80	50/50%	2409	8	Primary gonarthrosis, RA, posttraumatic arthrosis	-	One case	One case	10 0.41% Recurrent deep infection as the cause of amputation in 81% of cases
Pala et al. (2010) (51)	United Kingdom	Retrospective review	69.4 (54- 79)	55/45%	3913	9	Osteoarthritis	Two cases	One case	One case	Two cases
Houdek et al. (2019) (52)	USA	Retrospective									
		Teview	65	58/42%	5783		-		Previous periar- ticular fracture in 16 patients		Transfemoral amputation performed on 14 patients
Friedrich et al. (2017) (53)	Germany	Retrospective review	65 70.2 (43- 89)		5783	 32	-	-	rrevious periar- ticular fracture in 16 patients	-	Transfemoral amputation performed on 14 patients One of patients treated with knee amputation and died due to reasons unrelated to the surgery 12 months after index surgery
Friedrich et al. (2017) (53) Goldman et al. (2019) (54)	Germany USA	Retrospective review Retrospective review	65 70.2 (43- 89) 65		5783 37 23 (25 knees)	32		-	rrevous periar- ticular fracture in 16 patients 	-	Transfemoral amputation performed on 14 patients One of patients treated with knee amputation and died due to reasons unrelated to the surgery 12 months after index surgery one patient
Friedrich et al. (2017) (53) Goldman et al. (2019) (54) McQuail et al. (2018) (55)	Germany USA Ireland	Retrospective review Retrospective review Retrospective case series	65 70.2 (43- 89) 65 65 86)	 7/16	5783 37 23 (25 knees) 23	 32 23 19	 Osteoarthritis	-	Previous periar- ticular fracture in 16 patients One case	-	Transfemoral amputation performed on 14 patients One of patients treated with knee amputation and died due to reasons unrelated to the surgery 12 months after index surgery one patient Three above-the-knee amputations

in the selected studies within the range of 1-6% due to the number of patients with infected TKR in each study (23-29). Vascular complications were reported in some studies within the range of 0.1-3.4% due to the number of subjects with infected TKR (11, 16, 25, 27, 29-32). In addition, the compartment was observed only in one study (32).

Rate of amputation was reported within 0.1-10% in different studies (24, 33). Persisting infection and uncontrollable infection were the main factors of amputation. In addition, multi resistant staphylococcus aureus infection, massive tissue destruction at the time of admission, end-stage arterial occlusion, vascular reasons, developed sepsis uncontrollable infection, periprosthetic fracture, pain, severe bone loss, and vascular complication were the main reasons for amputation (11, 27, 31, 33-36). The data extracted from each included study were associated with the time and place of the study, research objective, sample size, age of the study population, male to female ratio, and other parameters [Table 1].

Table 1 listed all the original papers that reported amputation as a consequence or end result of knee replacement in nontumoral knee replacements. Moreover, the categorization of the original papers was conducted according to the reason for amputation. There have been few original studies that reported amputation in the infected group and total primary replacements at the same time. Table 2 tabulates the summary of the obtained results in the present study. Quality assessment of the entered articles is depicted in Figure 2. AMPUTATION IN TOTAL KNEE ARTHROPLASTY

Table 2. Studies reported amputation rate in infected and totalknee replacements

Year of publication	Primary total knee replacement	Infected total knee replacement	Amputation
Jeremy et al. (2012) (37)	12549	44	1
Laffer1 et al. (2006) (38)	534	13	1
Helito et al. (2015) (35)	1596	63	5
Jämsen et al. (2010) (57)	3137	24	0
Abularrage et al. (2008)4 (16)	24029	20	2
Westberg et al. (2014) (45)	107	6	1

Discussion

Prevalence of amputation as an irreparable complication of infected total knee replacement

Due to the irreparable complications of TKR, the discussion on this issue is very important. However,



Figure 2. Quality assessment of the articles included in the review process.

there is not enough data on the incidence of amputation due to the failure of knee arthroplasty (2). The TKR, in particular is a growing procedure in orthopedic settings. New versions of products, advancement in technique, and especially less time of recovery, compared to other reconstructive procedures make the replacement as an attractive procedure. However, after more than 40 years, there remain some hidden facts regarding the durability and prognosis of TKR. According to the literature, there have been few reports of amputation after replacement. No single study or expert opinion reported amputation as a real consequence or end result of this procedure. The present review showed that this risk is not negligible and may need to be discussed with the patient as other important complications.

Regarding all new advancements, the infection has remained the worst complication after the surgery with psycho-social and economic costs for the patients. Majority (>90%) of these infections are killed by accurate staged reconstruction. If the infection cannot be removed or multiple revision leads to severe unreconstructable bone or soft tissue loss, knee arthrodesis, spacer arthroplasty, and amputation will be three main viable salvage interventions with knee amputation as the final option for the failure of these salvage procedures (58-69). Based on the present review, the rate of amputation was estimated between 0.1-10% in different studies (24, 33).

Deep infection after TKR was assessed in a study by Bengston and Knutson. In the aforementioned study, an evaluation was performed on transfemoral amputation reported in 23 cases patients (out of 357 cases) with infected TKR. Rates of amputation were calculated at 0.18% and 6% in all cases and patients with infected arthroplasty, respectively (49). The aforementioned study was conducted in 1991; therefore, the high rate of amputation may be due to the failure to develop surgical procedures. Rate of amputation was reported as 0.18% in another study by Isiklar et al. (50). In addition, the rate of amputation was estimated at 0.14% in another study by Sierra et al. (11). In a study performed by Van Rensch et al., the prevalence of amputation in infected arthroplasties was reported as 0.41% (33). Identification of amputation as a complication of TKR or due to unrelated causes is a fundamental problem. Some included studies were multicenter, and the data did not contain the cause of amputation. Exact cause of amputation is unclear in several studies due to uncompleted medical records. It is recommended to perform future studies focused on the main causes of amputation.

Main cause and complication leading to amputation after total knee replacement

Generally, infection is identified as the main cause of amputation, which was observed in the majority of the patients who underwent TKR. In a study carried out by Paula Mozella et al., infection was identified as the main cause of amputation in 81% of cases (2). In the aforementioned study, the rates of primary knee replacement and arterial injury were reported about AMPUTATION IN TOTAL KNEE ARTHROPLASTY

0.49% and 0.08%, respectively (16). According to the evidence, the rate of infection is about 0.5% to 1.9% in primary TKRs and increases to 8-10% in revision TKRs (70-72). T. Amouyel et al. in a retrospective cohort study conducted on 72 chronic infected knee prostheses removal and considered fusion and spacer as salvage procedures. According to this study on chronic knee infections, the removal of implant leads to 38-46% failure rate either with fusion or spacer. At the end of 5 years of follow-up, they were reported with an amputation rate of 8% (48). Min-Sun Son et al. in a national registry database study followed the results of revision surgeries on 44,466 failed total knee arthroplasties retrospectively. Rate of above-the-knee amputations was reported as 4.1% according to the obtained results of the aforementioned study (46).our review showed 5.1% amputation rate in infected TKR and 0.025% amputation rate in primary TKR as a result of infection [Table 2].

Based on the obtained results of the entered studies, staphylococcus aureus has been the germ most frequently isolated in postoperative TKR infections (2, 50, 73). The germ was isolated in 54% of the cultures from patients amputated due to infection (2). Staphylococcus epidermidis is reported as another common germ isolated in infected TKR (50). Vascular complications in patients who underwent TKR are catastrophic; however, they are very rare. Accordingly, the prevalence of vascular complications is estimated within the range of 0.03-0.17% as reported in the literature (74). Based on a previous study, only 0.02% of infrapatellar amputations were related to vascular insufficiency (2). Commonly, vascular complications after TKR are observed in patients with previously undiagnosed atherosclerotic disease. Amputation due to the ischemia of the limb after arthroplasty was reported in two cases in a study by Paula Mozella et al. (2).

Another complication of infected TKR was the periprosthetic fracture associated with bone loss, which was reported in some studies, leading to amputation in 6.5% of the cases (2). Infection of the surgical site may be developed after the fracture. Risk of amputation in infected cases is much lower than that in patients with vascular injuries or compartment syndrome; however, infection in TKR is about 46 times higher than vascular complications. According to the present review, the risk of amputation in acute arterial injury is about 27%. There have been various rates of arterial complications after TKR (0.03-0.17) (16, 32, 74-76). These complications are mostly ischemia, thrombosis, and pseudoaneurysm, and few of them are the results of direct popliteal artery lesions. Most surgeons are not anxious about ischemic complications due to their rarity; however, if they occur, there will be a significant increase in the risk of amputation or mortality (77, 78). Moreover, this risk of amputation is about 15% in compartment syndrome and 2.6% in infected cases. Nevertheless, considering the prevalence of these complications, about 97% of the related amputations are the result of infection. Risk of amputation as the outcome of infection is about 81% in a study by Van Rensch (33). In our study amputation rate is 28% in direct vascular injury and 13% in compartment

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Table 3. Amputation rate based on complication									
complication	Rate in primary TKR%	Rate of Amputation	Amputation rate in complicated TKR						
infection	0.5	0.025%	5.1%						
Vascular injury	rare	rare	28%						
compartment	rare	rare	13%						

syndrome although these complications are very rare. amputation in infected cases is about 5.1% yet considering its prevalence, infection is the most common reason for amputation (0.025%) [Table 3].

May ethnicity and race affect the outcome of knee arthroplasty?

Ethnicity and race may affect the results of knee replacement. Dunlop et al. reported the role of ethnicity in the rate of joint replacement. They showed fewer rates of arthroplasty in African-Americans, compared to those in Caucasians of the same age (79). This disparity is mainly considered a matter of socio-economic differences; however, an American national database study revealed that this difference exists in the rate of above-the-knee amputation between these two groups (80, 81). The included studies in the present review were not able to prove any specific race as a risk factor for increasing the rate of above-the-knee amputation after knee replacement surgery.

Is arthroplasty identified as a safe procedure?

According to Sierra et al. (2003), only 0.36% of amputations occurred with reasons directly related to TKR, and about 64% of amputations resulted from unrelated reasons to TKR. According to the literature, there is not enough reports related to the real rate of amputations. There is no agreement on specific indications for amputation versus limb salvage procedures, and it is another source of different reported rates in various centers. Almost all mentioned related reasons are infection, severe bone loss, vascular injury, and compartment syndrome. Sierra suggested peripheral vascular disease as the most common reason for amputations (82). The present review demonstrated that infection is the leading cause of related amputations following TKR.

In failed arthroplasties, trying for multiple reconstructions or exact indication of arthrodesis and resection arthroplasty or amputation is not well understood and is different among studies. Even the trend toward both of these two salvage procedures has declined in recent years (83). Amputation may be preferred under certain conditions, such as for tall patients with long lower limbs or cases with extensive and persistent involvement of soft tissues, massive bone loss, or after failure of fusion (84). Most of knee replacements are conducted in older people with lower demand and retired; therefore, there is a need for performing costbenefit studies to achieve the best outcomes. Psychosocial and economic burdens of TKR are the main concerns for the application of this procedure. Legal issues are among other growing concerns when the patients are not told about the catastrophes (78).

According to the present review, it was shown that amputation is a real end result for knee replacements either in primary or revision knee arthroplasties that needs to be discussed with patients for decision-making. Prevalence of amputation to failure or complications after TKR procedures was estimated between 0.1-10% in different studies. Deep infection was the major cause of amputation. Vascular complications and fractures associated with bone loss and compartment syndrome were other reasons for amputation.

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