

Femoral Neuropathy after Kidney Transplantation: A Literature Review of Case Reports and Case Series

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Abstract

Kidney transplant (KT) surgery can increase survival probability more than any other transplant. In this context, neurological complications could occur in an important percentage of individuals because this surgery is considered one of the most common organ transplantations. One rare type of neurological complication, which can occur after KT surgery, is the femoral motor neuropathy. We aimed to evaluate the clinical epidemiological profile and pathological mechanisms of femoral motor neuropathy after KT surgery. Relevant reports in six databases were identified and reviewed by two reviewers without language restriction. Seventeen reports of 183 cases from ten countries, more one unpublished case from our institution were assessed. The mean age was 39 years (range 5–69) with male sex (62.5%) and Asiatic origin predominance. The central primary kidney disease leading to renal failure was essential hypertension. The mean time from KT surgery to the onset of femoral neuropathy was 1.78 days, and the time from the occurrence of neuropathy to recovery was 6 months. The incidence of femoral neuropathy after KT surgery was 1.85%. The current review provides four possible mechanisms related to this complication, but maybe these explanations lead to a misunderstanding of the main risk factors for the development of femoral neuropathy. Furthermore, studies with current surgical techniques should be investigated because most of the data come from the old literature. Therefore, prospective studies and reports assessing the graft-recipient ratio and management options should be done.

Keywords: Femoral nerve, incidence, kidney transplantation, literature review, neuropathy

INTRODUCTION

Chronic kidney disease (CKD) is an under-recognized public health crisis that affects about 15% of the United States adult population, and interestingly, more than 90% of these individuals do not know they have CKD.^[1] When kidney injury is severe enough to have a low estimated glomerular filtration rate, dialysis, or, for a minority of the cases, kidney

transplant (KT) are the two treatment options needed for the survival. In recent years, transplantation,

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compared to hemodialysis, shows a significant improvement in age and quality of life in the majority of the recipients, and even the living costs of the patients have decreased.^[2]

KT is one of the most common organ transplantations and increases survival probability more than any other transplant. Since 1988, more than 450,000 KTs have been performed in the United States.^[1] After the introduction of immunosuppression, limitations due to acute rejections were overcome, and it was possible to improve the outcomes for patient and graft survival. Today, the prognosis after transplantation is, in the majority of the cases, excellent. The 1-year graft survival rate is about 95%, and the 5-year survival rate is more than 85%.^[3] However, KT surgery is also associated with a significant risk of complications. The most common types of complications are infective diseases that affect more than 90% of individuals. In this context, it is worth mentioning that urinary tract infections are considered the most frequent infectious complications related to KT surgery.^[4]

Another type of complication is the neurological clinical manifestations, which may result in high morbidity and mortality in the post-KT period, despite current medical achievements in surgical techniques and immunosuppression.^[5] These complications could involve the peripheral and central nervous systems and are likely to result from comorbidity diseases of the patients such as diabetes mellitus, chronic uremia due to the renal injury,^[6] surgical methods during transplantation, side effects of immunosuppressive drugs, or even due to a combination of them. Posttransplantation neurological complications are common,^[7] with rates ranging from 30% to 60% of the patients having neurological eventualities.^[2] In this way, in a recent Chinese study about neurological complications after renal transplantation, the incidence of adverse neurological events was 4.8%. In this study, the complications found in the decreasing order were encephalopathy in almost half of the patients, cerebrovascular diseases, peripheral neuropathy, epilepsy, and central nervous system infections.^[8]

The peripheral neuropathies described after transplantations are not life-threatening conditions

but could cause severe morbidity and limit patients' quality of life. Peripheral mononeuropathy and polyneuropathy probably occur equally among individuals with CKD and mainly resulting from the patient's systemic primary kidney disease.^[9] The femoral neuropathy is the most frequent and debilitating neuropathy after KT surgery. This type of neurological complication is estimated to occur in about 2% of the recipients.^[10] This literature review aims to evaluate the clinical epidemiological profile, pathological mechanism, the best management, and prevent femoral motor neuropathy after KT surgery.

MATERIALS AND METHODS

Definition

Femoral neuropathy was defined using the Medical Research Council (MRC) Scale for Muscle Strength (from grade 0 to 5) as equal to or less than Grade 2 (partial movement with no gravity, <25% normal function). Patients with weakness in their leg, but maintaining the ability to flex their hip or extend their knee or walking without assistance, were not considered femoral neuropathy patients. Recovery was defined as a patient achieving an MRC scale equal to or greater than Grade 4, which indicates >50% normal motor function (complete movement against variable resistance).^[11,12] In the cases where the non-English literature was beyond the authors' proficiency (English, Portuguese, Spanish, Italian, French, and German) and the English abstract did not provide enough data such as Korean, Japanese, and Chinese Google Translate service was used.^[13]

Search strategy

We searched six databases to locate all existing case reports and series on femoral neuropathy after KT surgery published between 1976 and 2019 in the electronic form. Excerpta Medica (Embase), Google Scholar, Latin American and Caribbean Health Sciences Literature (Lilacs), Medline, Scientific Electronic Library Online (SciELO), and ScienceDirect were searched. Search terms were "neuropathy, femoral, femoral neuropathy, neurology, complication, neurological complication." These terms were combined with "transplantation, kidney transplantation."

Inclusion and exclusion criteria

Case reports, case series, original articles, and presentations published from 1976 to 2019 were included in this review with no language restriction. The two authors independently screened the titles and abstracts of all papers found from the initial search. Disagreements between the authors were resolved through the discussion.

We excluded cases where the cause of the femoral neuropathy was known as muscle hematoma in iliacus or psoas and cases describing neuropathy in any region previous to transplantation. Other exclusion criteria were cases about lateral femoral cutaneous nerve and only sensory femoral neuropathies. We excluded the reports that the disease or accident superimposed upon another without being specifically related to the KT surgery. Furthermore, cases that were not accessible by electronic methods, including a direct request to the authors of the study by E-mail, were excluded.

Data extraction

A total of 455 papers were found; 399 were irrelevant [Figure 1].^[10,11,14-28] When provided, we extracted author, year of publication, country of

occurrence, number of patients affected, primary kidney disease leading to renal failure, preexisting diseases that might have contributed to the neuropathy, time from surgery to neuropathy onset, time from neuropathy onset to recovery, patient's status at follow-up, and management. The majority of the reports did not provide information about the primary kidney disease and the time from surgery to onset. The data were extracted by two independent authors, double-checked to ensure matching, and organized by whether the femoral neuropathy was a complication of the KT surgery.

Incidence

The incidence was assessed in a second analysis. All 56 reports were rescreened. Only studies about femoral neuropathy after kidney transplantation with incidence percentages were included without language restriction. It is noteworthy that this analysis did not follow a protocol and was only performed after the literature review.^[8,10,14-17,20,24,26,27]

Statistical analysis

Categorical variables were represented as proportions; continuous variables were represented as mean, standard deviations (SD), median, and range.

RESULTS

For the years 1976 and 2019, 18 reports containing 184 individuals who developed femoral neuropathy secondary to KT surgery were identified from 11 countries [Table 1].^[10,11,14-28]

The mean and median reported age was 39.78 (SD 7.10) and 38 years (range: 5–69 years). The male was the predominant sex with a percentage of 62.5%. The primary kidney disease that possibly led the individuals to the renal failure was in decreasing order: essential hypertension (9 cases), chronic glomerulonephritis (7), idiopathic (5), autosomal dominant polycystic kidney disease (4), focal segmental glomerulosclerosis (4), diabetes mellitus (2), acute glomerulonephritis (2), and lupus erythematosus systemic (2). Other comorbidities were reported only once, such as proliferative glomerulonephritis, renal dysplasia, cystinosis, vesicoureteral reflux, nephrocalcinosis, and trauma.

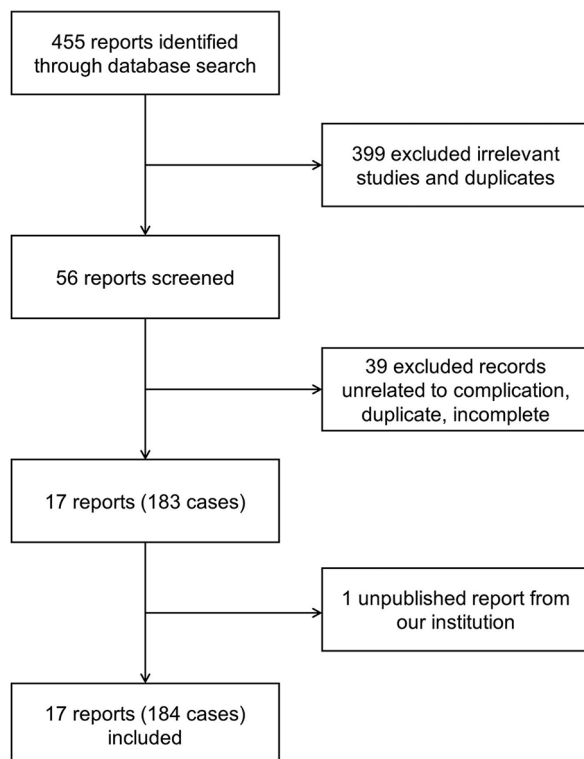


Figure 1: Flow chart of the screening process

Table 1: Reports presenting femoral neuropathy after kidney transplantation

References	Country	Year	Number of cases	Age in years (mean)	Sex (female/male)	Primary renal disease	Transplantation side (right/left/unknown)	Time from surgery to neuropathy (days)	Recovery time (months)
Present case	Brazil	2019	1	40	0/1	None	1/0/0	2	3
Kim <i>et al.</i>	Korea	2016	5	46.4	4/1	LES, CGN, none, ADPKD, FSGS	4/0/1	2.6	16.4
Veer <i>et al.</i>	Belgium	2010	5	60.2	5/0	2 DMII, 3 none	3/2/0	1.6	9
Li <i>et al.</i>	China	2010	83	38	23/60	-	-	-	2.69
Chang <i>et al.</i>	Korea	2008	12	-	-	-	-	-	-
Nikoobakht <i>et al.</i>	Iran	2007	35	40.45	20/15	-	-	1.6	-
Sung <i>et al.</i>	Korea	2002	7	39.14	3/4	-	7/0/0	-	-
Sharma <i>et al.</i>	USA	2002	4	48.5	3/1	4 HTN	3/0/0	1.25	6.25
Minz <i>et al.</i>	India	1996	3	-	-	-	-	-	104
Jog <i>et al.</i>	Canada	1994	5	33.8	2/3	2 HTN, 1 ADPKD, 1 proliferative GN, 1 none	1/4/0	1.9	6
Kumar <i>et al.</i>	India	1991	1	18	0/1	-	0/1/0	3	6
Meech <i>et al.</i>	New Zealand	1990	4	42.75	1/3	2 ADPKD, 1 FGS, 1 acute GN	-	-	9
Vogels <i>et al.</i>	Netherlands	1987	3	11	1/2	1 FSGS, 1 renal dysplasia, 1 cystinosis	1/2/0	2	4.6
Yazbeck <i>et al.</i>	Canada	1985	2	17	0/2	FSGS, reflux	2/0/0	1	1.5
Varizi <i>et al.</i>	USA	1981	3	34.33	2/1	CGN, LES, nephrocalcinosis	2/1/0	-	3.125
Sisto <i>et al.</i>	USA	1980	8	43	3/5	3 CGN, 3 HTN, trauma, acute GN	0/0/8	2.375	12
Pontin <i>et al.</i>	South Africa	1978	2	43.5	1/1	CGN, none	1/1/0	-	14
Vaziri <i>et al.</i>	USA	1976	1	33	1/0	CGN	1/0/0	-	8

ADPKD: Autosomal dominant polycystic kidney disease, CGN: Chronic glomerulonephritis, DM II: Diabetes mellitus type 2, FSGS: Focal segmental glomerulosclerosis, GN: Glomerulonephritis, HTN: Hypertension, LES: Lupus erythematosus systemic, -: Not reported

It is worth mentioning that this information is dubious since the data from Li *et al.* and Nikoobakht *et al.*, respectively, regarding 83 and 35 individuals, which represents the vast majority of the patients reported in the present review, do not mention the primary kidney disease.

The right-sided transplantation was the most commonly reported in association with the neuropathy after transplantation. The mean and median onset time from KT surgery to femoral neuropathy were 1.68 (SD 0.45) and 1.60 days (range: 1–3 days). The mean and median recovery time from femoral neuropathy occurrence to recovery was 7 (15.42) and 2.69 months (range: Days to years).

The management in none of the cases was reported systematically. Thus, we could not clearly describe percentages about it. In our case, we treated the patient conservative without starting a medication. Kim *et al.* mentioned that their individuals followed a rehabilitation program. Li *et al.* managed neuropathy with acupuncture, massage, unidentified medications, and hyperbaric oxygen in some cases.

Eleven studies (ten from the literature more our unpublished institutional incidence) assessed

the incidence of femoral neuropathy secondary to KT surgery. The mean general incidence, including all the studies of femoral neuropathy after kidney transplantation, was 1.85% [Table 2].^[8,10,14-17,20,24,26,27]

DISCUSSION

Anatomy and relations

The femoral nerve is the principal branch of the lumbar plexus. It arises from the posterior division of the ventral rami of the second, third, and fourth lumbar nerves. After, it runs transversely to the psoas major muscle and in front of the iliacus muscle. The nerve enters the femoral triangle by passing beneath the inguinal ligament, immediately lateral to the femoral artery. At the level of the lateral circumflex artery, it is divided into the anterior and posterior division. The anterior part supplies the sartorius muscle and gives off the anterior cutaneous branches, which provide sensory input for the thigh's anterior and medial side. The posterior division supplies the rectus femoris and the three vasti. In this context, the rectus femoris function is mainly responsible for hip flexion and the three vasti for the knee extension [Figure 2].^[29]

Table 2: Incidence of femoral neuropathy after kidney transplantation

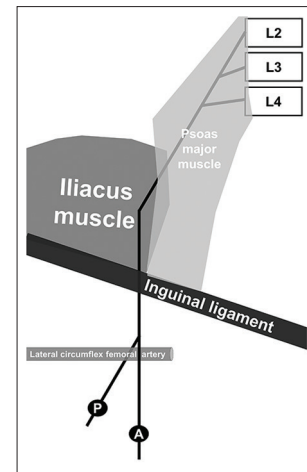
Reference	Number of cases reporter with neuropathy	Number of KT surgeries	Percentage of patients who develop femoral motor neuropathy
Jin <i>et al.</i>	9	1216	0.74
Veer <i>et al.</i>	5	3448	0.14
Li <i>et al.</i>	83	1830	4.5
Chang <i>et al.</i>	12	869	1.38
Nikooabakht <i>et al.</i>	35	129	27
Sharma <i>et al.</i>	4	184	2.17
Jog <i>et al.</i>	5	654	0.76
Yazbeck <i>et al.</i>	2	100	2
Sisto <i>et al.</i>	8	83	9.63
Pontin <i>et al.</i>	2	135	1.48
Our institution	1	306	0.32
Total	166	8954	1.85

KT: Kidney transplant

The segmental lumbar arteries vascularize the lumbar plexus. However, the intrapelvic femoral nerve's vascularity is by the iliolumbar artery and the deep circumflex iliac artery, which are branches from the internal and the external iliac arteries, respectively. Furthermore, in the infra-inguinal region, the nerve is supplied by the branches of the lateral circumflex artery. It is worthy of mentioning that on the right intrapelvic side, there are more branches and anastomoses with lumbar arteries than on the left side.^[30]

The isolated unilateral femoral neuropathy is an uncommon complication occurring in more than 1% of the individuals undergoing pelvic surgeries.^[31] Some of the procedures already reported in association with femoral neuropathy are aortic aneurysm repair,^[32] cystoprostatectomy,^[33] abdominal hysterectomy,^[34] inguinal herniorrhaphy,^[35] lithotomy position,^[36] total hip prosthesis,^[37] and ureteroneocystostomy.^[38] Furthermore, it was already associated with some cases of compression by retroperitoneal bleeding and muscle hematomas^[39] in hemophilia and patients using anticoagulants,^[40] Epstein-Barr virus infections,^[41] infiltrating muscle malignancy,^[42] complication posterior radiotherapy,^[43] trauma,^[44] and diabetes mellitus.^[45]

In the literature, numerous case reports and series about femoral neuropathy were already published in the association with the pathologies described above.

**Figure 2:** Schematic diagram of the femoral nerve anatomy and main correlations. A: Anterior division; P: Posterior division of the femoral nerve

Nevertheless, recent data about the incidence of its occurrence in surgery are scarce. The last systematic review about femoral neuropathy in association with surgical procedures, in general, was done in 2010 by Moore and Stringer, and only 38 articles were reviewed.^[46] Therefore, most of the discoveries we have today can only be theoretical as they are not based on substantial evidence.

Incidence

The incidence encountered by assessing eleven studies was 1.85%. It is noteworthy that it was only analyzed after the literature review, and a protocol was not followed. Thus, some bias could be present such as selection and the knowledge of previous studies. However, this is the first study to assess the incidence of femoral neuropathy after KT surgery with a combination of other reports and the first study of South America to report a case of femoral neuropathy after KT. In the literature, we found nine retrospective articles and one prospective.^[8,10,14-17,20,24,26,27]

After the review of the literature, we assume that this incidence is underestimated due to a combination of factors, which include early patient discharge, no checklist for patient discharge, unperformed or unknown neurological examination, negligence, under evaluation of the patient symptoms, and late follow-up with the first appointment being more than 30 days after the transplantation.

Pathophysiological mechanism

There are four theories to explain the femoral neuropathy after KT surgery. These theories are to

explain those cases with neuropathy after successful surgery proved by patient signs and symptoms with abnormal electroneuromyography, but normal abdominal imaging to exclude muscle hematomas in psoas and iliacus.

One of these hypotheses is the direct physical compression by traction or impinging of the femoral nerve during the surgery. This was first assumed concerning KT surgery by Vaziri *et al.*^[28] It could be explained by the blades of the self-retaining retractor^[47] compressing nerves during the surgery like the lateral blade compressing the lateral femoral cutaneous nerve and the inferior blade compressing the femoral nerve.^[46] However, this hypothesis does not explain neuropathy's presence even when only hand retractors were used or in reports that constant care about the blades was done during the surgery.^[21,25]

The second explanation is an ischemic injury. The middle portion of the femoral nerve is supplied by the internal and/or external iliac artery. When there is an anastomosis of the graft's renal artery to any region of the iliac artery, there exists the possibility of significant localized steal syndrome. In this way, anastomosis of the renal artery to the internal iliac artery should be done as far as possible from its origin to avoid injury to the iliolumbar artery and vasa nervosum.^[15] One interesting drawback of this theory is that the side of less vascularity is left, but the most commonly affected side in most studies is the right. Furthermore, this probably occurs in a minority of the patients because the mean recovery time is half a year, which the vascular damage probably needs more time than a temporary compression.

In 2016, Kim *et al.* studied the epidemiological profile of patients undergoing KT surgery that presented neuropathy with an aim in the pathological mechanism. They concluded that patients with lower body mass index (BMI) and higher graft-recipient weight ratio had more commonly femoral motor neuropathy.^[11] It is hypothesized that larger grafts and the fat tissue removal may compress the femoral nerve and induce the neuropathy;^[48] this compression is contributed by the patient's lying

position that starts during the surgery and continues within at least 24 h after the procedure. This explains the time of onset in days and the recovery time in months of this damage. Furthermore, lesions with long recovery periods may be vascular, and those with brief be due to compression of self-retaining retractor, higher graft-recipient weight ratio, or a combination of them. Another fact to be pointed out is that the majority of the individuals had on the right side, which can also support the compression theory because the right abdominal side has theoretically less space than the left.

We hypothesized another mechanism based on the immunological response. In some studies, the patients with femoral neuropathy presented a worse prognosis with a significant percentage of acute transplantation rejection in weeks after transplantation.^[14,21,26] Thus, neuropathy may be related to an inflammatory, misleading mechanism caused by the rejection, as was already described in the case reports. Besides, when major organs are being transplanted, probably there is more chance to occur and immunological response.^[49]

Even though these four hypotheses were by the majority of the authors explained isolated, we believe that each of them contributes with some percentage for the neuronal damage. In this context, the neuronal damage could be aggravated or have a delayed recovery by the patient's preexisting diseases such as diabetes and hypertension.^[50]

Age, sex, and country

The mean age that we encounter in the review was around 39-year-old with male sex and Asiatic origin predominances. These facts are interesting because CKD is more common in people with 65 or older, female sex, and non-Hispanic blacks.^[1] The renal injury leading to dialysis is estimated to affect only 7% of the population with <40 years.^[51] Therefore, after KT surgery, femoral neuropathy has a different epidemiological profile of the typical individuals undergoing transplantation. Moreover, based on these data, we can hypothesize that there is a possible genetic component contributing to these features.

The Asiatic predominance may be related to their lower BMI in general.^[52] We hypothesized that a

minor variation in kidney weight and anatomy with a major variation of BMI throughout the population could partially explain this interesting fact.^[53] In this way, they probably have less fat tissue, which could contribute to a higher compression until the stabilization period with the neuropathy recovery.

Prevention and management

In the period preoperation, the control of comorbidities and hemodialysis previous of the surgery showed a smaller number of femoral neuropathies after KT surgery.^[27] At the operation period, even though it is not proved that the blades of the retractors provoke neuronal damage, we believe that one should always be looking at the blades' position to decrease the possible damage. Also, if possible, use hand retractors instead of self-retaining.

Li *et al.* investigated the relationship between the mode and duration of iliac artery anastomosis and femoral neuropathy after KT surgery. They retrospectively studied 83 neuropathies from 6 transplantation centers in China. Their study revealed that the anastomose of the renal allograft artery and external iliac artery within 20 min might lower the incidence of femoral neuropathy.^[15]

Throughout the literature, none management was systematically studied. Some reports suggested that a rehabilitation program was started immediately after the diagnosis, but nothing was mentioned about the practices. Interestingly these reports, where physical therapy was attempted to alleviate the individuals' symptoms, showed better outcomes with faster recovery of almost 3 months difference than average.

Khalek *et al.* investigated the therapeutic efficacy of exercises and interferential stimulation as physical therapy approaches in improving neuropathy after KT surgery. Their results showed a significant increase in the nerve conduction velocity after 3 months of treatment application of exercise when compared with the control group. Physiotherapy is believed to allow continuous learning of movement by muscle and prevents its atrophy. This is an

essential fact for when the patient is recovered, as the muscle will be ready for use.^[54] We propose the mnemonic "FEMORAL" to help remember the main facts about femoral neuropathy after renal transplantation [Table 3].

CONCLUSION

Femoral motor neuropathy is an uncommon pathology after KT surgery affecting almost 2% of the individuals undergoing this surgery. We believed that more prospective studies with neurological examination and checklist should be done as well as reports assessing the graft-recipient ratio and management options. Furthermore, studies with the current surgical techniques of extracting the kidney from the donor should be assessed because the majority of the data that we have today are from older literature. We suggest that the neurological examination be done on the third hospitalization day; if a diagnosis of femoral neuropathy is made, early physical therapy is recommended.

Authors' contributions

Equal.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Table 3: The proposed mnemonic "FEMORAL" to help remember the main facts about femoral neuropathy after renal transplantation

Filter: Hemodialysis previous KT surgery showed better outcomes and shorter recovery time

Early physiotherapy: Physiotherapy is beneficial for the maintenance of muscle homeostasis

Measure strength: Neurological examination should be done at the third admission day; better evaluate during the checklist of patient hospital discharge

Over graft-recipient ratio: It could lead to femoral neuropathy due to compression

Retractors: One should always observe the position of the inferior retractor blade, and if possible, instead of self-retaining retractors, use hand retractors to decrease possible damage

Anastomosis: The anastomosis of the renal artery to the iliac artery within 20 min showed a smaller report number of femoral neuropathies

Lower BMI: Individuals with lower BMI should be cautiously observed during the hospitalization, and if possible, calculate the graft-recipient ratio to avoid complications

BMI: Body mass index, KT: Kidney transplant

Compliance with ethical principles

Not applicable.

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