Evaluation of Pain Syndrome in Patients after Total Knee Replacement

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Abstract

Total joint replacement is one the most effective methods for treatment of degenerative, systemic and posttraumatic diseases of the knee. However, up to 25% of patients remain dissatisfied with surgery outcomes. In the majority of cases the patients complain of pain in the operated joint. Identification of pain cause in the operated joint can turn to become a challenge for the surgeon. *Purpose of the study* – to identify the causes of pain syndrome basing on examination algorithm in patients after TKR as well as to assess the diagnostic value of each particular examination method. *Materials and Methods*. The authors analyzed results of comprehensive examination of 79 patients who complained of chronic knee pain after primary TKR and seeked medical help from the beginning of 2016 until December 2018. Inclusion criteria were as follows: knee prosthesis and presence of pain syndrome in the operated joint. Exclusion criteria: fistulous peri-prosthetic infection, suspected "culture-negative" infection and revisions. All patients included into the study were managed according to the standard algorithm of comprehensive examination. **Results.** The most likely causes of pain were identified during the examination. Infection was observed in 39 patients (49.4%), errors in three-dimensional positioning of components was considered as a probable cause of pain in 14 patients (17.7%), aseptic loosening was reported in 13 cases (16.5%), ligamentous instability - in 6 patients (7.6%), extraarticular pain origin was observed in 5 patients (6.3%) and peri-prosthetic fractures were reported in two patients (2.5%). The authors confirmed a combination of several pain causes in 17 patients (21.5%). Conclusion. Examination of patients with painfull knee prosthesis should be comprehensive due to potential combination of issues in each particular case. Integral and systematic approach to pain diagnostics in the operated joint is the "key to success" for planning further treatment tactics and for understanding the necessity and scope of revision procedure.

Keywords: total knee joint arthroplasty, pain, periprosthetic infection, component malposition.

Cite as: Murylev V.Yu., Alekseev S.S, Elizarov P.M., Kukovenko G.A., Dering A.A., Haptagaev T.H. [Evaluation of Pain Syndrome in Patients after Total Knee Replacement]. *Travmatologiya i ortopediya Rossii* [Traumatology and Orthopedics of Russia]. 2019;25(2):19-30. (In Russian). DOI: 10.21823/2311-2905-2019-25-2-19-30.

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Received: 06.04.2019. Accepted for publication: 28.05.2019.

Introduction

Total joint arthroplasty is one the most effective treatment options for degenerative, systemic and knee posttraumatic diseases. The outcomes of such procedure are stable pain relief, functional improvement and recovery of daily activities of patients. Over the nearly half-century history of condylar type prostheses the implant design and surgical techniques took a significant step forward. Despite this up to 25% of patients remain dissatisfied with surgery outcomes and revisions during first 2-5 years after the primary joint replacement are performed in 60-80% of cases [1, 2, 3, 4].

In the majority of cases the patients dissatisfied with treatment complain of pain in the operated joint [1]. Understanding of the pain nature is of key importance to determine treatment tactics. Based on the many years of the world experience it was agreed that revision is possible only after reliable identification of the problem. The causes may be related to the prostheses (mechanical, infectious, intraoperative) and can be extra-articular [5, 6, 7, 8]. Literature also describes rare cases of indefinable pain and cases of complex regional pain syndrome [9, 10].

Diagnosis of pain cause in the operated joint can be a challenge. Often the patients do not seek medical help for a long time or do not get proper attention and continue believing into the "better tomorrow" for their prosthesis and after some time turn to another institution. As a rule, such patients provide standard X-rays and discharge summary, so the identification of the pain cause might take much time and as a consequence affects the patient's status.

Purpose of the study – to identify the causes of pain syndrome in patients after knee arthroplasty using standard examination algorithm.

Materials and Methods

79 patients addressed the Botkin City Clinical Hospital in the period from the beginning of 2016 until the end of 2018 with complaints for chronic knee pain after total arthroplasty. Surgeries were performed in various hospitals of Moscow and Moscow region. Mean period of addressing from the moment of surgery was 24 months (from 3 to 127 months). Mean age of patients was 67 years (from 53 go 83). There were 60 women (76%) and 19 men (24%).

Criteria for inclusion of patients into the study were as follows: knee prosthesis and pain syndrome in the operated joint. Criteria of exclusion were as follows: fistulous periprosthetic infection, suspected culture-negative infection and revisions.

All patients included into the study underwent examination by the standard algorithm similar to the algorithm of S. Hofmann et al [4].

Prior to examination all patients were recommended to make standard X-rays and CT scanning.

Upon admission to the hospital the patients underwent general and biochemical blood tests and test for C-reactive protein. Examination started with detailed study of medical history data including discharge summaries and reports, archived X-rays and tests, defining chronology of pain origin. Pattern and location of pain, level of physical activity of the patient prior to surgery were also taken into account, as well as presence of risk factors for development of infection, any invasive procedures and injuries in preand postoperative period, period of origin of existing pain syndrome after the surgery, scope of rehabilitation [11]. Special attention was given to presence of concomitant infections and inflammations in the medical history.

Afterwards patients were asked to describe pain feelings basing on certain parameters. Location, pattern, intensity, onset and duration time, relation to certain movements and activities, efficient application of nonsteroid anti-inflammatory drugs for pain release and rate of its therapeutic use were considered.

Then followed a thorough clinical examination of the patients. The authors consecutively evaluated the bearing ability, walking on flat surface, walking up and down stairs; then continued with assessment of the range of active and passive motions in the operated joint. Clinical examination of the lumbar spine, hip and ankle joints as well as of neurological status were performed.

Then the latest standard X-rays in AP and lateral views were examined in comparison with the archive of pre- and postoperative X-rays, identified the stability of components fixation, presence of osteolysis signs, adequacy of size and three-dimensional positioning of the components, evaluated the patella positioning [12, 13, 14]. Careful CT scans analysis was made to evaluate positioning of components in axial plane according to the method described by R.A. Berger et al [15, 16]. Afterwards the authors took the decision on the need to perform supplementary radiological examinations such as weightbearing full leg standing radiographs [7, 17] and patella "sunrise view" radiographs [18].

All patients underwent diagnostics knee puncture while preadmission stage included identification of any contraindications to puncturing (receiving antibacterial agents during last 14 days). Fluid aspiration was done in aseptic conditions and without local anesthetics. Approach from the lateral patella margin was standardly used, however, in some cases the authors had to do puncture from different aspects of joint cavity (Fig. 1). Obtained aspirate was evaluated microscopically, then the material was sent in portions to the laboratory for cytological and bacteriological tests. The obtained data was evaluated by threshold criteria of chronic infection diagnostics AAOS/MSIS [19]. If necessary, considering microscopic assessment of the aspirate for blood presence, the authors made correction of white blood cell count by Ghanem formula [20].

Immediately prior to puncture the authors made a careful objective examination of the knee joint with palpation of surrounding soft tissues and identification of pain locations, and examination of postoperative scar. The knee joint stability, ligaments consistency, patella tracking were assessed. If needed secondary diagnostics punctures were performed every 14 days.



Fig. 1. Puncture from the lateral aspect of meniscus provided only 20 ml of synovial fluid of yellow color - 3338 leukocytes per mm³, 62,5% of polymorphonuclear neutrophils. Medial puncture of the same joint provided about 120 ml of brown-red fluid - 3,1% of polymorphonuclear neutrophils and 26586 leukocytes per mm³. Enterococcus faecium growth was observed only in the fluid obtained medially

After examination by the algorithm described above the patients were given recommendations for the period of awaiting results of cytological and bacteriological aspirate tests.

Results

In result of examination the most probable causes of pain syndrome in all patients were identified and options of treatment were suggested.

Diagnostic signs observed in the study are presented in Table 1. Several causes were identified in 17 (21.5%) patients. Table 2 demonstrated distribution of patients per main causes.

Infection was on the first place among all causes -39 (49.4%) patients. Besides, in 6 (15.4%) of those patients apart from infection the authors identified errors of components positioning, and in one patient – failure of medial collateral ligament. The results of bacteriological test of the aspirate from patients with peri-prosthetic infection are presented in the Table 3. Table 1 demonstrates that aspirate was not obtained from all examined patients ("dry tap") [21]. So, in 2 out of 8 such patients the diagnosis of peri-prosthetic infection was confirmed by other laboratory tests, data of clinical and radiographic examination and medical history.

Results of patients examination						
Examination	Diagnostic sign	Number of observed signs	% of total number of patients			
Objective physical examination	Ligament instability	7	8.9			
	Joint fibrosis	8	10.1			
	Signs of inflammation	9	11.4			
	Extraarticular causes	5	6.3			
X-ray observation	Errors in positioning of components	28	35.4			
	Loosening / osteolysis	31	39.2			
	Periprosthetic fracture	2	2.5			
	Ligament instability	7	8.9			
	Extraarticular causes	4	5.1			
Blood test	ESR>30 mm/hr	52	65.8			
	C-reactive protein >10 mg/l	41	51.9			
Puncture	Presence of the fluid	71	89.9			
	Leucocytes in synovial fluid >3000	38	53.5			
	Polymorphonuclear neutrophil >70%	33	41.8			
	Microorganisms growth in one culture	40	50.6			
	Microorganisms growth in two and more cultures	36	45.6			

Results of patients' examination

Table 1

Cause	Number of patients	%
Infection	39	49.4
Errors in positioning of components	14	17.7
Aseptic loosening	13	16.5
Instability of ligamentous complex	6	7.6
Extraarticular causes	5	6.3
Periprosthetic fracture	2	2.5

Distribution of	patients in	accordance to	o main	pain causes
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Second in frequency were isolated issues with positioning components in various planes including disorders in rotational relationships in 14 (17.7%) patients.

Aseptic loosening was diagnosed clinically and radiographically in 13 (16.5%) cases. In 6 (46.2%) of those 13 patients signs of incorrect 3D positioning of components were found in archive X-rays.

Ligaments instability of the knee joint was observed in 6 (7.6%) patients (excluding above mentioned female patient with combined infection and instability of medial collateral ligament). A rupture of medial collateral ligament in another female patient from this group occurred presumably due to incorrect positioning of components in the frontal plane (Fig. 2). Patella ligament instability in combination with mismatch of flexion and extension gaps due to incongruity in positioning of femoral and tibial components was observed in one more female patient. Also the authors diagnosed two cases of instability combined with coxarthrosis on the operated limb.

Table 2

Thus, after consolidation of all identified cases the incorrect placement of components in various combinations was observed in 28 (35.4%) out of 79 patients.

Among other extra-articular causes the authors reported 2 (2.5%) peri-prosthetic fractures: patella fracture and fracture of lateral condyle without displacement.

In remaining 5 (6.3%) cases the following extra-articular causes of pain were observed: 2 cases of hip osteoarthritis on the

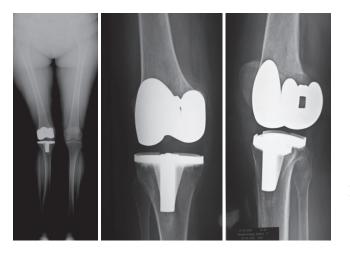


Fig. 2. X-rays confirming medial ligament instability and incorrect frontal positioning of components

side of replaced knee joint, 2 cases of spinal radicular semiology and one case of acute recurrence of urarthritis.

Discussion

All patients dissatisfied with the outcome of total knee arthroplasty complain of pain in the operated joint. Understanding the true cause of pain syndrome is often a challenge while description of pattern and location of pain almost never can precisely indicate the root of the problem. For example, complains of the patients with confirmed peri-prosthetic infection always varied. Some patients described the pain as burning along the anterior surface of the lower leg, others - as lancinating ("sharp glass") pain inside of the knee joint, others compared pain with electric current. Variety of pain pattern was observed in patients with peri-prosthetic infection and in patients with aseptic causes. At the same time, complaints on "start-up" pain often indicate loosening of prosthesis components. In the present study 7 (54%) out of 13 patients with radiographic signs of loosening confirmed reduced pain after a short walk.

Detailed study of medical history can provide a valuable information on the probable cause of the pain. For example, information about trauma with lesion of the knee ligaments in the preoperative period or about falling on the bent leg in postoperative period was reported in 3 (42.9%) out of 7 instability cases confirmed radiographically and clinically. In one case knee ligaments instability was identified in combination with incorrect positioning of tibial component which, presumably, was the cause for instability. In another two patients the ligaments instability was combined with diagnosed coxarthrosis which can be related to the changes in rotation center of mechanical leg axis. Besides, reference to infection and inflammation in the medical history of a patient can indicated development of hematogenic peri-prosthetic infection - all three patients with hematogenic infection (Tsukayama III) [22] had acute infection-inflammatory diseases reported in their medical records.

Objective physical examination is the most informative in cases of ligaments instability — standard tests allowed to confirm instability in all 7 patients including imbalance of flexion and extension gaps for walking up and down the stairs. Objective examination can also help to identify probable extra-articular pain cases — in the present study in 4 patients pain was localized in the area of pes anserinus in combination with clinical and X-rays signs of coxarthrosis on the operated side, and in one case the patient was recommended to see a neurologist for suspected radicular syndrome.

Objective examination of patients with peri-prosthetic infection can detect only minor diagnostic signs such as changes in skin pigmentation, pronounced edema and local hyperemia. All those signs are not very valuable for diagnosis, however, should be taken into consideration in case of doubtful periprosthetic infection due to concomitant diseases or absence of fluid in the joint which will be described further.

Sign of rigidity and complains of pain in the anterior portion of the knee joint (patella area) during getting out of a chair and walking on the stairs can indicate issues in patella-femoral joint due to rotational deviations. This requires mandatory confirmation by X-ray, CT scanning and tangential radiographs.

Knee joint fibrosis in the world literature is often considered as an independent cause for patient's dissatisfaction with treatment outcomes [4, 5, 7, 8, 23, 24, 25]. At the same time there are studies that describe joint fibrosis as the consequence of other infectious and mechanical causes [26, 27]. Presumably, it is related to the absence of precise universally accepted definition of joint fibrosis [25]. The most common criteria of this pathology are rigidity, flexion contracture and "excessive" intra- and para-articular scar tissue [23, 25]. 8 patients from the present study who had a clinical picture of marked fibrous joint remodeling demonstrated different causes of such condition: errors in positioning of components were identified in 5 patients, chronic infection — in 3 patients. Such condition was not always combined with limited range of motion and this fact demands further research and larger number of clinical cases.

Radiographic examination is the most valuable instrument to define biomechanical issues. Standard X-rays, however, allow to confirm only stability of components fixation and gross errors in positioning or height of articular line. In the group of patients with infection radiographic signs were identified in 18 (46,2%) out of 39 patients: 10 cases of loosening and 8 cases of osteolysis. Evaluation of X-rays of the patients with chronic low-grade infection in dynamics from the moment of surgery did not always indicate the correlation between time, elapsed after surgery, and osteolysis degree. At the same time examination of archive X-rays of patients with septic loosening demonstrated swift nature of this process — in 6 out of 10 patients with loosening it was chronologically confirmed that the period between stable fixation and loosening was less than 12 weeks. On the contrary, X-ray signs in patients with aseptic loosening demonstrated slow progression and often the images did not reflect the actual status when matching archive X-rays with data from medical history of the patient.

Full leg X-rays in 3 patients demonstrated errors in positioning of two components in the frontal plane, in one patients — only for femur component, and in three — only for tibial component.

According to the literature the following parameters are considered significant: internal rotation of only tibial component over $5-6^{\circ}$, internal rotation of only femoral component over 4° , overall internal rotation of components of $6-10^{\circ}$ and mismatch of rotational position of components starting of 5°

[16, 28–30]. In accordance to the above positioning errors in axial plane were confirmed in 19 patients (24%).

Study of "sunrise view" tangential radiographs are required to identify patella positioning [18]. According to literature overall internal rotation of components within 3-4° results in patella tilt, $5-9^\circ$ — in subluxation and over 10° – in dislocation [15, 30]. However, among the studied patients the dislocation of patella was observed only in one case at 13° of overall internal rotation of both components (10° for tibial and 3° for femoral component). Only tilt or subluxation of patella was observed in remaining 5 patients with overall internal rotation over 9° but the patella deformity was severe. In the only case of mismatch in rotation of components the authors observed patella instability – patella subluxation at 30° flexion, tilt at 60° and normal position at flexion of 90° and above, and excessive patella mobility at full extension.

In 2011 the American Academy of Orthopaedic Surgeons (AAOS) published diagnostic criteria for peri-prosthetic infection [31]. During the symposium of Musculoskeletal Infection Society (MSIS) in Philadelphia in 2013 these recommendations were revised [19, 32]. According to the recommendations without any significant signs of infection diagnostic punctures should be made with ESR above 30 mm/hr and/or C-reactive protein over 10 mg/l. Second International Consensus Meeting on Musculoskeletal Infection) took place in July 2018 where above recommendations were confirmed as relevant but with some limitations [22]. Those are related to a series of research reflecting low specificity and relatively low sensitivity of inflammation markers of blood serum against infection induced by low virulent agents [33, 34, 35, 36].

In the present study the ESR level was variously increased in 31 (79,5%) patient with infection and in 21 (52,5%) patients out of 40 patients without confirmed infection.

C-reactive protein was also increased in 31 (79,5%) patient with infection, and at that in three patients increased values were reported in respect of only one inflammation indicator (ESR or CRP). In patients with aseptic etiology of pain the level of CRP over 10 mg/l was reported in 10 (25%) patients, and in 8 (20%) patients the values were within 6-10 mg/l.

The data obtained confirm the fact that use of serum inflammation markers is limited by specificity and sensitivity [37, 38]. Increased level of indicators can be related to extra-articular causes (concomitant pathology, rheumatic diseases) and to lengthy trauma to bone and para-articular tissues in patients with aseptic loosening and instability. In certain cases, concomitant pathology can seriously complicate the diagnostics of the issue. For example, literature describes rare cases of acute inflammation of the operated knee joint along with recurrent uratosis [39, 40, 41]. The authors observed three such cases during the present study which resulted in the need to evaluate level of uric acid in the blood and, in necessary, to test synovial fluid for presence of tophus. Two out of three cases demonstrated swift loosening of components along with infection, and only in one case the diagnosis of peri-prosthetic infection was statistically reliably confirmed only during the procedure for spacer implantation. In the third case no signs of loosening or osteolysis were observed, peri-prosthetic infection was not confirmed and persisting reduction of inflammation and pain syndrome after puncture and conservative treatment.

According to the most actual diagnostic criteria of AAOS and MSIS [42] in case of no fistulas the diagnosis can be confirmed after double isolation of the same microorganism during bacteriological test or in presence of at least 3 out of 5 "minor" criteria. Out of five possible "minor" criteria, two are based on cytological test of the aspirate and another one — bacteriological test of aspirate of bi-

opsy material. Based on this, knee puncture is the necessary and the most valuable examination for diagnostic of peri-prosthetic infection.

The authors managed to get the aspirate from 71 (89.9%) out of 79 studied patients. In remaining 8 cases even a smallest fluid amount was not obtained («dry tap») due to severe scarring of the joint. Such situation poses significant differences for differential diagnostics of issues in the operated joint. Radiographic examination confirmed rapidly progressing loosening and components migration in 3 of 8 patients, raised level of ESR and CRP, which resulted in a decision for two stage revision. In one of the above cases the increased CRP level can be accounted for by concomitant pathology which complicated decision making even further and the final diagnosis could have been established only during surgery. Injection of normal saline solution into the joint with following aspiration and test was not performed due to high risk of iatrogenic complications and absence of strong evidence for efficiency of the present method in the literature [21].

Bacteriological culturing of obtained fluid is the most reliable method to identify periprosthetic infection which should be performed in all patients irrespective of serum inflammation markers. Besides, the bacteriological tests allow to determine antibacterial sensitivity which highly valuable for understanding tactics of further treatment [38].

Repeated puncture is necessary considering possible microbial contamination of the tested material, and in case of sufficient material quantity to make comparison to the results of cytological tests and macroscopic parameters. There were 4 cases of confirmed microbial contamination in the present study.

In 2004 A. Trampuz et al for the first time identified threshold parameters for leucocytes volume and percentage of neutrophils content in the aspirate — 1700 leucocytes per mm³ and 65% of neutrophils [43, 44]. Later on in 2011 AAOS also suggested thresholds for cytological tests which were modified during International Consensus Meeting on Peri-prosthetic Joint Infection and Second International Consensus Meeting on Musculoskeletal Infection. At present, leucocyte count over 3000 per mm³ and polymorphonuclear neutrophils volume over 70% correspond to "minor criteria" of AAOS/MSIS for diagnostics of chronic infection [19]. A key condition for cytological test is that aspirate, if possible, should not contain track blood inclusions while it might affect the result. In this regard E. Ghanem et al published a research in 2008 where they presented a formula for calculation of "true leucocytes" count in synovial fluid [20]. According to this data leucocyte count over threshold was observed in all 36 patients with confirmed periprosthetic infection who underwent cytology. In the majority of cases the leucocyte count significantly exceeded the number of 3000 per mm³. Percentage of polymorphonuclear neutrophils over threshold was observed in 33 (99.7%) of those patients. For some reason in 3 remaining patients neutrophil percentage was about 3-5% and the aspirated fluid microscopically was of brown color and exceeded the volume of 70ml. No correlation between those findings and type of pathogen were obtained — in two cases it was Staphylococcus epidermidis, and in one case — Enterococcus faecium.

In 30 patients with aseptic causes of pain who underwent cytological tests the leucocyte count did not exceed 2200 mm³ and percentage of polymorphonuclear neutrophils averaged 25-30%.

After recalculating "true leucocytes" by the Ghanem formula no values over or below the threshold were obtained during macroscopic and cytological verification for red blood cells presence in any patients with aseptic causes for pain as well as in patients with infection. At that it was observed that significant increase in red blood cells count in the aspirate can be related not only to traumatic puncture procedure («traumatic tap»). So, increased count of red blood cells in synovial fluid above 25000 per mm³ after adequate puncture procedure was observed in 15 (65.2%) out of 23 patients with aseptic or septic loosening of components. Presumably blood can get into the joint cavity in result of trauma to bone and para-articular tissues due to loss in rigid fixation of components to the bone. However, such assumption requires further research and in case of verification can be used for early diagnostics of aseptic loosening when X-ray signs are not obvious.

Due to the great variety of causes for pain syndrome after knee joint arthroplasty the identification of the true issue can be a challenge. Thus, chronic infection or errors in positioning of prosthesis components can be hidden behind the phenomenon of joint fibrosis. Those errors themselves remain acute and widespread issue often resulting in early aseptic loosening or ligaments instability. Besides, any detected mechanical or extra-articular causes can be combined with chronic infection which mandatory should be taken into consideration during examination of a patient. But even the availability of information on inflammatory process should be differentiated with respect of systemic or somatic pathology.

Patients with knee pain should undergo a full range examination. Integral and systematic approach to pain diagnostics in the operated joint is the key to success for planning further treatment tactics and for evaluating the need and scope of revision.

Ethics of publication: patients provided voluntary informed consent to the publication of clinical cases.

Competing interests: the authors declare that there are no competing interests.

Funding: state budgetary funding.

Authors' contribution

Murylev V.Yu. — study design, review of literature, analysis of obtained data, writing of the manuscript, correction and final editing of the manuscript

Alekseev S.S. — study design, review of literature, collection and analysis of the data, writing of the manuscript.

Elizarov P.M. — study design, analysis of obtained data.

Kukovenko G.A. – collection and analysis of the data.

Dering A.A. – collection and analysis of the data.

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