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Short Commentary

New trends for diagnosis and treatment of infected total knee arthroplasty

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Abstract

Periprosthetic joint infection (PJI) is a severe complication after total knee arthroplasty (TKA), occurring in approximately 0.3% to 3% of all cases. With growing populations and increasing age, this kind of pathology is worldwide growing its social and economic effects. Many risk factors have been identified but a proper and accurate diagnosis and choice of treatment seem to be characterized by an enormous evolution. Diagnostic features such as clinical and radiological elements are loosening their predictive value. New biomarkers and molecular elements seem to be more precise and accurate in confirming PJI. Anyway, lots of them are still under study. About treatments, decisions of surgeons should not be related to their experience or preference, but every choice should have proper indications. Double-stage treatments should be practiced only in few conditions. Cheaper management such as irrigation or single-stage surgery can be considered for several conditions.

Key words: Total knee arthroplasty, Infection, Diagnosis and treatment

INTRODUCTION

Total knee arthroplasty (TKA) is one of the most successful operations in current medicine. As the implantation of knee prostheses increases, rate of periprosthetic infections is also rising [1]. Infections rates following TKA range from 0.5% to 3% [2].

The reported incidence is low but it is probably underestimated due to the difficulty in diagnosis. Periprosthetic joint infection (PJI) has challenged the orthopedic community for several years and despite all the advances in this field, it is still a real concern with immense impact on patients, and the healthcare system. Eradication of infection can be very difficult. Therefore, prevention remains the ultimate goal [3].

The acutely infected knee replacement often presents to the on call Orthopedic Surgeon who can often lack the resources for the definitive management. Getting an early and accurate diagnosis and potentially performing an early treatment such as irrigation and debridement should be the most important objective for every surgeon. Management of these patients should include a team of specialists including Medical or Intensive Care, and specialists for infections. Management of PJI is extremely expensive and has a high morbidity [2].

In literature, there is a lack of proper criteria for diagnosis and for treatment. There are few RCT about this issue and guidelines and algorithms are poor too. Proper criteria and a standardized management for infections are missing.

Diagnosis and management need multidisciplinary approach. Nowadays, orthopedic community reports a great evolution in diagnostic strategies. Diagnostic elements such as radiographic features are loosening importance respect new biochemical biomarkers. Strategies for treatment too are evolving towards new cheap and safe surgical decisions.

NEW TRENDS IN "DIAGNOSIS"

The diagnosis of PJI is based on specific conditions related to infective disease suspicion. Parvizi et al. in 2014, [4] proposed laboratory and radiological criteria for the definite diagnosis of PJI. These criteria for a definite diagnosis are based on the possibility to point out the presence of sinus tract communicating with prosthesis at radiological evaluation and the evidence of a pathogen isolated by culture from two separate tissue or fluid samples obtained from the affected prosthetic joint.

Furthermore, the diagnosis is possible when four of the following six criteria occur: high ESR or CRP concentration, high synovial white blood cell (WBC) count, high synovial neutrophil percentage (PMN%), purulence in the affected joint, pathogen isolation in one culture of peri-prosthetic tissue or fluid, greater than five neutrophils per high-power field in five high-power fields observed in histologic analysis of periprosthetic tissue at 400 times magnification. But we have to consider that the lack of these conditions does not exclude definitely the infection. Imaging and physical examination have a poor role for the diagnosis.

Furthermore, we want to mark the importance of patients' clinical examination and the value of accurate clinical assessment of a suspected infection. The first clinical elements that create suspicion of infection are sinus tract or persistent wound drainage, acute onset of painful prosthesis or chronic painful prosthesis [5]. The first important step in presence of suspected infection is the examination of clinical history [6]: the physicians have to evidence peri-operative risk factors as prolonged surgical time, tissue morbidities, need for blood transfusion, and excessive use of antibiotics. Furthermore an accurate analysis of pathological risks is necessary; in fact, different pathologies can increase the risk of prosthesis infections: previous infections, obesity, diabetes mellitus, immunodeficiency, and malnutrition or drugs therapy. The clinical assessment provides more details for the suspicion of infection. During physical examination, the surgeon can find the typical inflammation signs as swelling, reddening, pain and loss of function [7]. Zajonz et al. found that the most frequent sign was loss of function (95%), followed by pain (85%) and swelling, furthermore only 22% of patients presented fever and 14% had feeling of illness but 19% had fistula as primary sign of infection [7].

In case of suspected infection, laboratory tests are mandatory. A lot of exams are available but different studies evidenced the role and the utility of each exam.

CRP and ESR seem to be tests with high sensitivity, but with a low specificity. In case of high values of ESR and CRP and clinical suspect for diagnosis, arthrocentesis for etiological diagnosis could be indicated [8].

So, for the definite and etiological diagnosis the physician has to perform an accurate arthrocentesis with adequate precautions (stopping antibiotics, add EDTA into the tube for the WBC count to be performed within 24 h) and obtain synovial liquid for biochemical, cytological and microbiological examinations. One of the most used and studied examination is the leukocytes count. Leukocytes Count in knee synovial fluid, cut-off positivity $\geq 1.7 \times 10^9$/l leukocytes ($\geq$ 65% neutrophils), showed in different studies high sensibility (from 78% to 94%) and high specificity (from 86% to 96%) [4].

New perspectives in IL-6 value, index of early infection, it seemed to have 100% sensibility but currently is not available in all laboratories. Actually, another perspective is represented from a synovial biomarker named Alpha Defensin, which demonstrates a high rate of specificity and sensibility [8].

Leukocytes Esterase shows a good sensibility and specificity but it's still undergoing study [9].

About microbiological examination, no predictive values found for Gram or Methyene Blue dye, instead of cultural examination that shows as the most reliable examination with a poor specificity [10].

To confirm the suspicion of infection, radiological findings with available serial images are important and useful in examination of patient with PJI. The most important and characteristic features, evidenced in different studies, to evaluate in X ray examination are periosteal thickening, osteolysis, trans-cortical fistulas [11]. Anyway, we have to consider that loosening of the prosthesis and areas of osteolysis can be present even in the absence of infection. Della Valle et al. in 2011, [12] demonstrated that Bone Scintigraphy with technetium-99m or marked leukocytes had an 81% diagnostic accuracy.

About PET, Reinartz, et al. evidenced a diagnostic accuracy of 83% [13], although it has yet a limited role and it's not mentioned in AAOS recommends.

The final step in diagnostic management of PJI provides intraoperative inspection, histopathology, 3 to 6 cultures and prosthesis ultrasonication. From literature, we can assert that intraoperative inspection with Gram stain has a good specificity (99%), although it has a low sensibility (27%) [8] and it's not mentioned in AAOS recommends [12]. The cultural examinations, instead, has a variable sensibility (60% to 80%) and a specificity depending from the number of samples [14]; some limitations to use this examinations are the necessary stopping of antibiotics 2 weeks before exam and a long time incubation of 7-14 days. At least, studies on sonication, used for prosthesis removal, demonstrated a sensibility of 78.5% and a not detected specificity [15].

If a microorganism is difficult to culture or identify by other

methods, pieces of the microorganism's genetic material it can be identified by genetic tests. This genetic material consists of nucleic acids: deoxyribonucleic acid (DNA) or ribonucleic acid (RNA) [16]. The PCR technique is used to produce many copies of a gene from a microorganism, making the microorganism much easier to identify [17].

Nucleic acid–based tests can sometimes be used to check the microorganisms for genes or gene mutations that make the microorganism resistant to a drug. However, these tests are not completely accurate because not all resistance mutations are known. Thus, tests cannot check for all the genes for resistance that may be present. Also, these tests are expensive, not widely available, and available for only a few microorganisms.

NEW TRENDS IN "TREATMENT"

The current literature confirms that the treatment of infected total knee replacement is still one of the worst complications in this type of surgery. These patients often need a complex and expensive treatment, associated with longer length of stay and lower outcomes.

The aim of the treatment is the eradication of the infection and the recovery to a functional knee.

The treatment options include the antibiotics therapy, irrigation and debridement, double-stage revision or single stage revision and rarely arthrodesis or amputation.

Antibiotics therapy cannot eradicate a deep infection alone and can be considered as an option only in few conditions such a low virulence microorganism or susceptible to oral antibiotics, very well-fixed implants, severe patient's conditions that contraindicate an operative procedure [18].

Irrigation and debridement recommended in cases with infection within 4 weeks after primary surgery or in case of acute haematogenous Gram + with stable implant. This treatment requires aggressive debridement of all foreign and affected periarticular tissues associated with irrigation with up to 9 litres of solution on pulsated washing [19].

Furthermore, a scrubbing of every retained component is recommended and every item, as scrub, gloves, etc., must be changed for every component [18].

This strategy is indicated only in immunologically optimized patients and low virulent organisms, always associated to antibiotics therapy and should be done in case of any other surgery. The results are hardly foreseeable and the success ranging is between 0% and 89% [20].

Double-stage revision is the most successful alternative for infected total knee replacement and is associated with success rate over 90% [21]. However, the current literature doesn't provide clear indication for double-stage revision. The author's opinion is to reserve this treatment to chronic infections, virulent organisms, immunosuppressed host and failure of the other less invasive treatment options [18].

The first step requires removal of all the knee components, irrigation and debridement and implantation of static or dynamic antibiotic-impregnated spacers (with vancomycin, tobramycin or gentamicin) [22]. These spacers release high concentrations of antibiotic locally promoting infection eradication. After surgery is mandatory to continue the antibiotic treatment for at least 6 weeks. After this period, if there are no signs of persistence of infection, a second stage is planned. The second stage requires removal of the cement depot, another irrigation and debridement time and new implant of knee components [23].

Single-stage revision consists of removal of all components, abundant irrigation and debridement, and implantation of new knee components impregnated with antibiotics cement. All the components are irrigated with dilute betadine antiseptic solution before suture. After surgery, the patients undergo to 6 weeks of antibiotics therapy (two weeks of I.V. and four weeks of oral therapy) [24]. This technique is used in case of mild symptoms of infection without fistulae, single Gram + bacteria, non-resistant and non-virulent, healthy hosts and adequate soft tissue coverage. The results are satisfactory, with rates of infection control between 73 and 93%. Several authors prefer this technique considering the need for a single operation, lower costs, decreased morbidity and improved functional results [25].

Arthrodesis is usually chosen after two-stage revision failure and is considered, with amputation, as a salvage option. There are no current guidelines about indications but the predominant opinion is to consider this surgery in case of disruption of extensor mechanism in young patients with immunosuppressed system, single joint disease and poor soft tissue that require wide reconstructions [26]. The arthrodesis can be done by external fixation, intramedullary nailing or plate fixation. The results of arthrodesis by intramedullary nailing are a union rate of 96% as compared to 67% with external fixation, but the risk of recurrency is higher in nailing (8.3% vs. 4.9% with external fixation). The success of the infection eradication reaches 94% [27].

Amputation should be only considered in life threatening systemic sepsis or persistent local infection associated with massive bone loss. 5% of patients with TKA infections need amputation [28].

CONCLUSION

In conclusion, the current guidelines about infection in total knee replacement are incomplete and don't offer to practitioners standardized treatment algorithms. The treatment's choice depends on several factors (patient conditions, virulence, bone loss, skin conditions, acute or chronic situation) but is mainly based on the prevention of infective complications to reduce the need of revision surgery [12].

Though no standardized guidelines exist about management of infected TKA, evidenced based practice towards this type of complication should be used. Clinical History and Clinical Examination are still at the base of all diagnostic algorithms.

The patients with painful implants must be considered possibly infected until contrary proves. ESR and RCP, after the clinical approach, are the second step. Proper timing and a clean practice should be conducted for arthocentesis. "Imaging", though not mentioned in recent AAOS recommends, could be still useful for indirect features.

Cultural exam is extremely reliable in intra-operative surgery, while sonication has good future perspectives

Good perspective has been found for synovial fluid biomarkers too, such as alpha-synuclein.

After diagnosis, every treatment should have specific indications.

Success rate of every kind of treatment depends on several factors, such as patient health, virulence, etc.

Today, the second-stage revision has the best success rate, but we think that the best treatment is surely "prevention".

CONFLICT OF INTEREST

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