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Original article

Acute periprosthetic knee infection: is there still a role for DAIR?

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Summary. *Background and aim of the work:* Periprosthetic knee infection is a rare complication associated with prosthetic failure; incidence change from 0,4-2% of primary total knee replacement and 5.6% in revisions. Indications for debridment, antibiotics and implant retention (DAIR) are early acute infections or acute delayed infection. Aim of the work is to check if this technique is still a successful in early infections. *Methods:* We have analyzed recent literature data on DAIR and all DAIR procedures in our clinic in the last 10 years, the mean time between onset of symptoms and surgery, the mean antibiotic therapy duration and results we have obtained. We evaluate the diagnostic process and different treatments in early knee periprosthetic infections, especially the DAIR approach. *Results:* If correct indications are followed, DAIR has a success rate in 31-100% of the cases; if it is applied in late chronic infection the success rate is 28-62%. In our experience DAIR has an 80% success rate: in 20 patients treated with DAIR we had 4 failures. *Conclusions:* DAIR can be considered a successful treatment, but it depends from individual patient factors, from the microorganisms involved, from the duration of antibiotic therapy and from correct choice in timing and in execution of DAIR by the orthopedic surgeon. (www.actabiomedica.it)

Key words: knee, periprostethic, acute infection, debridement

Introduction

Epidemiology

The stunning improvement in the last decades in knee replacement had unavoidably involved a significant rise in periprosthetic infections, although the rising in materials and techniques maintain a stable infection's rate.

Periprosthetic knee infection is a rare complication associated with prosthetic failure; incidence change from 0,4-2% of primary total knee replacement and 5.6% in revisions, even if these numbers seem to be underestimated in consequence of many asymptomatic infections that doesn't come to the attention of the surgeon (1). This improvement means that the absolute number of infections will remain significant, becoming an important complication, in terms of high morbidity and substantial costs to healthcare system (1, 2). Incidence of early knee Periprosthetic infections is 0,39% for first implants and 0,97% for revision knee replacement (3). An early diagnosis and a specific treatment represents than a primary goal in periprosthetic infections management.

Risk factors

We can identify many predisposing factors who can stand under a prosthetic infection. They are usually divided in generic and specific factor. General factors are all those conditions that may favor the onset of an infection, not necessarily periprosthetic: advanced

age, obesity, malnutrition, immunosuppression, therapy with steroid, diabetes, bladder catheter, high ASA score and concomitant skin infections. Specific factors are all those conditions that may favor a periprosthetic infection: rheumatoid arthritis, prosthetic revisions, duration of the surgery, hematomas and superficial wound infections (4, 5).

Classifications

Prosthetic joint infections were classified according to Tsukuiama's classification (6) on the base of the development of symptoms: early and late infections occur when symptoms appear within or after 4-6 weeks from the implantation respectively. Trampuz et al in 2008 (7) has modified temporal criteria of infection: he has defined early infection that occurs within 3 months from the surgery, with main involvement of highly virulent patogenous acquired during implant surgery (such as S. aureus or gram-negative bacilli); delayed infection that occur from 3 to 24 months from surgery, caused by less virulent organisms (coagulase-negative staphylococci) and late infections as the consequence of a haematogenous seeding from a remote infection.

Following Trampuz revision of Tsukaiama's classification, recently early infection temporal criteria have been back at 4 week from surgery and "acute delayed" infection has been added in all cases whose onset of symptoms are less than 4 weeks, not depending from the surgery data (8, 9). This classification evidence both situations (early and acute delayed infection) when debridement, antibiotics and implant retention (DAIR) may be used. For this reason, in our opinion this classification is the most reliable and it's used in our daily practice.

With this paper we analyze recent literature data and, considering results in our experience, we try to understand if DAIR is still useful or not.

Matherial and methods

We have analyzed recent literature data on early knee periprosthetic infection about diagnostic process and different treatments. We focus on DAIR technique, especially in temporal criteria, in surgery details and results of recent paper. Moreover, we have analyzed all DAIR procedures in our clinic in the last 10 years, the mean time between onset of symptoms and surgery, the mean antibiotic therapy duration and results we have obtained.

Results

Diagnosis

The diagnostic process of prosthetic joint infections is a complex challenge due to the absence of a clinical or laboratory test capable of achieving ideal accuracy for the diagnosis. Diagnosis is than obtained combining a variety of tests, including signs and symptoms, laboratory tests, histopathology, radiography. Often, in early infections, local signs may be clearer than in a chronic situation.

Symptoms

Local symptoms, like pain, swelling, hematomas or dehiscence of the surgical wound may alarm for an acute deep infection. The presence of systemic symptoms like fever or even a systemic septic picture, are highly suspect. The presence of a sinus draining purulent material must draw our attention for an infection not confined only at the skin (10).

Radiologic assessment

Radiography in early infection is usually useless. In fact, while chronic infections may cause bone loss and evidence of loosening, in acute forms are radiographically silent. It may help only to exclude other causes of joint pain. US may be helpful to study swelling area, synovial thickening, or to be a guide for aspiration or biopsy (2,10).

Laboratory findings

Routinely laboratory tests are aspecific in acute infections. High levels of CRP or a high count of WBC are unhelpful as they can usually be elevated for 30 to 60 days after a knee replacement. Persistent elevation, however, raises the possibility of infections (11).

Different biochemical markers have been suggested for use in the diagnosis of acute PJI. Peak of Interleukin-6 concentration are normally recognized two days after a knee replacement and rapidly return to normal values. Elevated levels of procalcitonine have been noted in patients with systemic bacterial infections. Soluble urokinase-type plasminogen activator receptor is a glycoprotein that has been found to increase in PJI (10).

Many studies pointed in synovial leukocyte count and PMN% in the differential. While in chronic infections these values have been reported from 1100 to 4000 cells an 64 to 69% respectively, in acute forms the levels are much higher (approximatively 20.000 cells and 89% respectively) (11). Synovial fluid leukocyte and granulocyte counts represents than a simple, rapid and accurate methods for differentiating PJI from aseptic failure (studies have shown this to be a highly discriminatory diagnostic test with a sensitivity of 89.5 to 94.0% and a specificity of 88.0 to 91.3% for the synovial fluid leucocyte count and a sensitivity and specificity of 89.7 to 97.0% and 86.6 to 98.0%, respectively, for the percentage of neutrophils).

Similarly, the alpha-defensin protein, an antimicrobial peptide, is secreted into the synovial fluid by neutrophils in response to pathogenic presence; its integration into pathogen's cell membrane causes rapid killing of the pathogen, giving an antimicrobial support to the immune system. The dosage of a-defensin in synovial fluid has shown a high sensitivity and specificity (97.4% and 95.8% respectively), confirmed by our experience data (12, 13).

The leukocyte esterase reagent (LER) test strip is an enzymatic test estimates the leukocyte count in urine. Although the leukocyte esterase reagent test wasn't developed for synovial fluid and is not a specific immunoassay, it has been found to be useful for the diagnosis of PJI and is being used clinically for that purpose. It's an economic (25 cent $) and a speedy (1 minute) test. We started using this technique few months ago so we still do not have definitive results (14-17).

Microbiology

Many microorganisms can sustain a peri-prosthetic infection. Coagulase-negative staphylococci (CoNS) are the bacteria most frequently isolated (30-43%), followed by Staphylococcus aureus (12-23%), mixed flora (10-11%), etc. In 11% of the cases no microorganisms are detected. Unusual pathogens like Candida spp or Brucella Spp have also been reported. A correct microbiological diagnosis is fundamental for an adequate therapeutic approach (18).

Diagnostic criteria

Obviously, the "gold standard" for the diagnosis of PJI is represented by the isolation of a pathogens from fluids or intraoperative periprosthetic tissues. The Infectious Diseases Society of America (IDSA) suggest that a set of five or six samples (minimum three). We can speak of PJI after the isolation of the same microorganism from two or more intraoperative specimens (10).

Musculoskeletal Infection Society (MSIS) (18) identified specific criteria for diagnosing a prosthetic joint infection. Thus, we can speak of PJI when:

1. There is a sinus tract communicating with the prosthesis; or
2. A pathogen is isolated by culture from at least two separate tissue or fluid samples obtained from the affected prosthetic joint; or
3. Four of the following six criteria exist:
   a) Elevated serum erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP) concentration,
   b) Elevated synovial leukocyte count,
   c) Elevated synovial neutrophil percentage (PMN%),
   d) Presence of purulence in the affected joint,
   e) Isolation of a microorganism in one culture of periprosthetic tissue or fluid, or
   f) Greater than five neutrophils per high-power field in five high-power fields observed from histologic analysis of periprosthetic tissue at x 400 magnification.

PJI may be present if fewer than four of these criteria are met.

Biofilm role

Microorganisms, after the adhesion to the orthopedic implants, starts to proliferate, organizing micro-

colines surrounded by a self-produced extracellular matrix (slime), composed of exopolysaccharides, proteins, teichoic acids, lipids and extracellular DNA (1). The growth of the colony and the maturation of the biofilm introduce the microorganisms in a slow- or non-growing (stationary) state, due to the low level of metabolic substances. The bacteria, submerged in biofilm, are protected from host immune responses and may demonstrate a reduced susceptibility to antibiotics because of changes in metabolic processes and poor diffusion (19).

The maturation of biofilm is not immediate, so in its development phase can be attacked with a careful debridement and a specific antibiotic-therapy, without the need to remove the whole implant.

The importance of an early and accurate diagnosis followed by a rapid management should be check, as already mentioned, in the possibility of a less radical treatment characterized by a DAIR treatment (debridement, antibiotics and implant retention) compared to the necessity for chronic infections of a 2 stages treatment.

Treatment

The target in the treatment of early periprosthetic infection are a least invasive surgery, an improvement in range of motion, a better quality of life and a reduction of mortality.

Various approaches exist to manage this kind of infection: debridement, antibiotics and implant retention (DAIR), one-stage revision, two-stage revision, permanent resection arthroplasty, antibiotic therapy alone, arthrodesis or amputation.

DAIR

According to Qasim et al (20), DAIR consists in retention of the implant, in an aggressive open surgical debridement of infected soft tissue, in a large volume high-pressure lavage and change of polyethylene in the last operation. Antibiotic therapy must be start as soon as possible and then changed after the result of microbiology cultures.

Kim et al (21) suggested some ideas to do a better DAIR, even if his paper is on total hip arthroplasty: lavage should be pulsatile and at least 3-6 L; if liner is replaced it should be submerged in 97% ethanol for 10-15 minutes; the surgical site should be irrigated with a povidone-iodine solution for 5-10 minutes and after with 3L of normal saline; use of drain at the end of the procedure. VAC medication can be considered as a safe procedure in these cases of acute infection (22, 23). The use pulsatile lavage is in discussion. Many authors (10, 20, 21, 24, 25) suggest a high-lavage system; Soriano and Schwecter (26, 27) showed the same results with high and low lavage system; Hassinger in 2005 (28) affirmed that pulsatile system causes a bacterial infiltration in soft tissues and Boyd (29) said that it cause a microscopically damage to soft tissue in 2004. In any case, most of author suggest pulsatile lavage system. Schwechter et al (27) suggest lavage with chlorhexidine gluconate 0.05% in MRSA colony: they found a most effective action in reducing bacterial colony.

Criteria

As indicate before, recently classification has been update with the definition of acute hematogenous infection or acute delayed infection. DAIR is recommended is these two situations (8, 9, 19). Persistence of a sinus has been shown to be a risk factor as the immunocompromised patients: they can be considered a risk for failure and a contraindication to DAIR (20).

Liner

Following correct indication and according to Qasim et al (20) and to Vilchez et al (30), our idea is to do DAIR only one time, using high-pressure lavage, and change in all of case the liner: Laas and al in 2014 (31), Choi in 2011 (32) and our experience with coltures of sonicated prosthetic components confirm that in most of cases cultures are positive in polyethylene liner; this suggest a predisposition of bacteria to join polyethylene surface, and in this way to develop the formation of bacterial biofilm and don't change it is a cause of early failure of the implant.

Antibiotic therapy

The antimicrobial agent should have activity against surface-adhering, slow-growing, and biofilm-

producing microorganisms. Antibiotic therapy must be started after the first surgery with a large specter therapy, waiting for result of analysis of intraoperatory samples to do a more precise therapy. Microorganism are different between early and late infection (33); in early infection Staphlococcus is the more frequent, with streptococcus and enterobacteriaceae; in late infection main microorganism are Propionibacterium, peptostreptococcus and aerobic gram positive bacillus. Duration of therapy is in dicussion. Generally, after 15-30 days of endovenous therapy, it is shifted in oral therapy and then continued for 3-6 months; some authors continue oral therapy until 2 years (19, 30, 34-36). In our clinic, according with Clinics of Infectious Disease of our hospital, we start antibiotic therapy after the debridement generally with daptomicin and rifampicin (in some case with piperacillina/tazobactam); use of daptomicin is recommended for its rapid action and use of rifampicin is recommended in association and not alone (37). We continue this therapy until the complete result of intraoperatory sample cultures; at this time, we shift in oral focused antibiotic therapy and we continue it for about 3-6 months. Generally, it's recommended to continue antibiotic therapy at least 5-6 months in infection of knee arthroplasty.

One-stage and two-stage surgery

In early infection one or two stage are not suggested. We consider this solution only if DAIR failed.

According to Bassetti et al (38) one stage should be done when we have intact soft tissue, with the presence of low virulence microorganism, in a patient with few comorbities; one stage is often used in hip infection. Following results of intraoperative frozen section (39), two stage revision is suggested when we have damaged soft tissue, with high virulence microorganism (38); generally, we find these condition in knee arthroplasty infection.

Results

A success in DAIR is consider if we have resolution of symptoms, normalization of blood exam and other sign of failure, like mobilization of the implant or osteolysis. Failure of DAIR is consider when there are recurrent symptoms of infection, isolation of the same or different organism in sequent cultures, surgery with remove of the implant, death. Stanley 2013.

Literature

Results are various and they are not homogeneous: the authors don't follow the same classification so the results can't be comparable.

In a recent paper, Qasim et al (20) in their review resume all recent works that analyze DAIR in infected total knee replacement: if correct indications are followed it has a success rate in 31-100% of the cases; if it is applied in late chronic infection the success rate is 28-62%. Furthermore, acute postoperative infection has shown better results than acute delayed infection. 7 studies of 23 has a low success rate (<50%) in early infection. It depends on microorganism, if MRSA or St. Aureus is involved the success rate is low. It depends on changing the liner or not. It depends on timing: there is no consensus in literature; most of authors consider the best time within a month from the onset of symptoms (6, 30, 35). Moreover, in our experience we note that it's not easy to establish the first day of onset infection, because symptoms and local signs of post-operative period can hide the begin of acute infection. Our idea, that find consensus in literature, is to suspect infection in each follow-up of the patient; if infection is confirmed surgery should be done as soon as possible.

Qasim et al. affirmed that DAIR should be do only one time and not repeated; if surgeon must repeat the procedure, it is considered a failure, and a success rate after the following two stage revision surgery is going to be lower.

Our experience

Since 2007 we had 20 patients treated with DAIR. 8 patients had a revision surgery and 12 had a first implant surgery. In all of cases we did DAIR by 4 weeks from first implant or symptoms appearance: mean time between onset of symptoms/first implant and DAIR was 21,4 days. In 4 cases we had an early acute infection, in 16 cases we have acute delayed in-

fection. In 8 cases we use VAC medication, 2 of this failed. Mean duration of antibiotic therapy was 5,1 months. We have 4 failure. We found Staphilococcus meticillinus sensible only in 4 case, and one of this failed. In 4 case cultures was negative.

Conclusion

DAIR yes or no?

In according with Qasim et al (20), we conclude that DAIR is good therapeutic choice, but temporal criteria are mandatory. Outcome of DAIR is better when duration of symptoms is short, when there are microorganisms with multiple and elevated sensibility to antibiotics and when implant has a good stability. In Putho et al paper (10), DAIR outcomes are better with careful patient selection and with the use of antibiotics active against biofilm-swelling bacteria. Bad outcome was find in patients with important co-morbidities, when S. Aureus is involved and when liner is not changed (1, 27).

However, there is no consensus in literature. Some author said that success rate of DAIR is comparable with 2 stage revision (40, 41); other author said that DAIR has an high success rate (10, 42, 43, 44), as shown in Qasim review, other authors affirm that DAIR has a bad outcome (11, 45, 46).

2 stage or one stage revision should be postponed as far as possible because they are long time treatments and because they are complex operations, with high risk of local complications and a long hospitalization (1, 20).

In borderline situations, when we visit a patient with onset of symptoms more than 1 months before or when we don't know the microorganism involved, we suggest a treatment attempt with DAIR, especially in patients without important co-morbidities.

Salgueiro et al in their study didn't find a significant difference in outcome in patients undergoing 2 stage revision following failed DAIR versus 2 stage revision as an initial approach (40).

In conclusion, DAIR can be considered a successful treatment, but it depends on individual factors of the patient, on the microorganisms involved, on the duration of antibiotic therapy and on correct choice in timing and in execution of DAIR by the orthopedic surgeon.

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