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Review

Periprosthetic joint infection in total ankle replacement: which are the current diagnostic criteria?

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Abstract. *Background and aim:* Periprosthetic joint infection (PJI) is among the most common complications of Total Ankle Replacement (TAR) and its management may be challenging. We set out to define which are the criteria currently used to diagnose PJI after TAR. *Methods:* This PRISMA-compliant systematic review was registered in the Open Science Framework. Multiple databases were searched including clinical studies in which PJI after TAR was diagnosed and treated. Data were harvested regarding the cohort, the study design and the diagnostic criteria for PJI. Risk of bias was assessed using the modified Coleman Methodology Score (mCMS). *Results:* Six papers (122 infected TARs) published between 2012 and 2022 were included in this review. Ankle pain with swelling and unexplained increased local temperature were the most common clinical findings leading to a suspicion of PJI. In 100% of cases the diagnosis was confirmed through synovial fluid analysis associated with positive blood tests. In all the revision surgeries intraoperative cultures (at least 3) were performed. In 109 ankles (90%) there was a microbiological isolation. Out of these, 38 (35%) were single organism infections by Staphylococcus coagulase negative and 37 (34%) were single organism infections by Staphylococcus Aureus. The mean mCMS was 37.6 out of 100. *Conclusions:* There is a lack of diagnostic criteria specific for PJI after TAR. Clinical and laboratory tests inspired to the knowledge in total knee and total hip arthroplasty are generally adopted in the field of ankle arthroplasty. The quality of evidence for studies included in this review was poor (www.actabiomedica.it).

Key words: ankle, replacement, prosthesis, infection, periprosthetic, joint

Introduction

Total Ankle Replacement (TAR) and Ankle Arthrodesis (AA) are the most common surgical option to tackle end-stage ankle osteoarthritis (1–4). While both techniques are effective at providing pain relief and improvement of function and quality of life (3), only TAR allows to preserve some range of motion of the ankle joint, which is considered an advantage since it theoretically improves the gait and reduces the knock-on effect on the adjacent joints (subtalar joint, Chopart joint, knee joint) and the risk of mechanical overload (3).

Complications of TAR have been widely described in literature. Among those, periprosthetic joint infections (PJI) are reported with a rate between 0 % to 13 % (5) and are feared as potentially devastating events, leading to the failure of the implant, difficult resolution of the infective process and complex revision surgery (5). Diagnostic criteria for PJI in TAR are inspired to the body of the knowledge built upon investigation of infected Total Hip Replacements and Total Knee Replacements (6). As a matter of fact, although the literature is constantly reporting and increasing number of TARs implanted throughout the world, the overall amount of prostheses of the ankle is certainly

way lower THRs and TKRs (7,8). Although fewer in numbers, the diagnosis of infection is usually impactful on the quality of life of the patient, as such it would be advisable to reach an agreement regarding the diagnosis and the treatment of these challenging conditions.

With this background, we set out to define which are the criteria currently used to diagnose PJI in TAR and to evaluate the trends in surgical management. We hypothesized that 1) specific diagnostic criteria have been proposed for PJI after TAR and that 2) such criteria have been commonly used in published studies in this area.

Methods

Protocol and registration

This systematic review followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement. It was registered in the Open Science Framework (Project: osf.io/57qks)

Eligibility criteria

The inclusion criteria were as follows: studies reporting data about cohorts of PJIs after TAR in patients aged between 18 and 85 years; studies including a sample size larger than 5 ankles; minimum follow-up of 12 months; randomized, quasi-randomized, prospective and retrospective cohort studies, case series, technical notes; published in any language; full text availability either on line either after direct contact with the authors.

Exclusion criteria were the following: data on skeletally-immature patients; case reports, biomechanical studies, cadaveric studies, expert opinions, letters to the editor, studies on animals and instructional courses. Narrative or systematic reviews were also excluded from the study but references were double checked in order to identify potential eligible studies.

Information sources and search

Pubmed, Embase, Cochrane Library and Scopus databases were searched from the earliest entries through October 13, 2022 with the following key words and Boolean operators: (ankle) AND (arthroplasty) AND (infection). Additional studies were identified in the bibliographies of articles. Two reviewers (AI and DDG) independently screened the results of the research, then the full text of eligible studies was analyzed. Disputes were resolved by the senior author (AB). Unpublished studies and gray literature were not considered.

Data charting and items

Data were charted independently by two investigators (AI and DDG) using an Excel sheet. Data were harvested regarding the cohort, the study design, the diagnostic criteria of infection. A particular attention was paid to the role of 1) clinical signs and symptoms leading to the suspicion of PJI, 2) synovial fluid analysis through arthrocentesis, 3) blood tests (White Blood Cells (WBC) count, C-reactive protein (CRP) and Erythrocyte sedimentation rate (ESR) and 4) histological findings and microbiological cultures.

Risk of bias

The modified Coleman Methodology Score (mCMS) was used to assess the quality of studies included, as in previous foot and ankle literature (9, 10), ranging from 0 to 100. Two investigators performed the mCMS assessment twice (AI and AB), with an interval of 10 days, then discussed the scores when more than a two-point difference was present, until consensus was reached. A score higher than 85 was considered excellent, good from 70 to 84, moderate from 50 to 69 and poor when less than 50.

Synthesis of results

Data were reported as average value, standard deviation (SD), range values and proportions. All analyses were performed using STATA statistical software package (Version 16.0, StataCorp, 2019).

Results

Studies included

The initial search yielded 536 papers, after duplicates removal 313 records were screened. Of these

only 6 studies met the including criteria for a total of 122 infected TAR (11–16). The selection procedure of the reviewed papers is summarized in Figure 1. The Level of Evidence of the included studies was Level III (3 studies) and Level IV (3 studies, 50%). Three studies (50%) had a retrospective noncomparative design (11,12,15).

Characteristics of cohorts

The mean sample size for studies included in this review was 20.3 ankles diagnosed with PJIs after TAR (SD 10, range 6 to 34). The mean age for patients included was 61.5 years (SD 3.5, range 55 to 65.5) and 48% were female (SD 12.3, range from 35 to 64). The mean follow-up reported was 37.9 months (SD 9.8, range from 26 to 50) (Table 1).

Diagnosis of PJI

The infection rate (reported only in 4 studies) ranged from 3.2% to 15% (mean 6.8%; SD 4.8). The type of infection was acute in most of the cases included (79 cases, 64.7%). Details regarding the diagnostic procedure adopted by different authors have been reported in 100% of the studies. Synovial fluid analysis and blood tests (WBCs, CRP and ESR) were performed in 100% of cases (Table 2). After microbiological culture, a microorganism was isolated in 109 cases (90%). Out of these, 38 (35%) were single organism infections by Staphylococcus coagulase negative and 37 (34%) were single organism infections by Staphylococcus Aureus. No authors have included imaging techniques as part of the criteria to diagnose PJI.

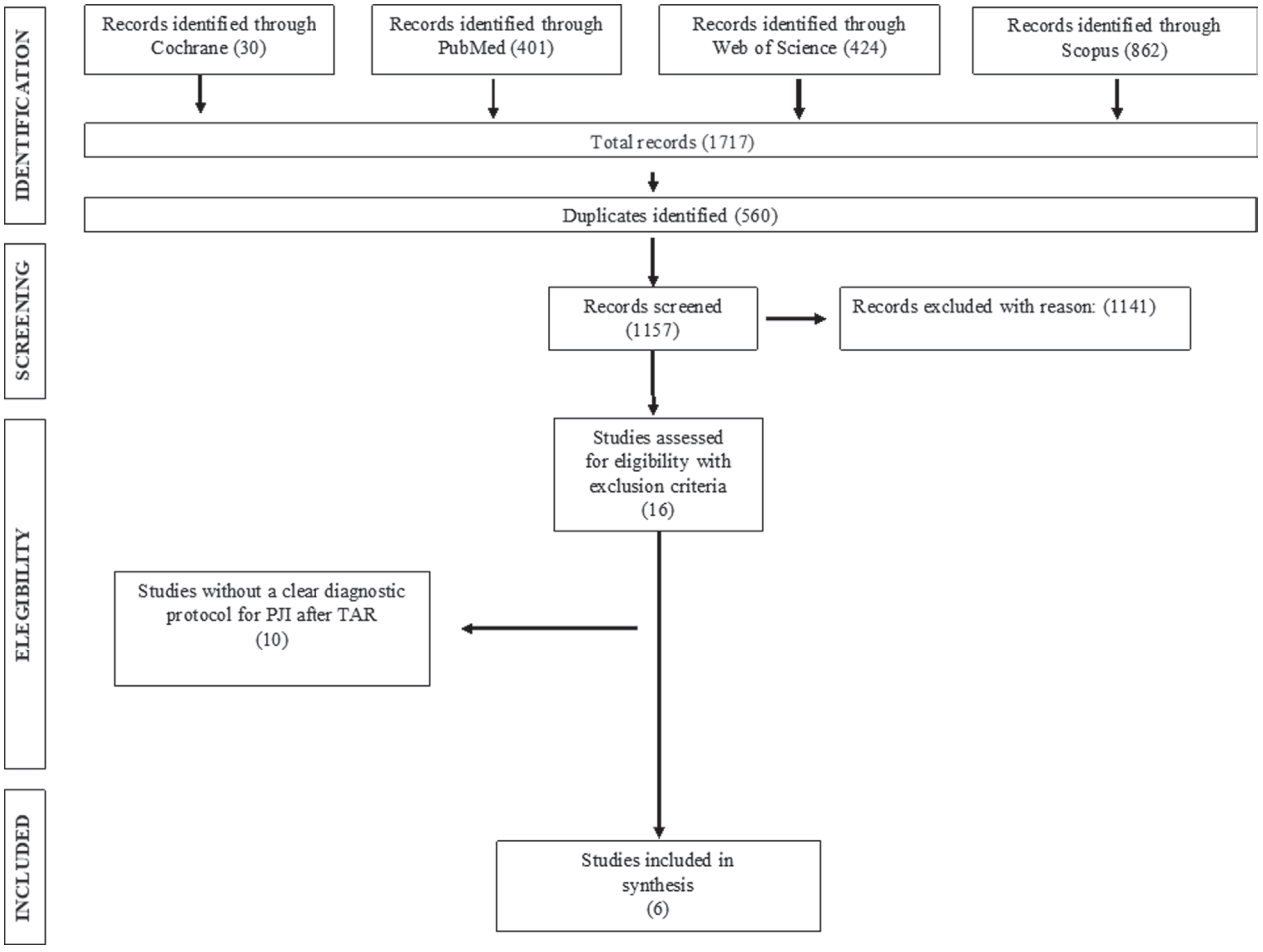

Figure 1. Flow chart for the selection of studies included in this review.

Table 1. Demographics and study characteristics for manuscripts included in this review.

First Author	Year	Study Design	LoE	Study Size	Female %	Age (y)	Acute Infect.	Chronic Infect.	Type of Implant	mCMS	Follow-up (m)
Ferrao et al.	2012	Retr – Non Comp	IV	6	-	63.5	3	3	-	39	34
Myerson et al.	2014	Retr – Non Comp	IV	19	42.1	65.5	15	4	Agility	34	26
Kessler et al.	2014	Retr – Comp	III	34	58.8	62.1	19	15	-	40	33.8
Patton et al.	2015	Retr – Comp	III	29	41.3	55	22	7	Agility	39	50
Lachman et al.	2018	Retr – Non Comp	IV	14	64.2	61	14	0	STAR	39	33.6
Pfahl et al.	2022	Retr – Comp	III	20	35	62.1	6	14	-	40	50

Study Design: Prosp, Prospective; Retro, Retrospective; Comp, Comparative; Non Comp, Non Comparative; LOE, Level of Evidence; mMCS: modified Coleman Methodology score

Table 2. Diagnostic parameters used by authors in primary studies for PJI after TAR.

First Author	Year	Joint Aspiration	ESR	CRP	WBC	Histology	Bacteria Isolation	Most Common Pathogen
Ferrao et al.	2012	6/6	6/6	6/6	6/6	6/6	5/6	S. Aureus
Myerson et al.	2014	10/19	19/19	19/19	19/19	19/19	7/19	S. Aureus
Kessler et al.	2014	34/34	34/34	34/34	34/34	34/34	34/34	S. Aureus
Patton et al.	2015	29/29	29/29	29/29	29/29	4/29	28/29	CNS
Lachman et al.	2018	7/14	14/14	14/14	14/14	14/14	14/14	S. Aureus
Pfahl et al.	2022	20/20	20/20	20/20	20/20	20/20	18/20	CNS

CNS: Coagulase-Negative Staphylococci; ESR: Erythrocyte sedimentation rate; CRP: C-reactive Protein; WBC: White Blood Cells

Discussion

Our literature research demonstrated a poor number of studies dedicated to the diagnosis of PJI in the setting of TAR. To date, all studies focusing in this area have adopted criteria proposed and validated in lower limb arthroplasty (7) but not specifically tested after TARs. Taking into account the growing number of TARs performed worldwide and the increasing life expectancy of the population (8) it's reasonable to expect a rise in the number of joint infections in this context, which is why a consensus aimed to establish which criteria should be adopted after TAR would be advocated.

To date, the criteria commonly adopted to diagnose a PJI after joint arthroplasty are the ones proposed by the Musculoskeletal Infection Society (MSIS) and then partly modified at the International Consensus Meeting (ICM) in 2013 (17). A further update has been introduced after the 2018 ICM through a scoring system aimed to quantify the risk of infection according to specific major and minor criteria (18). Upon review of the literature, we identified only one paper published in 2017 by Alrashidi et al. whereby the authors attempted to formalize the use of such criteria to diagnose PJI after TAR (6). However, in their Level V study the authors could only report data on the sensitivity and specificity of synovial fluid WBC in knee and hip arthroplasty, but no data was produced on TAR. Many other studies reporting results after TAR have included a few patients in which PJI occurred as

post-operative complication (19), however they generally did not report a subgroup analysis dedicated to infected ankles and as such we have decided to exclude them from our research protocol.

Of note, we noticed that all studies dealing with PJI after TAR mentioned a landmark paper published by Myerson et al. in 2014 (13) in which the clinical status was considered a crucial driver in the decision-making for cases where PJI was suspected but nor clearly confirmed by laboratory tests. In their paper, the authors stated that they considered swelling, inflammation, drainage or persistent wound problems as a possible sign of PJI. These findings led to perform a dry joint aspiration with subsequent culture and microscopy (12). Very importantly, if the aspirate was negative but the clinical suspicion was still present, the clinical findings were judged as more relevant to dictate the management protocol (12). It should be considered that this protocol was published just after the 2013 ICM definition for the diagnosis of PJI in which also inflammatory markers from blood tests were given a role as a minor criterion of infection. As compared to the PJI definition proposed by the 2013 ICM, the criteria proposed by Myerson appeared less strict and more based on the experience of the medical and surgical team. However, it should be emphasized that even the 2018 scoring system might bring to a 'grey area' where the diagnosis is uncertain and the final decision still depends on the physician.

This study is not without limitations. First, in this review we could include only 6 studies accounting for 122 ankles. However, this was due to strict inclusion criteria and to the paucity of literature available so far. Second, the lack of statistical analysis, which in turn was related to missing data in primary papers regarding the values of laboratory tests to diagnoses PJI. In the future, we would advocate that such values are reported in order to allow to test their sensitivity and specificity specifically in the area of TARs. Third, the final level of evidence of this review was only IV, since we could include only Level III and Level IV studies.

In summary, to date, the clinical suspicion of PJI after TAR (based on an inflammatory painful joint sometimes accompanied by systemic general symptoms) must always lead to perform blood tests and joint aspiration to test the synovial fluid. Until specific guidelines are produced, their interpretation should reflect what's been recommended by the International Consensus Meeting criteria for major lower limb joints. Of course, the presence of a sinus tract communicating with the joint should be considered a major criteria of infection for total ankle replacements as well.

Conclusion

There is a lack of diagnostic criteria specific for PJI after TAR. Clinical and laboratory tests inspired to the knowledge in the field of total knee and total hip arthroplasty are generally adopted after ankle arthroplasty. The quality of evidence for studies included in this review was poor. We advocate for clinical studies reporting raw data about all diagnostic and laboratory test used to confirm or disprove a suspicion of PJI after TAR in order to verify their sensitivity and specificity in this area and establish clear guidelines when approaching possibly infected TARs.

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