Follow us @BoneJointRes

Freely available online OPEN ACCESS

BJR

INFECTION

Can the oncology classification system be used for prosthetic joint infection?

THE PJI-TNM SYSTEM

V. Alt,
M. Rupp,
M. Langer,
F. Baumann,
A. Trampuz

Department of Trauma Surgery, University Hospital Regensburg, Regensburg, Germany

Cite this article: *Bone Joint Res.* 2020;9(2):79–81.

Keywords: Infection, Arthroplasty, Biofilm

Introduction

A major problem in prosthetic joint infection (PJI) is the lack of a generally used classification system although several different systems have been proposed in the literature.[1,2] The most frequently used classification of PJIs with early, delayed, and chronic infection proposed by Schafroth et al[3] only focusses on the time of onset of infection symptoms. However, PJIs are multifactorial complications after arthroplasty and involve different parameters, such as the host, the implant with the surrounding soft tissue and bone, as well as the causative microorganisms, which are of relevance for the treatment strategy and final outcome for the patient.[4,5] Therefore, these parameters should be taken into account in a classification concept for PJIs. McPherson et al[6] came up with a proposal for a staging system for PJIs that includes three categories: infection type (acute versus chronic), systemic host grade, and local extremity grade with significant correlation between the staging system and outcome parameters, particularly the relation of complication rates with worsening medical condition and a worsening local wound. This classification does not address the causative agent and the underlying implant, which both have an impact on the treatment decision process and outcome of PJIs. In conclusion, there is a strong need for an improvement in the classification of PJIs and the current editorial is intended to present a new idea for a new classification system for PJIs.

In general, new classification systems should allow professionals to derive treatment guidelines and prognosis for the disease. Another important aspect is that they should not be too complicated as this could prevent their use in clinical practice. On the other side, the use of established principles of other classification systems could help to enhance acceptance of a new classification.

One of the most widely and most successfully used classification systems in medicine is the TNM classification for malignant tumours in oncology. The basics of this system were developed in the late 1940s and early 1950s by Pierre Denoix and its eighth version was recently published in 2017,[7] which is used globally for the majority of malignant tumours. The principle of the TNM system is based on details of the primary tumour (T), regional lymph nodes (N), and distant metastasis (M). For each item, further details regarding the size and/or extent of the local tumour (T0 to T4), involvement of regional lymph nodes (N0 to N3), and differentiation on distant metastasis (M0 to M1) are used to guide treatment. Furthermore, the TNM system provides information for survival and helps to compare treatment outcomes from a clinical and scientific perspective. All these aspects are also of relevance for PJIs and the frequently used sentence “treat the infection like a tumour” describes certain similarities between tumours and PJIs, in particular the need for resection of affected tissue. These aspects have prompted the authors of this editorial to present the idea for a TNM classification for PJIs.

The above-mentioned crucial parameters for PJIs: type of implant including surrounding soft tissue conditions, the causative microorganism, and the host were taken into account and transferred to the three significant letters T, N, and M, which are the keystones of the TNM classification system in oncology and which are also used for the

Correspondence should be sent to V. Alt;
email: volker.alt@ukr.de

doi: 10.1302/2046-3758.92.BJR-2019-0134.R1

Bone Joint Res 2020;9:79–81.

PJI-TNM classification. 'T' represents the local situation of the tissue and the indwelling implant, 'N' stands for the causative non-human bacterial and/or fungal organisms, and 'M' for the morbidity of the patient for this new PJI-TNM classification. As with TNM in oncology, each item is further specified by numbers with increasing severity of the respective item, from 0 to 2 for T and N and from 0 to 3 for M. This is detailed in the accompanying infographic in this issue of *Bone & Joint Research*.[8]

Regarding the infected joint of the PJI, the name of the affected joint is put in front of the TNM letters in order to clearly state the affected body region, such as hip, knee, and shoulder. If it is a recurrence of infection, the letter 'r' is put additionally in front of the affected joint in order to emphasize reinfection.

T – Tissue and implant conditions

Local soft tissue and implant conditions are described and classified with the letter 'T' and significantly influence the treatment decision. T0 characterizes a situation with healthy soft tissue envelope (or small soft tissue defect not requiring plastic surgery coverage) with a stable implant. In T1 situations, the implant is loosened but sufficient soft tissue coverage is given. T2 cases are characterized by severe soft tissue requiring plastic surgery. For each item, the small letters 'a' and 'b' are used for the specification of the implant in order to allow for differentiation of standard implants ('a') versus revision implants ('b').

N – Non-human cells (bacteria and/or fungi)

Microbiological conditions and findings are considered in this category. It does not mainly focus on established but problematic classifications, such as early, late, acute, or chronic, but more on biofilm and antibiotic resistance profiles of the causative germs. N0 stands for an infection with immature biofilm formation. This is further specified to N0a and N0b as the pathogenesis in early postoperative (N0a) versus late haematogenous (N0b) should be acknowledged. N1 and N2 represent situations with mature biofilm formation, in which N1a stands for mature biofilm formation with 'non-difficulty to treat organisms' with bacteria being susceptible to biofilm-active antibiotics (e.g. rifampicin in staphylococci or fluoroquinolones in gram-negative bacteria).[9] In a so-called culture-negative infection, N1b is used. Infections with mature biofilm formation with difficult-to-treat bacteria (N2a) with resistance to the aforementioned antibiotics, polymicrobial infection (N2b), or fungi (N2c) are summarized under category N2.

M – Morbidity of the patient

The morbidity of the patient is of extreme importance for the treatment and prognosis of PJI and also for comparison of patient cohorts in clinical studies[10] and is, therefore, an integral part of this current classification as well.

The letter 'M' addresses the general health status of the patient using the Charlson Comorbidity Index as it enables reliable classification of the general health status of the host.[11] M0 patients are systemically not or only moderately compromised with a Charlson Comorbidity Index of 0 or 1. Patients with a comorbidity index of 2 to 3 are classified as moderately compromised M1 patients. M2 represents severely compromised hosts with a Charlson Comorbidity Index of 4 to 5. Patients who refuse surgical treatment (M3a) or would not benefit (M3b) or not survive surgical treatment (M3c) are categorized as M3 patients.

Treatment guidelines derived from the PJI-TNM system

Each classification should be able to derive treatment guidelines for specific situations. The PJI-TNM system offers this possibility with the following general recommendations.

In T0N0 cases, implant retention with irrigation and debridement can be considered as no mature biofilm formation, no difficult-to-treat bacteria, no soft tissue compromises, and a stable implant are present.

In all T1, T2, N1, and N2 cases, implant removal should be recommended due to loosened implants, severely compromised soft tissue, and/or major biofilm formation or fungi involvement.

M3a patients are not eligible for surgery and M3b hosts should be treated less aggressively as they do not benefit from major surgical treatment. M3c patients cannot be operated on due to host restrictions and are only eligible for non-surgical treatment, such as antibiotic suppression therapy.

There are certain limitations of this new classification. First, there is a risk of confusion of PJIs with malignant tumour disease when a patient's PJI is classified with the TNM system. However, the prefix PJI and the addition of the affected joint should minimize this risk.

Second, the use of the maturity of biofilm formation in the 'N' section cannot resolve the problem that exact time differentiation between immature and mature formation remains difficult to ascertain with current diagnostic methods. Nevertheless, its use is a step forward in the classification of PJIs, as it eliminates the need to limit classification to 'early' and 'late' and focusses more on the bacterial aspects of the underlying infection as mentioned above.

Furthermore, the use of the three letters T, N, and M with further sub-specification makes the classification more difficult to use than the simple differentiation between early, delayed, and late and seems to limit its practical use in daily clinical routine. However, the complexity of PJIs including details of the local infection situation, causative agent and biofilm maturity, plus the host comorbidity, justify a more detailed description of the situation.

In the next step, validation of this new PJI-TNM system regarding its accuracy and reliability in clinical routine is required, which is to be conducted by a planned prospective clinical trial.

In conclusion, we believe that this system contributes to significant improvements in the classification of PJIs for clinical routine and clinical studies in PJIs.

References

1. **Zimmerli W, Trampuz A, Ochsner PE.** Prosthetic-joint infections. *N Engl J Med.* 2004;351(16):1645-1654.
2. **Pellegrini A, Legnani C, Meani E.** A new perspective on current prosthetic joint infection classifications: introducing topography as a key factor affecting treatment strategy. *Arch Orthop Trauma Surg.* 2019;139(3):317-322.
3. **Schafroth M, Zimmerli W, Brunazzi M, Ochsner P.** Infections. In: Ochsner PE, ed. *Total hip replacement.* Berlin: Springer-Verlag. 2003:65-90.
4. **Kapadia BH, Berg RA, Daley JA, Fritz J, Bhave A, Mont MA.** Periprosthetic joint infection. *Lancet.* 2016;387(10016):386-394.
5. **Karczewski D, Winkler T, Renz N, et al.** A standardized interdisciplinary algorithm for the treatment of prosthetic joint infections. *Bone Joint J.* 2019;101-B(2):132-139.
6. **McPherson EJ, Woodson C, Holtom P, Roidis N, Shufelt C, Patzakis M.** Periprosthetic total hip infection: outcomes using a staging system. *Clin Orthop Relat Res.* 2002;(403):8-15.
7. **Amin MB, Greene FL, Edge SB, et al.** The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. *CA Cancer J Clin.* 2017;67(2):93-99.
8. **Alt V, Rupp M, Langer M, Baumann F, Trampuz A.** Infographic: Can the oncology classification system be used for prosthetic joint infection? *The PJI-TNM system.* 2020;9(2):in press.
9. **Zimmerli W, Sendi P.** Orthopaedic biofilm infections. *APMIS.* 2017;125(4):353-364.
10. **Cizmic Z, Feng JE, Huang R, et al.** Hip and Knee Section, Prevention, Host Related: Proceedings of International Consensus on Orthopedic Infections. *J Arthroplasty.* 2019;34(2S):S255-S270.
11. **Charlson ME, Pompei P, Ales KL, MacKenzie CR.** A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis.* 1987;40(5):373-383.

Author information
- V. Alt, Prof. Dr. med., Dr. biol. hom., Chairman and Head of Department,
- M. Rupp, Dr. med., Consultant,
- F. Baumann, PD Dr. med., Consultant, Department of Trauma Surgery, University Hospital Regensburg, Regensburg, Germany.
- M. Langer, Prof. Dr. med., Consultant and Deputy Director, Department of Trauma, Hand and Reconstructive Surgery, University Hospital Münster, Münster, Germany.
- A. Trampuz, Assist. Prof. Dr. med., Consultant, Charité – Universitätsmedizin Berlin, Berlin, Germany; Corporate Member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Center for Musculoskeletal Surgery (CMSC), Berlin, Germany.

Author contributions
- V. Alt: Formulated the idea for the new classification, Conceptualized the design, Wrote the manuscript.
- M. Rupp: Conceptualized the design, Wrote the manuscript.
- M. Langer: Created the figures, Wrote the manuscript.
- F. Baumann: Conceptualized the design, Wrote the manuscript.
- A. Trampuz: Provided scientific input from an infectious disease background, Wrote the manuscript.

Funding statement
- No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

ICMJE COI statement
- None declared

Acknowledgements
- None declared

Ethical review statement
- This study did not require ethical approval.