Original article

CD15 focus score: Infection diagnosis and stratification into low-virulence and high-virulence microbial pathogens in periprosthetic joint infection

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ABSTRACT

Introduction: The aim of the work was to validate the CD15 focus score for the infection pathology of periprosthetic joint infection in a large group and to clarify whether a stratification into low-virulence and high-virulence microbial pathogens is possible by means of the CD15 focus score (quantification of CD15 positive granulocytes).

Methods: The histopathology of 275 synovial tissue samples taken intraoperatively during revision operations (n=127 hip, n=141 knee, n=2 shoulder, n=5 ankle) was evaluated according to the SLIM consensus classification (SLIM = synovial-like interface membrane). Neutrophilic granulocytes (NG) were quantified by the CD15 focus score on the basis of the principle of focal maximum infiltration (focus) with evaluation of one field of vision (about 0.3 mm²). The quantification values were compared with the microbiological diagnoses taking into consideration the virulence groups of low-virulence and high-virulence microbial pathogens and mixed infection.

Results: The patients with positive microbiological findings (n=160) had significantly (p<0.001, Mann-Whitney U test) higher CD15 focus score values than patients with negative microbiological findings (n=115), the cut-off value being 39 cells per high power field (HPF). The CD15 focus score values of low-virulence microbial pathogens (n=94) were significantly lower (p<0.001, Mann-Whitney U test) than the values of high-virulence microbial pathogens (n=55), the cut-off value being 106 cells per HPF. Based on the microbiological diagnosis the sensitivity with respect to a microbial infection is 0.91, the specificity 0.92 (PPV=0.94; NPV=0.88; accuracy=0.92; AUC=0.95). Based on the differentiation of the CD15 focus score values between low-virulence and high-virulence microbes the sensitivity is 0.70 and the specificity 0.77 (PPV=0.63; NPV=0.81; accuracy=0.74; AUC=0.74).

Conclusion: As a result of the high sensitivity and specificity, the easy to use CD15 focus score is a diagnostically valid score for microbial periprosthetic infection. A differentiation between low-virulence and high-virulence microorganism of sufficiently high diagnostic quality is additionally possible as a result of the defined quantification of CD15 positive granulocytes (the CD15 focus score) histopathological diagnosis of microbial infections is possible, which on the one hand supports the microbiological diagnosis and on the other hand by the stratification into low-virulence and high-virulence microbial pathogens could represent an additional basis for a pathogen-specific antibiotic treatment in the event of unclear constellations of findings.

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1. Background and objective

According to international criteria histopathology is a constituent of the diagnosis of periprosthetic joint infections.
positive virulence to low-virulence pathogens, the CD15 focus score was validated in a medium-sized group of patients [8]. The aim of this analysis was:

1. to validate the CD15 focus score on a larger group and
2. to investigate whether it is possible to differentiate between low-virulence and high-virulence microbial pathogens by means of the CD15 focus score. For this, 275 cases were diagnosed by means of the CD15 focus score and the results were correlated with the diagnoses from the microbiological findings.

2. Material and method

2.1. Adherence to ethical guidelines

This work includes no studies on humans or animals. The Ethics Commission of the Rheinland-Pfalz Medical Board, Mainz has given a positive vote under case number 837.400.15 (10168), in particular that there are no objections in relation to professional ethics or professional regulations. This work was supported by the ENDOVEREIN e.V., Hamburg, Germany.

2.2. Statistics

Statistical evaluation of the data recorded was performed with SPSS 23 (IBM, SPSS, Chicago, USA).

2.3. Investigation material and patient group

Tissue samples (SILM synovial interface membrane in the sense of synovial and periimplant tissues) from 275 patients (135 female and 140 male) in the context of histopathological diagnosis were analysed in the ZHZMD-Trier under accredited conditions (quality standard: DIN ISO/IEC 17020). The average age was 68.9 years (19–91 years, SD = 11.2). The 1–8 tissue samples were taken intraoperatively during endoprosthetic revision operations on hip joints (n = 127), knee joints (n = 141), shoulder joints (n = 2) and ankle joints (n = 5). In all cases (n = 275) there had been no preoperative or prediagnostic antibiotic treatment. The mean prosthesis life was 52 months (SD = 6.41).

2.4. Microbiological diagnosis

The microbiological cultivation of the samples takes place as standard for a period of 14 days; the microbiological finding was positive if the same pathogen could be detected in at least two samples [18,20,22]. The microorganisms were classified into high- and low-virulence microbial pathogens according to the published criteria [19,20].

2.5. Microbiological microorganism identification

The microbiological cultivations were negative in 115 cases; after incubation for 12 days microbes, respectively bacteria could be detected neither aerobically nor anaerobically. Positive findings existed in 160 cases; these were categorised into low-virulence microbial pathogens, high-virulence microbial pathogens [19,20], mixed infections (granulomatous inflammation pattern, non-low-virulence and non-high-virulence).

2.6. Histochemistry

The histochemical, the immunohistochemical methods and tissue processing were carried out in a certified and accredited context, the quality standard conformed to DIN ISO/IEC 17020. After fixing in formalin (4%) the tissue samples were embedded in paraffin. The microtomised sections with a section thickness of 1–3 µm were stained with haematoxylin and eosin (HE), and a periodic acid-Schiff (PAS) staining was additionally performed.

2.7. Immunohistochemistry

The immunohistochemical staining is carried out in a fully automated staining system (Benchmark XT, IHC Slide Stainer of the Roche brand, Ventana Medical Solutions). The sections were first deparaffinised with xylene and an ethanol series, and cell conditioning was carried out using Cell-Conditioning 1 (CC1) at 95 °C for 8 min, followed by a mild cell conditioning for 30 min. The anti-CD15 antibody (clone MMA, Roche, Basle, Switzerland) – a monoclonal murine antibody – was used as the primary antibody (ready-to-use, according to Roche undiluted). The primary antibody serves for specific identification of CD15. The sections were incubated with the antibody for 32 min. DAB (3,3-diaminobenzidine; DAKO Denmark) was used as the chromogen for the reaction with the peroxidase. The endogenous peroxidase was blocked by prior addition of H2O2. Haematoxylin (Harris, from Surgipath, Richmond, Illinois, USA) was used for counter-staining. Negative controls were produced by omitting the primary antibody and were examined.

2.8. Evaluation method by the CD15 focus score

The quantifying evaluation method of the CD15 focus score [8] follows the principle of focal maximum infiltration (focus) which is detectable beyond doubt under magnification (e.g. lens power of 10). The area in which the most CD15 NG are detectable was thus initially searched for. The focus is then established using the lens with a power of 20, and the field of vision is thus magnified 200-fold. The cells are counted directly in a single field of vision or by means of digitally assisted interactive morphometric analysis using a microscope of the Leica DM 2500 brand (Standard Microsystems Framework 2007). The image field corresponds to a slide section of about 0.3 mm². Both intra- and extravascularly located NG were quantified. Unambiguous demarcation of the CD15 NG, which have an intensive, coarse granular reactivity with covering of the cell nucleus and cytoplasm, from the CD15 positive macrophages (weak brownish sometimes also non-granular reactivity without complete covering of the cell nucleus and cytoplasm) is possible [8].

3. Results

3.1. Histopathological diagnosis according to the consensus classification

In total, 59 cases (21.5%) of type 1, 138 cases (50.2%) of type 2, 26 cases (9.5%) of type 3, 36 cases (13.1%) of type 4 and 17 cases (6.2%) of type 5 could be diagnosed according to the consensus classification.
3.2. Prosthesis life in relation to the consensus classification

The prosthesis lives were available for 40.7% of all cases (n = 112) in total (M = 52.3, SD = 64.1). Considering the prosthesis life in relation to the consensus classifications, 23 patients could be assigned to type 1 (M = 92.3, SD = 78.6), 56 patients to type 2 (M = 51.4, SD = 63.8), 7 patients to type 3 (M = 45.3, SD = 60.1), 16 patients to type 4 (M = 24.4, SD = 23.3) and 10 patients to type 5 (M = 12, SD = 10.7).

3.3. Investigation material and patient group

Tissue samples (SLIM synovial interface membrane in the sense of synovial and periimplant tissues) from 275 patients (135 female and 140 male) in the context of histopathological diagnosis were analysed in the ZHZMD-Trier under accredited conditions (quality standard: DIN ISO/IEC 17020). The average age was 68.9 years (19–91 years, SD = 11.2). The 1–8 tissue samples were taken intraoperatively during endoprosthetic revision operations on hip joints (n = 127), knee joints (n = 141), shoulder joints (n = 2) and ankle joints (n = 5). In all cases (n = 275) there had been no preoperative or prediagnostic antibiotic treatment. The mean prosthesis life was 52 months (SD = 64.1).

3.4. Microbiological findings

3.4.1. Positive microbiological findings

The group comprised 160 patients (75 female, 85 male), the average age was 69.6 years (22–91 years, SD = 11.7). A pathogen could be detected by cultivation of samples taken intraoperatively from the hip (n = 82), knee (n = 74), shoulder (n = 2) or ankle (n = 2).

3.4.2. Negative microbiological findings

The group is composed of 115 patients (60 female, 55 male). The average age is 67.9 years (19–87 years, SD = 10.5). In these patients no pathogen could be detected by cultivation of the samples taken intraoperatively from the hip (n = 45), knee (n = 67), shoulder (n = 0) or ankle (n = 3); the microbiological finding was negative.

3.4.3. Microbiological microorganism identification

The microbiological cultivations were negative in 115 cases; after incubation for 12 days microbes, respectively bacteria could be detected here neither aerobically nor anaerobically. Positive findings existed in 160 cases; these were categorised into low-virulence microbial pathogens, high-virulence microbial pathogens [19,20], mixed infections (granulomatous inflammation pattern, non-low-virulence and non-high-virulence).

3.4.4. Low-virulence microbial pathogens

In 94 cases the isolated germs were low-virulence microbial pathogens: Staphylococcus epidermidis (n = 59), Staphylococcus capitis (n = 8), Staphylococcus caprae (n = 3), Propionibacterium acnes (n = 12), Corynebacterium glauacum (n = 1) and Bacillus pumilus (n = 1), Corynebacterium jeikeium (n = 1), Staphylococcus hominis (n = 3), Staphylococcus lugdunensis (n = 3) and Kocuria kristinae (n = 1), Listeria monocytogenes (n = 1), Brucella (n = 1).

3.4.5. High-virulence microbial pathogens

In 55 cases high-virulence microbial pathogens were detected: Staphylococcus aureus (n = 28), Streptococcus pyogenes (n = 1), Escherichia coli (n = 6), Enterococcus faecalis (n = 7), Gemella haemolysans (n = 1), Candida parapsilosis (n = 1), Enterobacter cloacae (n = 1), Enterococcus hirae (n = 1), Klebsiella pneumoniae (n = 1), Pseudomonas Aeruginosa (n = 1), Strepococcus agalactiae (n = 3).

3.4.6. Mixed infections

In 11 of the 115 patients (4% of all cases) mixed infections were diagnosed. Staphylococcus epidermidis in combination with Parvimonas micra (n = 1), Staphylococcus hominis (n = 1), Staphylococcus pettenkoferi (n = 2), Staphylococcus aureus (n = 1), Staphylococcus haemolyticus (n = 1), Staphylococcus warneri (n = 1), or a mixed infection consisting of Staphylococcus epidermidis (n = 1), Escherichia coli (n = 1), Enterococcus faecalis (n = 1), or mixed infections with Staphylococcus warneri and Bacillus humenis (n = 1) or mixed infections from Staphylococcus capitis and Staphylococcus saccharolyticus (n = 1) were involved in these.

3.4.7. Graph 1A: CD15 focus score with positive and negative microbiological findings

The CD15 focus score in the cases of the group with a positive microbiological finding (n = 160) with 131.7 cells was greater than the mean of the SLIM cases with negative microbiological findings with 14.3 cells (n = 115), Fig. 1. The difference in the cell count per focus between the two groups is 117.4 cells. The SLIM cases of the group with a positive microbiological finding have significantly higher CD15 focus scores (p < 0.001 Mann-Whitney U test) than the cases with negative microbiological findings (n = 115), Figs. 2 and 3.
Fig. 3. Immunohistochemical presentation of CD15 positive NG. Infectious type (type II): CD15 focus score = 361, high-grade infection. High-virulence microbial pathogen: Immunohistochemical CD15 staining in NG. Microbiological finding positive: *Escherichia coli*. (image size shown: about 0.26 mm²)

3.4.8. **Graph 1B:** Sensitivity and specificity for the periprosthetic microbial infection

If the microbiological finding functions as the gold standard, the sensitivity is 0.91, the specificity 0.92 and the sum of the two 1.83 (PPV = 0.94; NPV = 0.88; accuracy = 0.92; AUC = 0.95). The 14 falsely negative cases are exclusively low-virulence microbial pathogens. In the falsely negative cases there were no high-virulence microbial pathogens. The numerical value of 39 cells per HPF was specified as the limiting value between positive and negative microbiological findings.

3.4.9. **Graph 2A:** CD15 focus score with low- and high-virulence microbial pathogens

The mean of the cell count of CD15 positive NG per focus (CD15 focus score) was lower in the SLIM cases of the group with low-virulence microbial pathogens (n = 94) with 94.6 cells than the mean of the SLIM cases with high-virulence microbial pathogens (n = 55), here with 192.6 cells. The numerical value of 106 cells per HPF was specified as the limiting value between high- and low-virulence.

3.4.10. **Graph 2B:** CD15 focus score: Sensitivity and specificity for the differentiation between low- and high-virulence microbial pathogens

If the microbiological finding functions as the gold standard for differentiation between low- and high-virulence microbial pathogens, the sensitivity is 0.70, the specificity 0.77 and the sum of the two 1.47 (PPV = 0.63; NPV = 0.81; accuracy = 0.74; AUC = 0.74). The limiting value for germ stratification between high- and low-virulence is 106 cells per HPF.

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3.4.11. CD15 focus score with mixed infections

In 11 of the patients mixed infections were diagnosed. The mean of the cell count of CD15 positive NG per focus (CD15 focus score) is 144, with a standard deviation of 117.4 (min = 17, max = 350) [Graph 3].

3.4.12. Graph 4 and 5: Comparison of microbiological findings and SLIM types

The comparison of microbiological findings and SLIM types gave the following results: Microbiological finding with type I 59 cases (1 high-virulence pathogen, 2 low-virulence pathogen, 0 mixed infection, 0, therefore 3 positive and 56 negative findings), with type II 137 cases (49 high-virulence pathogen, 71 low-virulence pathogen, 9 mixed infection, therefore 129 positive and 8 negative findings), with type III 26 cases (5 high-virulence pathogen, 17 low-virulence pathogen, 2 mixed infection, therefore 24 positive and 2 negative findings), with type IV 36 cases (0 high-virulence pathogen, 4 low-virulence pathogen, 0 mixed infection, therefore 4 positive and 32 negative findings) and with type V 17 cases (0 high-virulence pathogen, 0 low-virulence pathogen, 0 mixed infection, therefore 0 positive and 17 negative findings). The comparison of microbiological findings and the infectious SLIM types, type II and type III, is illustrated in Graphs 4 and 5.

4. Discussion

4.1. Histopathological diagnosis of the joint prosthesis failure

The consensus classification of endoprostheses-associated pathologies defines a comprehensive etiological spectrum of endoprostheses-associated pathologies [9,12,13]. These diagnostic criteria are readily reproducible and this classification is used in histopathological diagnosis, also in German-speaking countries in particular, as the standard for a causal classification of the joint prosthesis failure. This classification takes into account synovial periprosthetic joint infections in two forms: Periprosthetic microbial infection, so-called infectious type II, and the combination of periprosthetic microbial infection and periprosthetic particle condition, so-called mixed type, type III.

4.2. Histopathological infection diagnosis of periprosthetic joint infection

The Histopathological infection diagnosis has been specified as a defining diagnosis constituent of periprosthetic joint infection [2,18,19,22,23]. This form of infection diagnosis is to be regarded as an essential supplement to microbiological infection diagnosis and is not based or lesser based to only a small extent on direct detection of pathogens, but is based on the evaluation of infection-characteristic infiltrate patterns of leukocytic cells [14,16,17]. The detection and quantification of NG is foremost. A so-called direct germ typing by special enzyme histochemical staining is possible in principle, but in the majority of cases is limited to fungal infections and mycobacterial infections due to the peculiarities of the method [10].

The essence of histopathological infection diagnosis (detection of the pathological infection substrate) especially of acutely infectious non-specific microbial infections thus lies in NG detection by means of HE staining, the PAS reaction, chloroacetate esterase staining and immunohistochemical CD15 detection [8].

The diagnostic method repertoire generally depends, however, on the differential diagnosis objective. The identification and quantification of immunohistochemically detected NG by CD15 are to be regarded as valid methods of microbial infection diagnosis [8]. Enzyme histochemical staining in particular is subject to qualitative variations, although also depending on the staining procedures and the decalcification time, so that an automated, standardised immunohistochemical detection of the specific antigen CD15 should be given preference for NG detection [8]. An immunohistochemical detection of CD68 for detection of epitheloid cells and macrophages may be necessary for investigations and differential diagnosis involving granulomatous epitheloid cell reactions. This includes in particular abraded particle granuloma, granulomatous infections, such as e.g.: brucellosis, mycobacterial infections and mycoses [10].

4.3. Various forms of NG quantifications for diagnosis of periprosthetic joint infection

Although histopathology is a diagnosis constituent of periimplant material, it is incumbent upon the pathologist to decide which of the various NG quantifications is used for diagnosis of the periprosthetic infection [18]. The most important quantifications of NG are presented.

4.4. More than 2 NG

More than 2 NG per HPF (400x) in the analysis of 10 HPF (high power field = field of vision at a defined microscope magnification):

This NG quantification is based on more than 2 NG per HPF (400x) in the analysis of 10 HPF [16]. The value of 5 NG per HPF in 5 HPF has been proposed as an alternative [6,17]. The high diagnostic value of this evaluation method in combination with clinical parameters is published [4,5].

4.5. 23 neutrophilic granulocytes in 10 HPF

This NG quantification is based on counting of 10 HPF (visual field count 20, field of vision diameter 0.625 mm). A maximum of 10 NG per HPF are counted; if for example 50 NG are found in one HPF this is nevertheless counted as 10 NG. If more than 23 NG are found in total in 10 HPF, the diagnosis of a periprosthetic membrane of the infectious type is to be made with a sensitivity 73% and specificity 95% [14].

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4.6. CD15 focus score

The CD15 focus score validated and further developed is a comparatively simple counting algorithm. This is based on a cell count of CD15 NG independently of location in a single image field and is orientated towards a specific property of NG, the intensive and coarse granular CD15 expression [8]. Finally, this score follows the relatively easily convertible principle of maximum degree (“worst area grading”), an almost universal principle in histopathological diagnosis, and by this means also takes into account the focal nature of microbial infections in periimplant tissue [8].

The CD15 focus score is characterised by a high diagnostic quality, and due to the intensive CD15 reactivity the development of a CD15 quantification software, “CD15 Quantifier”, was possible [8,21]. The limiting value between a positive and negative microbiological finding is 39 cells per HPF. In contrast to the previous publication [8], this work includes a larger data set, whereby the risk of outliers has been minimised, which resulted in a new limiting value deviating slightly from the first value for the diagnosis of a microbial infection. With a CD15 focus score limiting value of 39 cells per HPF the sensitivity is 0.91, the specificity 0.92, the sum is 1.83 (PPV = 0.94, NPV = 0.88, accuracy = 0.92, AUC = 0.95). At a CD15 focus score limiting value of 106 for differentiation between low-virulence and high-virulence microbial pathogens the sensitivity is 0.70, the specificity 0.77, the sum is 1.47 (PPV = 0.63, NPV = 0.81, accuracy = 0.74, AUC = 0.74).

Summarising, by using the CD15 focus score a comparatively high diagnostic sensitivity and specificity [8] of a microbial infection diagnosis results, with the possibility of differentiation into low-virulence and high-virulence microbial pathogens. This additionally offers the advantage of a simplified quantification of NG since it is independent of location. An involved differentiation into intra- and extravascularly located granulocytes therefore is no longer necessary [14]. Since this quantification follows the principle of maximum degree, it also takes into account the focal nature of microbial infections such as is discussed in the literature [20].

4.7. Low-virulence and high-virulence microbial pathogens

The microbial spectrum detected in this group coincides well with the data for periprosthetic joint infection described in the literature [20]. The CD15 focus score allows for the first time a histopathological differentiation between an infection by low-virulence and high-virulence microbes [19,20]. Although the virulence of microbial pathogens is also to be evaluated as a relative phenomenon (virulence relativity), as an expression of the guest-host relationship [3] it emerges from the data available that at the tissue level a relatively stereotypical reaction pattern exists.
with respect to the pathogen-induced inflammatory infiltration by NG. The relatively high scatter of the CD15 values, however, can be interpreted in the sense of this virulence relativity.

4.8. Types (type II and III) and comparison of low- and high-virulence microorganisms

No significant differentiation of low- and high-virulence microbial pathogens into type II and type III cases was to be found in this analysis. A relative accumulation of high-virulence microorganisms was found in type II cases, and this finding coincides well with data published on the distribution of the microbe species [20,22]. Since type III cases are characterised by an additional abraded particle reaction, a secondary infection in the sense of a delayed infection is probable, and the relatively high proportion of low-virulence microorganisms would suggest this. It is debated in the literature whether low-virulence microorganisms can lead secondarily to colonisation of the periimplant tissue in the context of bacteraemia [20]. Nevertheless, an intracellular persistence with secondary bac- teraemia is also described for high-virulence microorganisms (e.g. Staphylococcus aureus) in the current literature [7], which could explain the relatively high proportion of Staphylococcus aureus in type III cases.

Based on the differentiation of the CD15 focus score values between low-virulence and high-virulence microbes the sensitivity is 0.70 and the specificity 0.77 (PPV = 0.63; NPV = 0.81; accuracy = 0.74; AUC = 0.74). The CD15 focus score therefore can be used not only for infection diagnosis of the periimplant joint infection as such, but also for an orientating stratification of the microbial species (low-virulence versus high-virulence microbes). The limitation is that microbial mixed infections and microbial infections with a granulomatous inflammation reaction cannot be demarcated by this means.

4.9. Type II a/IIa as low grade infection and type II b/IIIb as high grade infection

The CD15 focus score could be of diagnostic importance for periprosthetic joint infection especially if the microbiological findings are unclear or there is a discrepancy in the constellation of findings between the clinical and microbiological diagnosis of the infection. It can contribute to an increased diagnostic certainty and in cases where the microbiological finding is negative it can be the basis for a targeted antibiotic treatment. Therefor the values of the CD15 focus score should be implemented in the histopathological consensus classification where infectious periprosthetic membranes are classified as type II [9]. Including this stratification in low- grade infection and high- grade infection we propose two types of type II. Type II a/IIa as low grade infection and Type II b/IIIb as high grade infection. In both subtypes the quantification values of the CD15 focus score should be stated in order to give the clinician a precise information of the histopathologic diagnosis which should be the basis for the therapy.

Further information and acknowledgements

Some of these data (n = 91) have been published in a German language journal under a different focus (software development, CD15 focus score). Financial assistance has been received from ENDO-Verein Hamburg.

References


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