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OPTIMIZATION OF PROGNOSTIC INDICATORS OF DENTAL STATUS IN PATIENTS WITH CHRONIC LEUKEMIA

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Abstract: Chronic leukemia is a hematological malignancy associated with profound immunosuppression, thrombocytopenia, granulocytopenia, and microcirculatory disorders, which collectively create a favorable background for the development of severe, rapidly progressive, and recurrent oral complications. The optimization of prognostic indicators of dental status in this patient population is a pressing clinical challenge that requires a multidisciplinary approach integrating hematological and dental assessments. This literature review analyzes current scientific data on clinical, immunological, and microbiological prognostic markers of oral pathology in patients with chronic leukemia. Key prognostic indicators include the severity of gingival bleeding (BOP index), periodontal pocket depth, salivary flow rate, levels of immunoglobulins (particularly IgG and IgE), proinflammatory cytokine profiles (IL-1β, IL-6, TNF-α), and the degree of colonization by periodontopathogens (Porphyromonas gingivalis, Treponema denticola, Aggregatibacter actinomycetemcomitans). The review substantiates the need for early diagnosis, risk stratification, and personalized treatment protocols to improve clinical outcomes and quality of life in this vulnerable patient group.

Keywords: chronic leukemia, periodontitis, prognostic indicators, dental status, immunoglobulins, cytokines, oral microbiota, risk stratification, personalized medicine.

Introduction

Chronic leukemia, encompassing chronic lymphocytic leukemia and chronic myeloid leukemia, is a hematological disease characterized by the clonal proliferation of malignant lymphocytes or myeloid cells. Despite significant advances in chemotherapy, targeted therapy, and hematopoietic stem cell transplantation, the disease remains associated with substantial morbidity and a high prevalence of secondary complications, including oral manifestations.

The oral cavity is often a mirror of systemic disease, and this is particularly true for chronic leukemia. Immunosuppression, neutropenia, thrombocytopenia, and microcirculatory disturbances lead to a wide spectrum of oral complications: gingival bleeding, spontaneous hematomas, mucosal ulcers, candidiasis, herpetic infections, and, most importantly, severe and rapidly progressive periodontitis. Unlike periodontitis in immunocompetent individuals, the leukemic counterpart is characterized by early onset, aggressive course, poor response to conventional treatment, and high recurrence rates.

The prognostic assessment of dental status in patients with chronic leukemia is essential for several reasons. First, oral complications significantly impair patients' quality of life by causing pain, interfering with nutrition, and causing psychological distress. Second, oral foci of infection can serve as portals for systemic dissemination of pathogens, leading to sepsis – a potentially fatal complication in immunocompromised hosts. Third, active oral pathology may delay or interrupt anti-leukemic therapy, negatively affecting overall prognosis.

Despite the clinical importance of this issue, standardized protocols for the prognostic assessment and management of oral diseases in chronic leukemia patients remain insufficiently developed. Traditional dental indices designed for the general population do not account for the unique pathogenetic features of leukemia-associated periodontitis. Therefore, the identification and optimization of specific prognostic indicators are crucial for improving patient care.

This literature review aims to analyze current scientific evidence on prognostic indicators of dental status in patients with chronic leukemia, including clinical, immunological, and microbiological parameters, and to propose an optimized approach to risk stratification and personalized treatment.

Clinical prognostic indicators

Bleeding on Probing (BOP)

Bleeding on probing is one of the most reliable clinical indicators of active periodontal inflammation. In patients with chronic leukemia, BOP positivity is observed in nearly 100% of cases, with mean index values reaching 87.3±9.2%. The prognostic significance of BOP in this population is twofold. First, persistent BOP indicates ongoing inflammatory activity that may not respond adequately to standard periodontal therapy due to underlying immunosuppression. Second, bleeding risk is exacerbated by thrombocytopenia – a common feature of chronic leukemia observed in approximately 42.9% of patients. The combination of active inflammation and reduced platelet count increases the risk of spontaneous gingival bleeding and complicates periodontal interventions.

Optimization of BOP as a prognostic indicator involves regular quantitative assessment (percentage of bleeding sites) combined with monitoring of platelet count. Patients with BOP >70% and platelet count $<50\times10^9$/L require the most intensive monitoring and a multidisciplinary approach to treatment planning.

Periodontal Pocket Depth

Periodontal pocket depth measured using a standardized periodontal probe (WHO probe, 0.5 N pressure) at six sites per tooth is a critical prognostic parameter. In chronic leukemia patients, pocket depths ≥5 mm are considered prognostically unfavorable. Deep pockets (≥6 mm) are associated with a higher risk of disease progression, tooth loss, and systemic dissemination of periodontopathogens.

The prognostic value of pocket depth in this population is enhanced when combined with assessment of vertical bone loss on panoramic radiographs. The presence of intrabony defects (vertical bone loss >3 mm) indicates a more aggressive disease course and poorer response to non-surgical therapy.

Tooth Mobility

Tooth mobility, graded on a scale from 0 (physiological mobility) to 3 (vertical mobility), is a late but important prognostic sign. In chronic leukemia patients, mobility develops earlier and progresses faster than in immunocompetent individuals due to accelerated bone resorption mediated by RANKL/OPG imbalance and increased osteoclast activity. The presence of grade 2

or 3 mobility in any tooth indicates advanced periodontal destruction and a guarded prognosis for tooth retention.

Oral Hygiene Status (OHI-S)

The Simplified Oral Hygiene Index (OHI-S) assesses the presence of dental plaque and calculus on six indicator teeth. In chronic leukemia patients, mean OHI-S values of 3.00±0.00 (maximum score) indicate uniformly poor oral hygiene. Poor hygiene is prognostically unfavorable as it perpetuates the cycle of microbial colonization, inflammation, and tissue destruction. However, optimization of this indicator involves not only patient education but also consideration of physical limitations – fatigue, weakness, and oral pain may prevent patients from maintaining adequate hygiene.

Salivary Flow Rate

Hyposalivation (salivary flow rate <0.30 mL/min) is a common finding in chronic leukemia patients, with mean values of 0.127±0.078 mL/min – representing a 2.5–3.5-fold reduction compared to healthy controls (0.45±0.10 mL/min). Reduced salivary flow impairs natural self-cleaning mechanisms, reduces buffering capacity, decreases antimicrobial protein concentrations (lysozyme, lactoferrin, secretory IgA), and promotes colonization by aciduric and periodontopathogenic bacteria.

Prognostically, a salivary flow rate below 0.15 mL/min is associated with a significantly higher risk of severe periodontitis, rampant caries, and oral candidiasis. Optimization of this prognostic indicator includes regular measurement at each dental visit and objective assessment of xerostomia using validated questionnaires.

Immunological prognostic indicators

Immunoglobulin G (IgG)

Serum IgG is the main immunoglobulin responsible for long-term humoral immunity and opsonization of pathogens. In chronic leukemia patients with periodontitis, IgG levels are significantly reduced, often falling below the lower limit of normal (6.0 g/L). Mean values of 5.98±0.81 g/L have been reported. Low IgG is a prognostically unfavorable marker indicating impaired systemic humoral defense and increased susceptibility to periodontal and other infections.

Optimization of IgG as a prognostic indicator involves regular monitoring (every 3–6 months) and correlation with clinical periodontal parameters. Patients with persistently low IgG (<6.0 g/L) despite treatment may require intravenous immunoglobulin replacement therapy in addition to periodontal care.

Immunoglobulin E (IgE)

IgE is associated with allergic and type I hypersensitivity reactions. In chronic leukemia patients with periodontitis, IgE levels are markedly elevated, often exceeding 150 ng/mL – three times the upper limit of normal (≤50 ng/mL). Elevated IgE reflects systemic inflammatory and

immune dysregulation and is prognostically associated with more severe periodontal disease and poorer response to standard therapy.

A reduction in IgE following treatment is a favorable prognostic sign. Studies have shown that a decrease of >70% from baseline IgE levels after therapy correlates with clinical improvement (reduced bleeding, pocket depth reduction) and longer relapse-free intervals.

Proinflammatory Cytokines (IL-1β, IL-6, TNF-α)

Interleukin-1β (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α) are key mediators of the inflammatory response in periodontitis. In chronic leukemia patients, serum and salivary levels of these cytokines exceed normal values by 6–14 times, reflecting systemic and local hyperinflammation.

Prognostically, the following thresholds have been identified as unfavorable:

· IL-1β >50 pg/mL
· IL-6 >40 pg/mL
· TNF-α >45 pg/mL

Patients with cytokine levels above these thresholds are at higher risk for rapid disease progression, poor response to non-surgical therapy, and early tooth loss. Conversely, a reduction of at least 50% in all three cytokines following treatment is associated with favorable outcomes.

Secretory Immunoglobulin A (sIgA)

Secretory IgA in saliva is the first line of specific immune defense in the oral cavity, preventing bacterial adhesion to the epithelial surface. In chronic leukemia patients, sIgA levels are often reduced due to defective synthesis of the secretory component. Low sIgA (<0.5 g/L) is prognostically unfavorable, correlating with higher rates of mucosal infections and more severe periodontitis.

Circulating Immune Complexes (CIC)

Elevated levels of circulating immune complexes are detected in chronic leukemia patients, reflecting immune dysregulation and chronic antigen stimulation. High CIC levels (>50 IU/mL) are associated with more severe periodontal inflammation, including increased bleeding, deeper pockets, and greater bone loss. Normalization of CIC levels following treatment is a favorable prognostic sign.

Microbiological prognostic indicators

Quantification of Periodontopathogens

Molecular methods, particularly real-time PCR, allow precise quantification of key periodontopathogens in subgingival plaque samples. In chronic leukemia patients, the following pathogens are consistently detected at high frequencies:

Pathogen Detection rate (%) Prognostic significance
Treponema denticola 67.4% Very high – associated with deep pockets and bone loss
Porphyromonas gingivalis 61.5% High – keystone pathogen, associated with severe disease
Prevotella intermedia 60.5% High – associated with acute exacerbations
Aggregatibacter actinomycetemcomitans 52.5% High – produces leukotoxin, associated with aggressive periodontitis
Tannerella forsythia 51.5% Moderate – co-aggregates with other pathogens

Prognostically, the following microbiological findings are unfavorable:

· Detection of ≥3 periodontopathogens simultaneously
· High bacterial load (>10^5 copies per sample for any pathogen)
· Persistence of pathogens despite standard therapy

Optimization of microbiological prognostication involves quantitative PCR testing at baseline and after treatment. A reduction in pathogen load of >50% following therapy is a favorable prognostic sign, whereas persistent high loads indicate the need for additional antimicrobial interventions or repeated VLOK courses.

Microbiome Diversity

Beyond individual pathogens, overall microbiome diversity is an emerging prognostic indicator. Patients with chronic leukemia typically exhibit reduced oral microbiome diversity (lower Shannon diversity index) compared to healthy individuals. Low diversity is associated with more severe and refractory periodontitis. Restoration of diversity following treatment is a positive prognostic marker, though currently not widely available in routine clinical practice.

Integrated prognostic scoring system

Given the multifactorial nature of periodontitis in chronic leukemia, an integrated approach to prognostication is necessary. The following scoring system has been proposed, assigning points to key prognostic indicators:

Clinical domain (maximum 6 points):

· BOP >70% – 2 points
· Pocket depth ≥5 mm in ≥6 teeth – 2 points
· Tooth mobility grade ≥2 in ≥2 teeth – 2 points

Immunological domain (maximum 6 points):

· IgG <6.0 g/L – 2 points
· IgE >100 ng/mL – 2 points
· IL-1β >50 pg/mL or IL-6 >40 pg/mL or TNF-α >45 pg/mL – 2 points

Microbiological domain (maximum 6 points):

· Detection of ≥3 periodontopathogens – 2 points
· High bacterial load (>10^5 copies) for any pathogen – 2 points
· Persistence of pathogens after standard treatment – 2 points

Interpretation:

· 0–5 points: Low risk – standard periodontal care, monitoring every 6 months
· 6–10 points: Moderate risk – intensified therapy, consider VLOK, monitoring every 3–4 months
· 11–18 points: High risk – aggressive multimodal therapy, VLOK indicated, monitoring every 1–3 months

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Optimization strategies for prognostic indicators

Early Diagnosis and Baseline Assessment

All patients with newly diagnosed chronic leukemia should undergo a comprehensive dental examination within 1–2 months of diagnosis. Baseline assessment should include:

· Complete clinical periodontal examination (BOP, pocket depths, mobility, OHI-S)
· Salivary flow rate measurement and pH
· Panoramic radiography
· Serum immunoglobulins (IgG, IgA, IgM, IgE)
· Proinflammatory cytokines (IL-1β, IL-6, TNF-α) – in moderate/severe cases
· Quantitative PCR for periodontopathogens (minimum panel: P. gingivalis, T. denticola, A. actinomycetemcomitans, P. intermedia)
· Platelet and neutrophil counts

Risk-Stratified Monitoring

Based on baseline assessment, patients are assigned to one of three monitoring schedules:

Low-risk patients: clinical examination every 6 months, annual immunological and microbiological reassessment.

Moderate-risk patients: clinical examination every 3–4 months, biannual immunological and microbiological reassessment, consider preventive VLOK course.

High-risk patients: clinical examination every 1–3 months, quarterly immunological and microbiological reassessment, VLOK therapy indicated (5–10 sessions), consider immunoglobulin replacement if IgG persistently low.

Personalized Treatment Protocols

The optimization of prognostic indicators requires personalized treatment approaches:

For patients with predominant immunological abnormalities (low IgG, high IgE, elevated cytokines): VLOK therapy is particularly beneficial due to its immunomodulatory effects. A course of 5–10 VLOK sessions normalizes immunoglobulin profiles and reduces cytokine levels.

For patients with predominant microbiological abnormalities (high pathogen load, multiple pathogens): VLOK combined with targeted antimicrobial therapy (based on antibiotic susceptibility testing) is recommended. Repeated microbial testing guides treatment adjustments.

For patients with thrombocytopenia (platelet count $<50\times10^9$/L): Non-invasive periodontal management (avoiding subgingival instrumentation), platelet transfusion before invasive procedures, and VLOK therapy (which reduces bleeding tendency by improving platelet function).

For patients with hyposalivation (salivary flow <0.15 mL/min): Salivary substitutes, stimulation of residual salivary function (sugar-free lozenges, pilocarpine if not contraindicated), intensive fluoride therapy to prevent caries, and VLOK (which improves salivary gland function).

Role of VLOK Therapy in Optimizing Prognostic Indicators

VLOK therapy has been shown to improve all three domains of prognostic indicators:

Clinical domain: VLOK reduces BOP by 4.8-fold, decreases pocket depth, reduces tooth mobility, and increases salivary flow rate from 0.127 to 0.28 mL/min.

Immunological domain: VLOK reduces IgE by 79.9% (from 152.70 to 30.64 ng/mL), increases IgG by 29.3% (from 5.98 to 7.73 g/L), and reduces proinflammatory cytokines by 4.4–4.7-fold.

Microbiological domain: VLOK reduces detection rates of T. denticola by 63.6%, A. actinomycetemcomitans by 57.0%, and P. intermedia by 49.5%.

Thus, VLOK therapy is a key tool for converting high-risk patients to lower-risk categories and improving long-term outcomes.

Conclusion

The optimization of prognostic indicators of dental status in patients with chronic leukemia is a critical component of comprehensive patient care. Key prognostic indicators span three domains: clinical (BOP, pocket depth, tooth mobility, OHI-S, salivary flow rate), immunological (IgG, IgE, proinflammatory cytokines, sIgA, CIC), and microbiological (detection and quantification of periodontopathogens, microbiome diversity).

An integrated prognostic scoring system incorporating these indicators allows risk stratification into low, moderate, and high-risk categories. This stratification guides monitoring frequency, treatment intensity, and the indications for VLOK therapy.

VLOK therapy has demonstrated significant efficacy in improving all three domains of prognostic indicators, converting high-risk patients to lower-risk categories and reducing the frequency of periodontitis exacerbations. Personalized protocols based on individual prognostic profiles are essential for optimal outcomes.

Future research should focus on prospective validation of the proposed prognostic scoring system, identification of additional biomarkers (genetic polymorphisms, microbiome metagenomic profiles), and development of point-of-care tests for rapid prognostic assessment in clinical settings.

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