Dental Evaluation Prior to Hematopoietic Stem Cell Transplantation

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SUMMARY

Hematopoietic stem cell transplantation (HSCT) is an established treatment for various hematologic malignancies, but is associated with significant mucosal complications related to immunosuppression and toxicity. The oral cavity is both a frequent site of HSCT-related adverse effects and a potential source of systemic infection. Consequently, pretransplant dental evaluation has traditionally been recommended to eliminate oral foci that may increase morbidity and mortality. However, most existing guidelines were developed during an era of more intensive conditioning regimens, prolonged neutropenia, and higher treatment-related mortality than is typical today. This review examined current evidence regarding the risks and benefits of dental evaluation and intervention prior to HSCT, with particular attention paid to differences between autologous (ASCT) and allogeneic stem cell transplantation (AlloSCT). While there is general agreement that acute or symptomatic oral infections should be treated before conditioning, the management of asymptomatic dental disease remains controversial. The available literature includes a few randomized controlled trials and suggests a low incidence of oral-origin infections during HSCT. Non-randomized studies and systematic reviews question the benefit of extensive dental clearance, particularly when it may delay transplantation or increase morbidity. Current evidence supports a selective, risk-adapted dental approach. For AlloSCT recipients, targeted intervention for high-risk conditions appears appropriate, whereas low-risk asymptomatic lesions may be monitored. In ASCT, transplantation may often proceed safely without comprehensive dental clearance. Overall, individualized decision-making may be preferable to uniform aggressive dental protocols.

KEYWORDS

Hematopoietic stem cell transplantation; Pretransplant dental evaluation; Oral infection risk

Introduction

Hematopoietic stem cell transplantation (HSCT) involves replacing bone marrow cells previously destroyed by high doses of chemotherapy or radiation (conditioning) with new cells derived either from the patient (autologous stem cell transplantation — ASCT) or form another person, i.e. a donor (allogeneic stem cell transplantation — AlloSCT). In the case of ASCT, hematopoietic stem cells need to be harvested and stored before conditioning. Autologous stem cell transplantation is mostly used in the treatment of lymphoid malignancies — multiple myeloma and lymphoma — and AlloSCT in the treatment of acute leukemias.

Oral health has a dual relation with HSCT. On the one hand, high-dose chemotherapy with or without radiotherapy is harmful to other tissues and organs besides the bone marrow, most commonly affecting the gastrointestinal tract aside from hematopoiesis. The oral cavity is a part of the gastrointestinal tract and a frequent site of HSCT-related side-effects[1]. The most common ones, affecting 80% of patients undergoing HSCT, are oral mucositis, bleeding, xerostomia, and taste alterations[2]. The risk of these complications is increased in patients with poor oral health. On the other hand, the mouth is colonized by a large number of different microorganisms, some of which are conditionally pathogenic and able to cause opportunistic infections[3]. These complications usually arise in patients with prolonged severe neutropenia and immunosuppression, and can increase the morbidity and possibly the mortality of HSCT, prolong hospital stay, as well as increase the cost of the procedure[4]. Therefore, dental evaluation prior to HSCT is considered the standard of care and is recommended by the European Society for Blood and Marrow Transplantation (EBMT)[5]. The primary goal of pretransplant dental evaluation is to identify and remove foci which increase the risk of local and systemic complications. However, the ability to perform complicated and prolonged dental treatments in patients undergoing HSCT is limited by their general health, stage of malignancy and antineoplastic therapy. Inappropriate dental interventions might be harmful to patients in two ways. First, unnecessary interventions might delay HSCT, reducing the efficacy of the procedure and increasing the risk of tumor progression and death. Second, in some cases, the dentist might opt for pretransplant tooth extractions, even though it might be reasonably safe to delay dental treatment until the patient recovers from HSCT and then perform more appropriate and less mutilating endodontal or periodontal interventions[5].

The purpose of this paper was to review available studies of pretransplant dental evaluation and interventions, and analyze their risk-benefit ratio — both in relation to different dental problems and the type of HSCT (ASCT vs AlloSCT), and underlying malignancy. A comparative overview of ASCT and AlloSCT as well as dental management is shown in Table 1.

Methods

For this review, eligible articles were searched in PubMed using the following keywords: “dental evaluation” AND “allogeneic” OR “autologous” AND “transplant” AND “infection” OR “complication” AND “risk”. Other databases searched were Google Scholar, Embase, Biosis Previews, and Derwent Drug File. All articles were manually checked for content, and 23 articles were ultimately included in this review. All articles were published in English, and conference reports were not discarded. The literature search was conducted in June 2025. Article selection followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) (Supplementary Materials File S1).

Table 1. A comprative overview of transplant type and dental management.

Parameter	ASCT (autologous)	AlloSCT (allogeneic)
Conditioning regimen	High-dose chemotherapy primarily for lymphoid malignancies (e.g., multiple myeloma)	Myeloablative (MAC) or reduced intensity (RIC) regimens targeting hematological malignancies
Post-transplant immunosuppression	Minimal and short-term; mainly influenced by pre-transplant treatments	Prolonged and significant, lasting a year or longer due to donor-derived immune cells
Duration of neutropenia	10–15 days; shorter recovery due to autologous cells	Longer in MAC (~20–30 days); variable in RIC
Risk of infections	Lower due to shorter neutropenia and minimal immunosuppression	Higher; prolonged immunosuppression increases infection risk
Recommendations for acute infections	Treat all symptomatic infections pre-transplant if time permits	Mandatory treatment of all symptomatic infections before transplant initiation
Recommendations for asymptomatic conditions	Observation acceptable for minor caries or asymptomatic issues if HSCT cannot be delayed	Proactive treatment required for potentially infectious conditions, especially periodontal
Delaying HSCT for dental treatment	Avoid unnecessary delays; treat high-priority conditions only	Delay acceptable for high-risk dental issues to prevent post-transplant complications

Hematopoietic stem cell transplantation

Despite having similar names, important fundamental differences exist between ASCT and AlloSCT. The antitumor effect of ASCT is based on the pretransplant high-dose chemotherapy conditioning regimen. Autologous hematopoietic stem cells, nowadays almost exclusively derived from peripheral blood, are used to enable the recovery of blood counts in time to prevent patient deaths from infections induced by prolonged agranulocytosis. The exact type and toxicity of the conditioning regimen depend on the underlying malignancy. Conditioning is usually less intensive and toxic in multiple myeloma than in lymphoma. The median time to granulocyte recovery is between 10 and 15 days. Immunological dysfunction after ASCT is usually not profound and is more dependent on pretransplant therapy than on the procedure itself [6,7,8].

Two types of pretransplant conditioning are nowadays used prior to AlloSCT[9,10,11]. The older type is myeloablative conditioning (MAC), designed to destroy the recipient's hematopoiesis, thereby inducing prolonged severe granulocytopenia and mucositis that is usually longer and more severe than in ASCT. A newer approach is to use reduced intensity conditioning (RIC), which does less damage to the recipient's hematopoiesis and gastrointestinal system, resulting in a shorter period of agranulocytosis and less mucositis. However, due to the fact that immunocompetent cells are derived from the donor and that patients have to take immunosuppressive agents for months, the period of significant immune dysfunction after AlloSCT lasts at least one year — and frequently longer. Treatment-related mortality for ASCT is less than 5% (and in some instances, e.g. ASCT for multiple myeloma, less than 1%)[12]. The treatment-related mortality of AlloSCT is around 10% nowadays; substantially less than 30 years ago[13].

Guidelines

Both European and American guidelines recommend dental evaluation and the elimination of foci prior to HSCT[5,14]. No differentiation is made between ASCT and AlloSCT, between different types of AlloSCT nor between underlying diseases in patients referred for ASCT. These guidelines have remained essentially unchanged since the 1990s. At that time, the treatment-related mortality of AlloSCT was substantially higher (around 30%) and RIC was unknown. Autologous stem cell transplantation was only starting to be used, the preferred source of stem cells was bone marrow, and the median time to neutrophil recovery was around 30 days.

There are ongoing debates regarding the uniformity of these guidelines. Some clinicians argue that the recommendations do not adequately reflect the advancements in transplants methods, such as RIC regiments, which have less severe complications[9,10,11]. Others point out that the risk of delaying HSCT due to dental interventions can be substantial, especially in cases where the underlying malignancy is aggressive. For example, a delay in AlloSCT could increase the risk of tumor progression or relapse, which may outweigh the benefits of addressing certain asymptomatic dental conditions[17,18]. Contrary to this, proceeding with untreated dental foci, particularly in patients undergoing myeloablative conditioning, may result in serious systemic infections[15,19]. In practice, clinicians and dental experts often differ on the threshold for intervention. Some prefer a conservative approach, treating only acute and highly symptomatic dental issues, while others advocate for more aggressive protocols to prevent even minor risks and infections during immunosuppression. The lack of randomized controlled trials addressing these divergent practices further complicates reaching a consensus[19,22].

The impact of oral health on hematopoietic stem cell transplantation complications and outcomes

All recommendations agree on the fact that infection should be cured prior to the start of pretransplant conditioning. This is due to the fact that infections are the main cause of treatment-related deaths during HSCT procedures and that, because of the myelosuppressive and immunosuppressive effects of conditioning, localized infections might easily become systemic and potentially lethal. However, there are very few data on the systemic dissemination of oral infections during HSCT, or even cancer treatment in general. Severe oral and periodontal disease was shown to be a risk factor for *Streptococcus viridans* and coagulase-negative *Staphylococcus* bacteremia in patients undergoing AlloSCT[15]. However, none of the patients affected by these infections died of them[16]. A review concluded that the weighted prevalence of dental infections during cancer therapy is relatively low (5.4%)[17]. It did not specifically analyze the outcomes of patients undergoing HSCT. Some studies have shown a higher incidence of bacteremia, especially streptococcal bacteremia, in patients with dental pathology. Fujeda et al. highlighted a higher incidence of bacteremia caused by streptococcal species among transplant recipients who did not receive basic periodontal treatment[18]. However, other studies have shown no correlation between bacteremia and periodontal status. In a study published by Akintoye and colleagues, no relationship was found between radiographic periodontal status and septicemia or mortality within the initial 100 days after transplant[19]. It seems that periodontitis is prevalent in patients with hematopoietic diseases. Despite its association with oral mucositis, the occurrence of systemic infection remains low and controllable.

Endocarditis is an extremely rare complication after HSCT. The data on endocarditis after HSCT is scarce: only a few older publications are available in literature search, which show very low numbers of patients developing endocarditis. For example, Kuruvila et al. report that only 5 out of 1 547 patients were diagnosed with endocarditis post-HSCT[20].

Based on these propositions, it is generally accepted that acute, relatively easily curable local infections — like pulpitis, significant or symptomatic apical periodontitis or pericoronitis, and acute ulcerative gingivitis — need to be resolved before starting the transplant procedure or, for that matter, any aggressive treatment leading to profound myelosuppression or immunosuppression. To our knowledge, this is a generally accepted rule and no study has ever tried to prove otherwise. Also, these conditions cause a lot of pain and discomfort to patients and are considered dental emergencies, even in immunocompetent individuals, making it almost impossible to postpone their treatment.

Dental caries, asymptomatic apical periodontitis, residual roots, shallow periodontal pockets, and impacted third molars are not acute infections, but can become doorways for intraoral microbes during periods of immunosuppression and neutropenia, enabling them to cause bone and systemic infections. There is no general consensus on whether and in which patients these conditions should be treated prior to HSCT. Some of the most frequent dental conditions, the risks they carry, and recommendations on how to address them are shown in Table 2. Below, we reviewed the available data on the risks and benefits of such interventions.

Table 2. Risks and recommendations for common dental issues in HSCT patients

Condition	Risk if untreated	Recommended pretransplant intervention
Acute pulpitis	Pain, systemic infection due to immune suppression	Immediate root canal treatment or pulpectomy
Asymptomatic apical periodontitis	Risk of systemic dissemination during neutropenia or immunosuppression	Root canal treatment or extraction depending on lesion size (> 5 mm) and transplant urgency
Residual roots	Potential infection nidus during transplant-related immune suppression	Extraction recommended
Advanced marginal periodontitis	Risk of bacteremia and systemic infection	Scaling and root planing; extraction for teeth with severe mobility or deep pockets (> 8 mm)
Partially erupted third molars with pericoronitis	Potential abscess formation and systemic spread	Extraction recommended
Moderate/severe caries	Progression to pulpitis or apical infections during immunosuppression	Restoration, pulpectomy, or root canal treatment
Minor caries	Low risk of systemic impact; potential progression during prolonged neutropenia	Observation or restoration if time permits
Shallow periodontal pockets (< 5 mm)	Minimal systemic risk, but potential local inflammation	Scaling and oral hygiene instruction

Complications of dental interventions

Treating periodontal disease can lead to bacteremia and systemic infection, but the risk of this occurring seems to be low. On the other hand, wounds after root and tooth extractions need to heal for up to 14 days before it is safe to start pretransplant conditioning. Also, complications after tooth extractions occur in up to 40% of patients scheduled for HSCT, which delays the procedure even further[21].

Clinical trials on pretransplant dental interventions

We performed a thorough literature search, but failed to identify a single randomized trial exploring the value of pretransplant dental evaluation and foci elimination in patients undergoing transplantation or intensive chemotherapy.

A non-randomized comparative trial comparing the outcomes of 58 patients undergoing HSCT concluded that those without dental foci or with eliminated dental foci had similar outcomes as those who did not undergo foci elimination. The paper did not differentiate between ASCT and AlloSCT, nor did it describe the way in which patients were allocated to the two groups. The incidence and severity of oral mucositis, infections and post-SCT survival were not correlated with the presence of dental foci. Based on these findings, the authors recommended not to perform radical dental treatment prior to HSCT[22].

A prospective study in patients scheduled to undergo HSCT examined the outcomes of partial dental interventions. The study included 41 patients of which 38 needed dental interventions. Treated conditions included advanced caries, pulpitis, symptomatic or large apical periodontitis, advanced marginal periodontitis, and impacted third molars with pericoronitis. None of the patients developed systemic problems related to oral health problems. The authors therefore concluded that radical dental treatment prior to transplantation should not be recommended[23]. Again, there was no distinction between AlloSCT and ASCT or underlying disease types.

Toljanić et al.[24] demonstrated that oncologic treatment outcomes were not affected by the presence of untreated chronic dental disease or its acute exacerbations. However, a substantial majority of the patients included in their study received only standard chemotherapy, which did not result in a degree of granulocytopenia and immunosuppression comparable to HSCT.

Several older studies have shown that the time at which dental status evaluation is initiated is crucial for the decision on the further management of oral pathology[25]. If treatment of the dental pathology would lead to a postponement of the transplant, a conservative approach is chosen more frequently. Therefore, it would be important to start the dental evaluation as early as possible in order not to affect the treatment plan and potentially curative therapy. However, new studies — such as a retrospective analysis from two big centers in the US — identified low levels of dental need prior to alloHCT. Their findings suggest high access to care in this population. The role of antibiotic prophylaxis in patients undergoing bone marrow transplantation is controversial[26]. Approaches differ between centers, and the centers that use prophylaxis most often use quinolones. There are no specific recommendations for patients with dental pathologies. The Infectious Diseases Society of America and the American Society of Clinical Oncology recommend against routine prophylactic antibiotics before dental procedures in neutropenic patients, while Samim and collegues published a review article that recomends the profilactic use of antibiotics in patients with neutropenia gr IV[27].

Data reviews and meta-analyses

The Committee on Medicare coverage extensions of the Institute of Medicine found little published scientific evidence that directly assessed the effectiveness of dental service in the prevention or management of systemic health outcomes in patients with different types of cancer, including those undergoing HSCT[28]. Elad et al. performed a decision tree analysis on data from published case series and case reports on patients scheduled to receive treatment for hematological cancer or HSCT[29]. They found that the elimination of dental foci results in 1.8 lives saved per 1 000 treated patients. However, they failed to differentiate between underlying disease and HSCT types. A recent systematic review concluded that — in view of the relatively infrequent dental infections during cancer therapy and the complications after third molar extractions — partial dental evaluation/treatment protocols prior to anti-neoplastic therapy and HSCT whereby minor caries (within dentin), asymptomatic third molars or asymptomatic teeth without excessive probing depth (< 8 mm), mobility (I and II) or with periapical lesions of < 5 mm, appear to be a viable option if there is insufficient time for complete dental evaluation/treatment protocols[17].

Conclusions

All the listed facts, coupled with the low degree of evidence on the usefulness of aggressive dental pretransplant treatment, suggest that it is reasonable to modify the recommendations on the need for pretransplant dental health assessment and elimination of foci. In patients planned to undergo AlloSCT, partial intervention seems sufficient. This should include:

- restoration of teeth with moderate and severe caries in patients with enough time before HSCT, and observation in those in whom the procedure should not be delayed;
- extraction of residual roots;
- pulpectomy and root canal treatment for teeth with pulpitis;
- root canal treatment or extraction (depending on the urgency of AlloSCT, number of teeth affected, and disease severity) for teeth with recently symptomatic apical periodontitis or asymptomatic apical periodontitis and periapical radiolucency with a maximal diameter > 5 mm;
- extraction of teeth with gingival swelling, pain, and purulent discharge, with a probing depth greater than 8 mm, or severe mobility;
- oral hygiene instruction and scaling for asymptomatic marginal periodontitis;
- extraction of partially erupted third molars affected with pericoronitis or purulent drainage;
- tooth brushing instructions.

In patients scheduled to undergo ASCT, a similar approach can be used, provided it can be performed easily and without delaying the transplant procedure. Otherwise, due to the low risk of severe complications, the short duration of neutropenia, and no severe immunosuppression posttransplant, it seems that ASCT can be performed safely even without prior dental clearance.

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SAŽETAK

Stomatološka evaluacija prije transplantacije krvotvornih matičnih stanica

Ivana Jurčić Čulina, Boris Aurer, Lana Desnica, Ante Vulić, Barbara Dreta, Sandra Bašić-Kinda, Dino Dujmović, Toni Valković i Josip Batinić

Transplantacija krvotvornih matičnih stanica (HSCT) etablirana je terapijska metoda u liječenju različitih hematoloških malignih bolesti, ali je povezana sa značajnim komplikacijama sluznice uzrokovanima imunosupresijom i toksičnošću. Usna šupljina predstavlja čestu metu nuspojava povezanih s HSCT-om, ali i potencijalni izvor sustavnih infekcija. Zbog toga se stomatološka procjena prije transplantacije tradicionalno preporučuje radi uklanjanja oralnih žarišta koja mogu povećati morbiditet i mortalitet. Međutim, većina postojećih smjernica potječe iz razdoblja intenzivnijih kondicionirajućih režima, dulje neutropenije i veće transplantacijski povezane smrtnosti nego što je to uobičajeno danas. Ovaj pregledni rad analizirao je dostupne dokaze o rizicima i koristima stomatološke procjene i intervencije prije HSCT-a, s posebnim naglaskom na razlike između autologne (ASCT) i alogene transplantacije (AlloSCT). Iako postoji opći konsenzus da akutne i simptomatske oralne infekcije treba sanirati prije kondicioniranja, pristup asimptomatskim stomatološkim stanjima ostaje kontroverzan. Dostupna literatura uključuje malo randomiziranih kontroliranih studija te upućuje na nisku incidenciju infekcija oralnog podrijetla tijekom HSCT-a. Nerandomizirane studije i sustavni pregledi dovode u pitanje korist opsežne stomatološke sanacije, osobito ako ona dovodi do odgode transplantacije ili dodatnog morbiditeta. Trenutni dokazi podupiru selektivan, individualiziran pristup. U bolesnika podvrgnutih AlloSCT-u razumno je ciljati visokorizična stanja, dok se niskorizične asimptomatske lezije mogu pratiti. U bolesnika planiranih za ASCT, transplantacija se često može sigurno provesti i bez sveobuhvatne stomatološke sanacije.

KLJUČNE RIJEČI

Transplantacija krvotvornih matičnih stanica; Prijetransplantacijska stomatološka obrada; Rizik infekcije oralne sluznice