



# Oral surgery in liver transplant candidates: a retrospective study on delayed bleeding and other complications

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**Objective.** Untreated dental infections pose a threat for immunocompromised liver transplant (LT) recipients. Therefore, pretransplant dental evaluations are recommended. However, risk of bleeding should be considered among patients with end-stage liver disease, and prophylactic blood transfusions may be used to prevent bleeding. We performed a retrospective study of the incidence of and risk factors for oral surgery–related bleeding in candidates for LT and hypothesized that complications may occur despite preoperative and perioperative hemostatic actions.

**Study Design.** One hundred thirty-four patients who had tooth extractions performed by oral and maxillofacial surgeons before LT were studied. The primary endpoint was bleeding between 24 hours and 2 weeks after extraction. Bleeding risk was analyzed by preoperative platelet (PLT) count and international normalized ratio (INR). Invasiveness of procedures, severity of liver disease, PLT, INR, prophylactic transfusions of PLT, fresh frozen plasma, and tranexamic acid (TA) were included in univariate and multivariate logistic regression analyses to further assess risk.

**Results.** Twelve patients exhibited minor bleeding; four despite PLT  $>100 \times 10^9/L$  and INR  $<1.5$ . Increased bleeding associated with INR and prophylactic transfusions by univariate analysis; by multivariate analyses, prophylactic TA (odds ratio [OR] = 8.0; 95% confidence interval [CI] 1.7–37.0), and PLT (OR = 8.3; 95% CI 1.1–62.7) remained significant.

**Conclusions.** Most extractions were safe, but prophylactic transfusions did not ensure adequate hemostasis. Local hemostatic measures and close follow-up are warranted. (Oral Surg Oral Med Oral Pathol Oral Radiol 2016;121:490–495)

Pretransplant dental treatment is a prerequisite in many liver transplantation (LT) programs. This requirement aims to prevent posttransplant infectious complications, such as bacteremia and sepsis, which could be fatal in immunocompromised patients.<sup>1,2</sup> In particular, patients with chronic liver disease (CLD) have shown poor oral health with a high prevalence of dental infections in pre-LT dental evaluations.<sup>3</sup> Often, teeth with obvious severe infections are extracted after administering antibiotic prophylaxis. Although there is no scientific evidence in the literature to support antibiotic prophylaxis for this patient group, our clinic has adopted this protocol to prevent serious postoperative infectious complications in these high-risk patients. Patients with CLD also run a high risk of bleeding after oral surgery because of CLD-associated coagulopathy.<sup>4</sup> Reported incidences of bleeding after oral surgery in

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patients with CLD vary from 0% to 56%.<sup>4–8</sup> However, previous studies were limited by small cohorts (9–90 patients), and those patients often had well-compensated CLD.<sup>6</sup> Earlier studies that specifically studied LT candidates, that is, patients with advanced or end-stage liver disease, included only 23 to 36 patients.<sup>4,5,7,8</sup>

Platelets (PLT), fresh frozen plasma (FFP), and tranexamic acid (TA) are typically administered before oral surgery in an attempt to prevent bleeding despite the lack of firm evidence to support this strategy. It has been suggested that the risk of bleeding might be predicted by an elevated international normalized ratio (INR) or thrombocytopenia; therefore, prophylactic transfusions of FFP and PLT have been justified to prevent bleeding complications. Because of the high fibrinolytic activity in the oral cavity, systemic antifibrinolytics, such as TA, are sometimes used in addition to the local antifibrinolytics. However, the systemic

## Statement of Clinical Relevance

International normalized ratio and platelet count do not reliably predict bleeding after tooth extractions in liver transplant candidates because of rebalanced hemostasis. Hence, routine prophylactic replacement therapy may be ineffective. Alternatively, local hemostatic measures and close postoperative follow-up by a skilled clinician are recommended.

approach remains controversial because of the risk of thrombotic events. Nevertheless, the effect of these blood products lasts for only a few hours; consequently, they may not have an impact on delayed bleeding that can occur several days later.

The primary aim of the current retrospective study was to investigate the incidence and risk factors of bleeding complications following tooth extractions in candidates for LT. We also investigated the effects of preprocedural transfusions to prevent post-oral surgery bleeding. A secondary aim was to investigate other complications related to oral surgery. We hypothesized that complications might occur, despite preoperative and perioperative hemostatic actions.

## MATERIALS AND METHODS

This retrospective study was conducted in agreement with the Declaration of Helsinki and was received exemption from institutional review board approval. The primary endpoint of the study was oral bleeding related to oral surgery that appeared within 2 weeks from surgery. Replacement therapy was considered effective when good hemostasis was achieved during the procedure and the patient did not show any delayed bleeding.

During 2000–2006, a total of 306 adult LTs were performed in Finland. Of these patients, 263 had dental evaluations before LT at the Department of Oral and Maxillofacial Diseases, Helsinki University Hospital, Helsinki, Finland. As part of routine practice before LT the Transplantation and Liver Surgery Clinic referred patients to an oral and maxillofacial (OMF) surgeon in our department for dental treatments.

We retrieved data from patient medical records, tomographic radiographs, and the hospital laboratory database. Medical records were reviewed when any oral surgery-related bleeding complication required hospital care. These events were considered bleeding complications in the present study. We defined “bleeding” as continuous or delayed bleeding, observed at least 24 hours following tooth extractions, which required a return visit to an OMF surgeon for treatment. The bleeding was recorded by either a medical doctor or nurse at the hospital ward. The amount of blood loss was not recorded.

Data collected from the patient records included type of liver disease, number of teeth, number of extracted teeth, number of difficult extractions (impacted wisdom teeth, representing invasive procedures), oral surgery related complications, and preoperative PLT and INR values, as well as intravenous (IV) preprocedural replacement therapies: PLT (8–16 IU), FFP (2–4 IU), and TA (1–3 g oral or IV administration). These replacement therapies were given prophylactically, based on the anesthesiologist’s individual clinical

assessment of bleeding risk, when the PLT count was low and the INR was high.

The Model for End-stage Liver Disease (MELD) was used to categorize patients in this study. MELD scores reflect the severity of liver disease, and they are used to predict the risk of death. The scores were calculated with the Mayo Clinic online calculator. The calculation included blood creatinine, bilirubin, and INR values recorded at the time the patient was listed for LT. The MELD equation assumed an upper limit of 350  $\mu$ M for plasma creatinine.

## Statistical analysis

Data were analyzed with PASW statistical software, version 17.0 (SPSS Inc., Chicago, IL). The  $\chi^2$  test was used to evaluate categorical variables, and the Mann–Whitney test was used for continuous variables. The effect of various factors on bleeding risk was assessed by univariate and multivariate logistic regression analyses. A two-sided  $P < .05$  was considered significant.

## RESULTS

Patient demographic characteristics are given in [Table I](#). The final study population comprised 134 patients who required tooth extractions before LT. Most patients returned to the in-patient clinic for at least one night following tooth extractions. In some cases, patients stayed overnight at the Department of Oral and Maxillofacial Diseases. In either case, postoperative follow-up was readily available. TA was routinely used locally. It was applied in liquid form to saturate gauzes, which were then placed tightly over alveolar sockets after tooth extractions. Other local hemostatic measures were provided to all patients, including careful, tight suturing of the wounds and close follow-up in the recovery room.

One patient had acute liver failure, and all others had CLD. Of the patients, 12 exhibited bleeding complications more than 24 hours postoperatively, which required treatment from an OMF surgeon. In the present study, all bleeding complications were minor and fairly simple to treat. In most cases, bleeding occurred 1 to 2 days postoperatively, but one case exhibited excessive bleeding 8 days postoperatively. That patient had remained in the ward; thus, treatment was easily available. In cases of delayed bleeding, an OMF surgeon was called, and the alveolar socket was either resutured or local hemostatic agents were administered (e.g., with local TA surges/rinse or with gelatin sponges), and tight gauze pads were placed on bleeding alveolar sockets.

The average number of teeth extracted was five (range 1–20); four patients required full mouth

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