



# Major relationships of tooth extraction in patients with cardiovascular diseases: a concise systematic review

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## Abstract

**Introduction:** Cardiovascular diseases (CVD) are the leading cause of death worldwide. The number of tooth extraction patients with cardiovascular disease in our country is increasing year by year. Blood pressure control, determination of cardiac function, recognition of arrhythmias, glycemic control, and use of antiplatelet agents or oral anticoagulants need to be investigated.

**Objective:** It was to carry out a concise systematic review of the main relationships of tooth extraction in patients with cardiovascular diseases, to emphasize the main risk predictors. **Methods:** The systematic review rules of the PRISMA Platform were followed. The search was carried out from February to March 2023 in the Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases, using articles from 2009 to 2022. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed accordingly, according to the Cochrane instrument.

**Results and Conclusion:** A total of 124 articles were found, 38 articles were evaluated and 24 were included and developed in this systematic review study. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 26 studies with a high risk of bias and 40 studies that did not meet GRADE. It was concluded that the cardiovascular response of elderly outpatients with systemic diseases during tooth extraction is quite significant. Age, sex, systemic diseases, and some tooth extractions may be risk factors closely associated with cardiovascular response. It is necessary for the dental treatment of these patients

with heart disease a good knowledge of the subject and requires medical and dental coordination. Dental surgeons need to be prepared to identify possible medical and dental emergencies and take steps to prevent or treat them effectively and quickly.

**Keywords:** Cardiovascular diseases. Dental extraction. Tooth extraction. Exodontia. Elderly.

## Introduction

Cardiovascular diseases (CVD) are the leading cause of death worldwide [1]. Endothelial dysfunction is the first step in the development of atherosclerosis and precedes intravascular inflammatory and prothrombotic changes linked to atheroma formation and evolution. Acute and chronic inflammation are the main drivers of endothelial dysfunction and plaque evolution, leading to acute cardiovascular events such as myocardial infarction (MI), ischemic stroke, and peripheral arterial disease. The risk of an acute cardiovascular event increases considerably during periods of acute infection or influenza season. Chronic dental infections have been associated with systemic inflammation, endothelial dysfunction, and increased incidence of future cardiovascular events [2].

In this scenario, the number of tooth extraction patients with cardiovascular disease in our country is increasing year by year. Safety is paramount for these patients, and there is no uniform standard of risk assessment and management for tooth extraction patients with cardiovascular disease during the

perioperative period. Blood pressure control, determination of cardiac function, recognition of arrhythmias, glycemic control, and use of antiplatelet agents or oral anticoagulants need to be investigated [3-5].

In this aspect, the correct evaluation of patients with cardiovascular impairment is based on a detailed anamnesis and prior knowledge of the main coronary disorders and their sequelae. Complications such as myocardial infarction and bacterial endocarditis may be described in clinical dental procedures. The management of this information is important in determining the patients' cardiac risk to classify it as high, moderate, or minimal [6].

Thus, the dental professional must plan the clinical consultations according to the preestablished individual risk [6,7]. Short-term consultations and limitation of stress and anxiety levels, with the use of anti-anxiolytic drugs and complementary sedation, may be important for an uncomplicated trans and postoperative period. Emergency procedures, in cases where coronary changes occur during a clinical procedure, are also evident [7].

Also, cardiovascular diseases can present a congenital origin, that is present from birth, such as interatrial and interventricular communication, defects of the artery, coronary arteries, or acquired coronary artery anomalies that involve several risk factors such as smoking, alcohol, old age, sedentary lifestyle, which contribute to the aggravation of these diseases Hypertension, atherosclerosis, arrhythmia, angina pectoris, myocardial infarction, heart failure, stroke [7,8].

Thus, the acquired ones are the most frequent in the routine of a dental practice, so the dentist should be able to attend to those patients who need special care, regarding the correct use of medications due to the risk of drug interactions, the type of local anesthetic to be used and the management of patients who use anticoagulant therapy [1,9].

In this context, dentistry has surgical procedures such as the extraction of supernumerary teeth, removal of third molars, wisdom teeth, and residual root, with or without odontostomy and osteotomy, which, because they are more complex procedures, cover even more care in patients with heart disease, especially in the preoperative, in the trans-operative and the postoperative period, so all care is essential [10].

The recommendations of the American Heart Association emphasize that some surgical procedures, dental procedures, and instrumentations involving mucosal surfaces or contaminated tissues may cause transient bacteremia [11]. While recognizing that the efficacy of antibiotic protection is uncertain in some

cases, it recommends the administration of antibiotics to patients with a potential risk of developing endocarditis. Continued administration of antibiotics should be considered in patients with the established infection before the procedure. However, it is not possible to predict which patients will develop this infection or which particular procedure will be responsible [11,12].

Given the above, the present study carried out a concise systematic review of the main relationships of tooth extraction in patients with cardiovascular diseases, to emphasize the main risk predictors.

## Methods

### Study Design

This was followed by a systematic literature review model on the main clinical findings of mandible fractures, according to the PRISMA rules.

### Data Sources and Research Strategy

The literary search process was carried out from February to March 2023 and was developed based on Scopus, PubMed, Science Direct, Scielo, and Google Scholar, using scientific articles from 2009 to 2022, using the descriptors (MeSH Terms): *Cardiovascular diseases*. *Dental extraction*. *Tooth extraction*. *Exodontia*. *Elderly*, and using the Booleans "and" between the descriptors (MeSH Terms) and "or" between the historical findings.

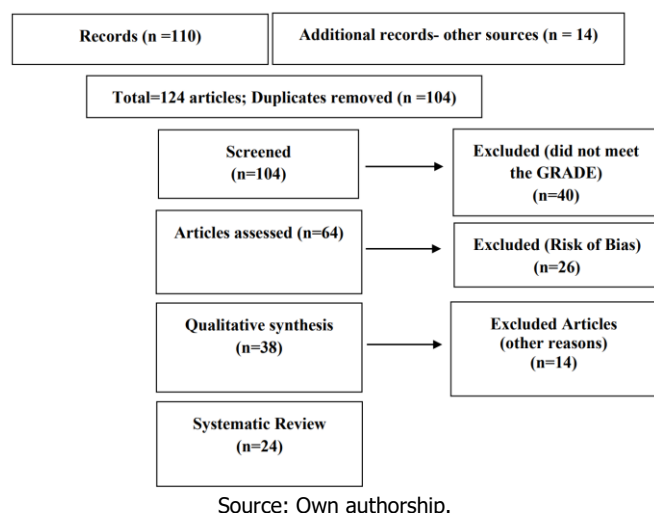
### Study Quality and Risk of Bias

The quality of the studies was based on the GRADE instrument, with randomized controlled clinical studies, prospective controlled clinical studies, and studies of systematic review and meta-analysis listed as the studies with the greatest scientific evidence. The risk of bias was analyzed according to the Cochrane instrument.

## Results and Discussion

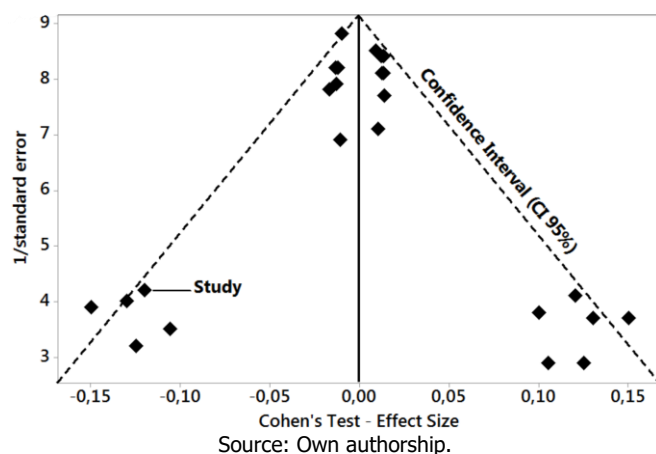
### Summary

A total of 124 articles were found. Initially, duplication of articles was excluded. After this process, the abstracts were evaluated and a new exclusion was performed, removing the articles that did not include the theme of this article, resulting in 64 articles. A total of 38 articles were evaluated and 24 were included and developed in this systematic review study (**Figure 1**). Considering the Cochrane tool for risk of bias, the overall assessment resulted in 26 studies with a high risk of bias and 40 studies that did not meet GRADE.

**Figure 1.** Selection of studies.

**Figure 2** presents the results of the risk of bias in the studies using the Funnel Plot (Effect Size - Cohen's Test). The sample size was determined indirectly by the inverse of the standard error. The graph showed symmetric behavior, not suggesting a significant risk of bias in studies with small sample sizes, which are shown at the bottom of the graph.

**Figure 2.** The symmetric funnel plot does not suggest a risk of bias between the small sample size studies that are shown at the bottom of the graph (N = 24 studies).



### Major Clinical Findings

A retrospective clinical study by Li et al. 2022 [13] evaluated the cardiovascular response of elderly people during tooth extraction and analyzed risk factors to provide clinical guidance. The heart rate (HR), systolic blood pressure (SBP), and diastolic blood pressure (DBP) of elderly patients significantly increased during local anesthesia and tooth extraction. During the operation, older patients ( $\beta = 2.011$ ,  $P = 0.005$ ) and diabetics ( $\beta = 3.902$ ,  $p < 0.0001$ ) were associated with higher SBP, while those with more tooth extractions had higher HR ( $\beta = 0.893$ ,  $P = 0.007$ ). Female patients had significantly increased HR ( $\beta = 1.687$ ,  $P < 0.0001$ ) and

SBP ( $\beta = 2.268$ ,  $P < 0.0001$ ).

However, for patients with coronary artery disease, HR ( $\beta = -2.747$ ,  $p < 0.0001$ ) and blood pressure [SBP ( $\beta = -4.094$ ,  $p < 0.0001$ ) and DBP ( $\beta = -0.87$ ,  $p = 0.016$ )] were markedly lower than in patients without a diagnosis of coronary artery disease. Therefore, the cardiovascular response of elderly outpatients with systemic diseases during tooth extraction is quite significant. Age, sex, systemic diseases, and some tooth extractions may be risk factors closely associated with cardiovascular response.

In addition to these findings, a retrospective observational study developed by Tang et al. 2019 [14] established a prediction model based on the Random Forest (RF) algorithm for the risk of cardiac complications of tooth extraction in elderly patients with CVD. A total of 603 patients who met the inclusion criteria were used to create a training set. Predictors were identified using logistic regression (LR) with penalized LASSO variable selection (smallest absolute shrinkage and selection operator). The training set, based on 603 participants, including 282 males and 321 females, had a mean participant age of  $72.38 \pm 8.31$  years. Using resource selection methods, 11 risk predictors of cardiac complications were selected. When the RF model was built, its overall classification accuracy was 0.82 at the optimal cutoff value of 18.5%. Compared to the LR model, the RF model showed superior predictive performance. The AUROC (area under the receiver operating characteristic curve) scores of the RF and LR models were 0.83 and 0.80, respectively, in the independent test set. The AUPRC (area under the accuracy recall curve) scores of the RF and LR models were 0.56 and 0.35, respectively, in the independent test set.

Furthermore, a retrospective clinical study carried out by Kubota et al. 2021 [15] evaluated the cardiovascular response in patients using warfarin and hypertensive patients not using warfarin during tooth extractions. We included 53 patients who had undergone tooth extraction while using warfarin (mean age  $78.8 \pm 6.3$  years, 26 men) and 66 with hypertension who had undergone tooth extraction but were not in the use of warfarin (mean age  $77.4 \pm 6.8$  years, 22 men). The highest values of systolic blood pressure (SBP) (mean of  $150.1 \pm 21.1$  mmHg) were observed in patients using warfarin before (9.0%) and after (10.3%) administration of local anesthesia (AL), during extraction (39.7%), and during (33.3%) and after (7.7%) suturing ( $n = 78$ ;  $p < 0.01$ ), and in hypertensive patients who did not receive warfarin ( $160.6 \pm 24.8$  mmHg) before (19.2%) and after (27.3%) LA administration, during extraction (29.3%) and during (18.2%) and after (6.1%) suture ( $n = 99$ ;  $p < 0.01$ ).

The highest SBP was linearly correlated with SBP before LA administration in patients on warfarin (highest SBP =  $0.9415 \times \text{SBP before LA} + 23.243$ ,  $R^2 = 0.75481$ ) and in hypertensive patients without warfarin (highest PAS =  $1.0027 \times \text{PAS before LA} + 15.789$ ,  $R^2 = 0.60341$ ). Therefore, higher SBP was not evenly distributed between patients on warfarin and hypertensive patients not on warfarin during tooth extraction and was strongly associated with SBP before AL, regardless of anticoagulant status [15].

In all cases of patients with cardiovascular diseases, the preoperative anamnesis should be done with all the details, always observing the risk factors that progress to include the medications used, if the patient makes use of cardiac prostheses, monitoring the vital signs before and after dental procedures, always recording all occurrences and procedures in medical records [16].

Based on the study by Kamatani et al. (2017) [7], although cardiac arrhythmias are occasionally associated with dental extractions and dental anesthesia, an atrioventricular block is rarely seen during dental procedures. In this study, a rare case of type I second-degree atrioventricular block (Wenckebach's phenomenon) was reported after bilateral extraction of mandibular third molars retained under general anesthesia in a 16-year-old Japanese girl. Extubation of the nasotracheal tube or oral/pharyngeal suctioning could have triggered a vagal reflex that caused a type I second-degree atrioventricular block. Thus, standard cardiovascular monitoring is imperative for patients undergoing dental treatment under general anesthesia.

Still, according to Forresti et al. (2017) [8], a trigger for hereditary angioedema is dental treatment with tooth extraction. Clinical symptoms may not manifest for many hours or even days after the procedure. In the example of this author, the problem resulted in death after tooth extraction, highlighting the need for dentists to be aware of this condition.

In a review of episodes of bacterial endocarditis involving litigious procedures against dental surgeons, it was found that the dental procedures that resulted in bacterial endocarditis were exodontia, periodontal scaling, root canal treatment with over instrumentation, and minor oral surgery [17-20]. The authors observed that the dentists involved in the cases failed to prescribe a prophylactic antibiotic therapy, prescribed incorrect antibiotics, or at inappropriate times. There was only one episode of correct antibiotic prophylaxis that resulted in bacterial endocarditis. These data highlight the importance of correct prophylaxis with antibiotics, as there is adequate evidence that this procedure reduces the risks of transient bacteremia. In addition,

the dentist needs to record all procedures and behaviors in the patient's clinical record because, in any litigious proceedings, the medical record is the most reliable document used to defend the professional [19,20].

Besides, regarding the use of anticoagulants and platelet anti-aggregates, patients with heart disease usually use acetylsalicylic acid medication, sodium warfarin that interferes with blood clotting, making it difficult to perform dental surgery. In this case, the dental surgeon must request a pre-operative laboratory test called a Coagulogram for International Normalization Ratio (INR), which is recommended by the World Health Organization (WHO) to unify the prothrombin time blood clotting tendency [1]. Also, in the trans-operative, the dental surgeon must always be prepared with hemostatic measures: 10.0 mL tranexamic acid for irrigation, collagen sponge, and bone lock. In cases of bleeding, the patient should be referred to an outpatient clinic for intravenous administration of fresh frozen plasma and vitamin K (1mg) [1].

Regarding the use of vasoconstrictors, every cardiopathy patient is at greater risk of endogenous adrenaline release due to local anesthesia improperly than the small amount of local anesthetic the use of vasoconstrictors in a small amount. The dental surgeon, however, cannot exceed the limit of 0.04mg adrenaline, and perform negative aspiration so that there is no intramuscular injection. In this context, anxiety is a factor that interferes with cardiovascular systemic homeostasis; in the preoperative period, the use of anxiolytics can be used [6].

In hypertensive patients, the disease is asymptomatic and defined as the elevation of blood pressure in the arteries, systolic pressure is the maximum pressure, while the diastolic pressure is the minimum, with values at rest above 140mmHg (systolic) and 90mmHg (diastolic), is considered a hypertensive individual. Checking the pressure before the consultation, even if the patient is controlled, always opt for consultations in the morning, and are brief, to avoid the use of NSAIDs (non-steroidal anti-inflammatory drugs) for a long period and in patients who use the medications for pressure: propranolol and captopril, etc, as there may be interference in the mechanism of action of hypertensives [11].

In dentistry, the most used antibiotic prophylaxis is for the prevention of infective endocarditis. Infective endocarditis is a remote infection involving the heart valves and may lead to death [19,20]. Recent studies emphasize changes in the profile of infective endocarditis from a streptococcal disease in patients with prior heart disease to a staphylococcal disease associated with performing dental and medical



procedures in elderly patients with multiple comorbidities [17].

In this sense, the American Heart Association (AHA) suggests the adoption of antibiotic prophylaxis for the prevention of infective endocarditis under certain conditions [19,20]. This therapeutic resource has now been indicated only for patients at high cardiac risk in invasive dental procedures. Thus, a restricted number of patients is selected, only those in whom endocarditis would lead to an increased risk of morbidity and mortality [20].

The indication of the use of antibiotic prophylaxis before invasive dental procedures is well established in patients with cardiovascular conditions predisposing to the development of infective endocarditis, such as patients with prosthetic heart valves or repaired with prosthetic material, previous history of endocarditis, cardiac transplantation that develops with dysfunction valvular heart disease, uncorrected or corrected cyanotic congenital heart disease, but evolved to a residual lesion, corrected with prosthetic material or device, during the first six months after the procedure, any corrected congenital heart disease with a residual defect at or adjacent to the prosthesis [19].

Some clinical conditions may predispose patients to the development of remote infection. In these individuals, antibiotic prophylaxis is indicated and should be discussed with the attending physician, considering comorbidities and vulnerabilities. This includes patients with Acquired Immunodeficiency Syndrome-AIDS ( $CD4 < 1,000/mm^3$ ), in chemotherapeutic treatments, transplanted solid organs or bone marrow, in radiotherapy treatments of head and neck, using immunosuppressants, autoimmune disease, Skeletal anemia, splenectomy, use of bisphosphonates, injecting drug users, chronic renal failure, severe facial infection, chronic or active hepatitis, diabetes mellitus and patients with orthopedic joint prostheses [20].

Another important issue is the dosage of anesthesia, to avoid complications, the maximum dose of anesthetics must be respected. In those with severe risk, it is recommended that the physician in charge request anesthetics without vasoconstrictors avoid undesirable complications, such as tachycardia and even cardiac arrest. This brings with it some disadvantages during the treatment because, in addition to decreasing the time of action of the drug, due to the rapid leakage of the anesthetic components into the bloodstream, it provides a potential increase in systemic toxicity [1-3].

In the case of lidocaine, the maximum dose is 4.4 mg/kg or 300mg; mepivacaine is 4.4 mg/kg or 300mg; prilocaine is 6 mg/kg or 400mg; and articaine is 7 mg/kg or 500mg. Likewise, vasoconstrictors should be well-adjusted. Adrenaline, for example, has a maximum

recommended dose of 0.2mg, while noradrenaline is 0.34mg per session [9,10]. The use of anesthetic prilocaine should be carefully monitored because doses above 600 mg may cause episodes of methemoglobinemia (Meta-hemoglobin is a form of hemoglobin protein, in which the iron in the heme group is in the  $Fe^{3+}$  state and not in  $Fe^{2+}$  of normal hemoglobin. In this disorder, iron atoms in the form of ferric ions lose the ability to release oxygen to tissues causing episodes of tachycardia, cyanosis, dyspnea, fatigue, headache, vomiting, and dizziness, and may progress to coma and death. of this table can be obtained by intravenous administration of 1% methylene blue (1.5 mg/kg) [17].

In this context, in the case of endodontic procedures, it is also verified that the absence of hemostatic action promotes greater bleeding of the pulp tissue and less control of pain during treatment. In cases of stress, pain, and tension can generate an amount of endogenous adrenaline greater than that administered in local dental anesthesia when the correct dosage is respected. Thus, if the patient can tolerate the stress of the dental procedure, he may receive local anesthesia with a vasoconstrictor [4,17].

In this scenario, for the patient with a history of angina or previous myocardial infarction, every effort should be made to reduce stress levels through efficient and deep anesthesia for dental and soft tissue procedures. During the consultation with the patient's physician, the dental surgeon may report the intention to prescribe anxiolytic medication before the dental procedure. The prescription of anxiolytics and preventive medication for angina helps in the comfort and stability of the patient. Monitoring of blood pressure and heart rate should be performed during the procedure and for the next 30 minutes [10,17].

The dental care of patients with cardiovascular impairment requires correct planning of the clinical procedures to be performed. To this end, prior contacts with the patient's physician and a detailed anamnesis will provide crucial information for the determination of the risk factors. These will depend on the choice of care in the office or hospital setting and the determination of the need for antibiotic prophylaxis [5,17].

Thus, short-term visits and the use of complementary sedation may make the service safer and more comfortable for both the patient and the professional [21-23]. It is also worth remembering that the more informed and prepared the dentist is at the moment of the clinical consultation, the lower the chances of trans and postoperative complications. In addition, there will be more tranquility and speed to deal with possible emergencies, increasing the patient's chances of survival [24].

## Conclusion

It was concluded that the cardiovascular response of elderly outpatients with systemic diseases during tooth extraction is quite significant. Age, sex, systemic diseases, and some tooth extractions may be risk factors closely associated with cardiovascular response. It is necessary for the dental treatment of these patients with heart disease a good knowledge of the subject and requires medical and dental coordination. Dental surgeons need to be prepared to identify possible medical and dental emergencies and take steps to prevent or treat them effectively and quickly.

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## Informed consent

Not applicable.

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No additional data are available.

## Conflict of interest

The authors declare no conflict of interest.

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