



Emma O'Donnell,¹ **Shazia Kaka**,² **Helen Patterson**³ and **Carole Ann Boyle**⁴ provide dental teams with knowledge on the background and process of cardiac transplant and explain the implications for oral health and dental management.

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Abstract

Cardiac transplantation replaces a severely damaged non-functioning heart with a healthy heart from a donor. Within the UK, the number of cardiac transplants being performed each year is increasing, with significant improvements in longer-term survival. Dental professionals are therefore more likely to see and manage these patients in the pre- and post-transplant periods. This paper proposes

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Introduction

What is a cardiac transplant?

A cardiac transplant is a surgical procedure that replaces a severely diseased heart with a healthy heart from a recently deceased donor.¹ It is most commonly indicated for people with advanced heart failure or those with recurrent, symptomatic, life-threatening arrythmias, which are unresponsive to maximal medical and/or surgical treatment.² Coronary artery disease, congenital heart disease, valvular heart disease, or myocardial disease can all produce these end stage complications where the diseased heart fails to support a physiological circulation. Poor quality of life ensues with symptoms including breathlessness, fatigue, dizziness, chest pain, cough and risk of sudden death (1% per year).³

Cardiac transplant is the recommended treatment option to help restore cardiac function and prolong life. In 2021/22, 179 heart transplants were performed across seven centres in the UK (Table 1), with five-year survival rates of 71%.

When donors are not immediately available, ventricular assist devices (VADs) can be used

as a short-term measure to help support life. These are battery operated, mechanical pumps surgically implanted into the heart's left ventricle, to either partially or completely replace the function of a heart. While results are variable, a recent systematic review reported 12-, 24- and 48-month survival rates of 82%, 72% and 57%, respectively.⁵

Those at high risk of developing dangerous arrythmias may have an implantable cardioverter defibrillator (ICD) in place. These devices, on detecting an abnormal rhythm, deliver either small rapid pacing impulses or a larger electric shock to restore normal rhythm. If an ICD is in place, it is useful to ascertain the frequency of shocks and how recently these have occurred. This allows the clinician to risk assess the possibility of shocks in the dental surgery and ensure they are treated in the most appropriate environment.

Acceptance for cardiac transplantation

The multidisciplinary cardiac transplant team carries out a thorough medical assessment and decides, within 18 weeks, whether to list the patient for a heart transplant. If deemed suitable, the patient is assigned to either the super-urgent, urgent, or non-urgent heart transplant list.

The majority of non-urgent patients are out of hospital and stable. Those on urgent lists tend to be inpatients in hospital on intravenous (IV) medication, while those on the super-urgent list are commonly in intensive care units (ICUs), with IV monitoring equipment or left VADs to sustain heart function.

How is a cardiac transplant carried out?

Cardiac transplantation is complex, high-risk and takes 4–6 hours. During the surgery, the patient is placed on a heart-lung bypass machine to keep blood circulating with adequate oxygen. The patient's damaged heart is removed and the donor heart put in place. The patient is moved to an ICU for further medical support and optimisation of recovery before being stepped down over the course of 2–3 weeks. During recovery, high dose immunosuppressive regimes are used to reduce the risk of transplant rejection. This rejection risk is highest within the first 3–6 months post-transplant and subsequently reduces with time.⁶

The post-transplant period

Rejection of the transplanted heart is a major cause of morbidity and mortality.⁶ An important balance must therefore be struck throughout the patient's life between ensuring sufficient immunosuppression to avoid rejection while minimising the main sequelae of immunosuppression, namely infection and malignancies.

Induction regimes provide intense early post-operative immunosuppression, with drugs including monoclonal antibodies (eg basilixamab, daclizumab, alemtuzumab) and polyclonal antibodies (eg antilymphocyte and antithymocte globulin). These usually continue for 2-3 weeks, resulting in significant depletion of a patient's T- and B-cells. During this period, prophylactic antibacterials, antifungals and antivirals are commonly used to reduce infection risks. Maintenance regimes are subsequently commenced which continue through the patient's life. While regimes will vary, combination therapies consisting of a steroid, a calcineurin inhibitor (cyclosporin A, tacrolimus, sirolimus, everolimus) and an antimetabolite (eg mycophenolate mofetil or azathioprine) are most commonly used. Therapy is gradually decreased over time, with efforts now being made to discontinue steroid therapy 6-12 months after heart transplantation.6 The numerous medications patients may be taking and their significance is summarised in Table 2.

Cardiac transplant protocol

Dental assessments make a significant contribution towards the workup for cardiac

Table 1 Location for cardiac transplants within the UK				
City	Hospital			
London	Great Ormond Street Hospital (children)			
	Royal Brompton and Harefield Hospital (adults)			
Cambridge	Royal Papworth Hospital			
Birmingham	University Hospital Birmingham NHS Foundation Trust			
Manchester	University Hospital of South Manchester			
Newcastle	Freeman Hospital			
Glasgow	Golden Jubilee National Hospital			

Table 2 Dental considerations of post-transplant medications					
Drug	Drug type	Regime	Significance in dentistry		
Mycophenolate mofetil (Cellsept)	Inosine monophosphate dehydrogenase inhibitor	Lifelong	Immunosuppressant Altered taste		
Tacrolimus (Prograf)	Calcineurin inhibitor	Lifelong	Immunosuppressant Oral ulceration Drug interactions: carbamazepine, clarithromycin, erythromycin, fluconazole, miconazole		
Sirolimus (Rapamune)	mTOR inhibitor	Lifelong	Immunosuppressant Drug interactions: clarithromycin, erythromycin, fluconazole, miconazole		
Everolimus (Afinitor)	mTOR inhibitor	Lifelong	Immunosuppressant Drug interactions: carbamazepine, clarithromycin, fluconazole		
Ciclosporin (Neoral)		Lifelong	Immunosuppressant Gingival hypertrophy Drug interactions: aciclovir, carbamazepine, clarithromycin, doxycycline, fluconazole, miconazole		
Prednisolone	Corticosteroid	Six months post-transplant	Immunosuppressant Risk of adrenal crisis Avoid non-steroidal anti-inflammatory drugs (NSAIDs) if possible Drug interactions: carbamazepine, clarithromycin, erythromycin, fluconazole		
Alendronic acid (Fosamax)	Bisphosphonate	While on prednisolone to prevent secondary osteoporosis	Medication-related osteonecrosis of the jaws Increased risk of gastrointestinal irritation with NSAIDs		
Statin		Lowers cholesterol	Drug interactions: carbamazepine, clarithromycin, doxycyclin, erythromycin, fluconazole, miconazole, tetracycline		

transplantation. There is, however, little guidance on which dental teams should do this, where it should be done, and the factors that require consideration when deciding which treatment should be carried out.

Tables 3, 4, 5, 6 and 7 present a proposed protocol to answer these questions through a patient's transplant journey.

Cardiac transplant and the role of the general dental practitioner

Care of this unique patient group requires a shared approach between the general dental practitioner (GDP), specialist dental teams and cardiac transplant teams. Regardless of setting, all clinicians should prioritise prevention, disease stabilisation, removal of any potential or

Table 3 Cardiac transplant dental protocol for patients being considered for cardiac transplant • The patient should be seen within two weeks of referral Referral Consider co-ordinating dental appointments with other pre-transplant appointments in the same location to reduce the patient's appointment burden Full dental examination, including caries, periodontal and oral cancer risk assessment, plus soft tissue baseline should be established If seen by Special Care Dentistry (SCD), details of patient's GDP should be known, or registration encouraged. The patient should be informed of the need to continue to attend their own GDP for regular screening Radiographic examination is strongly encouraged unless the patient is unable to Assessment attend the clinic or a radiology department. A panoramic is required with intra-oral radiographs as indicated7 Should the patient be unable to attend clinic, the patient should be assessed on a ward with consideration of radiographs via a mobile unit if available If the patient is considered not for transplant, consider discharge to GDP for ongoing care unless the patient fulfils other SCD referral criteria • Establish a prevention regime with the patient A treatment plan where the patient is accepted for a cardiac transplant may differ/ Treatment plan be more invasive than one where they are not accepted If seen within a centralised national clinic, consider referring for treatment to SCD colleagues at a location closer to patient's home Exclude current and potential acute or chronic bacterial, fungal and viral infections Treat dental pathology prioritising any sources of dental sepsis Consider adjustment or removal of dentures, orthodontic appliances and brackets if transplant is likely to be imminent8 If not fit for treatment pre-transplant, complete a dental assessment where possible, note treatment requirements and follow-up soon after transplant Patients may be on anticoagulants and relevant guidance should be sought prior to invasive treatment (Management of dental patients taking anticoagulants or antiplatelet drugs guidance by Scottish Dental Clinical Effectiveness Programme) Patients may have an implanted cardiac device to regulate abnormal heart rhythm's these may activate without warning, potentially causing patients to perform sudden movement, including biting down. These generally do not require antibiotic cover. Use of adrenaline should be considered in lower dosages with careful monitoring Consider that bisphosphonates and concurrent corticosteroids are likely to be prescribed post-operatively. **Treatment** protocol When to consider extractions: Any potential source of acute or chronic infection Teeth of poor or uncertain prognosis Deep or extensive caries9 Abscess/swelling Irreversible pulpitis Unrestorable tooth/root Retained root in communication with oral cavity Perio-endo lesions9 Periodontally involved teeth with furcation involvement, Grade 2 and 3 mobility or those with pocketing over 4 mm with bleeding on probing Asymptomatic and symptomatic periapical periodontitis9

waiting list · A two-week healing period is advisable following any invasive dental treatment, prior to surgery. This may not be possible due to the unpredictable nature of Following cardiac transplant, with the final decision remaining with the cardiac surgeon dental Letter to cardiology stating patient is dentally stable for cardiac surgery treatment Correspondence to GDP to inform of treatment provided and encourage regular review Patients on the transplant waiting list should be reviewed by SCD annually, whilst

Table 4 Cardiac transplant dental protocol for patients then placed on routine

Teeth with technically difficult root canal (curves, sclerosed)

Root caries

Partially erupted third molars

While on transplant waiting list

- also attending their GDP six-monthly, unless there are clinical indications for more frequent review
- Treat any dental pathology quickly and definitively so as to not compromise the patients place on the transplant waiting list
- Inform the cardiac team if the patient requires dental treatment while on cardiac transplant waiting list

active infective sources, and ensure a thorough soft tissue assessment. Generally, the dental workup before waiting list acceptance will occur in a hospital setting; however, if medically fit for primary care, the GDP could optimise oral health for transplant using the principles found in Table 3. Regular oral health examinations in primary care should be implemented alongside specialist dental team review, in keeping with enhanced prevention and recall schedules. Close surveillance of this cohort will ensure early detection of dental disease development which may influence their suitability for transplant, with potential suspension from the transplant waiting list. Should the GDP find evidence of infection or dental disease, the cardiac and specialist dental team should be made aware urgently. Following transplant, the patient should not receive any invasive dental treatment outwith a hospital site until medically stable. Post-transplant, the patient, if stable, is generally appropriate for treatment in general practice after two years. Non-invasive dental treatment is suitable in general practice pre- and posttransplant, should the patient be medically well enough to attend primary care. Additionally, patients with VADs require regular recall and to be managed by the specialist dental team should they require treatment alongside prophylactic antibiotics for invasive procedures that could cause bacteraemia.

Cases

The case series below illustrates the practical application of the cardiac transplant dental protocol and the holistic approach to care considered for these patients throughout their journey.

Case 1

A 49-year-old attended the dental clinic with a cardiac nurse following a referral from the specialist cardiac centre. They were an inpatient at the time, having been admitted two weeks prior due to acute heart failure on a background of ischaemic cardiomyopathy. They had an implantable cardioverter defibrillator in situ with no shocks to date and were being considered for cardiac transplantation. The patient was anticoagulated with warfarin, with a target international normalised ratio (INR) of between 2-3. Additionally, they were on clopidogrel and heart failure medications. They had not attended a dentist in 20 years as they had experienced no discomfort from their dentition.

Clinical and radiographic examination revealed extremely poor oral hygiene with multiple retained roots. The patient wore an upper acrylic denture, beneath which was food packing and evidence of denture stomatitis.

The treatment plan included oral hygiene

Table 5 Cardiac transplant dental protocol for those on cardiac transplant waiting list with ventricular assist device in situ

Referral and assessment	As above	
Treatment protocol	If active treatment is required, the patient should be seen within SCD No elective treatment within first six months of VAD placement Establish prevention regime Consider referral to SCD colleagues at location closer to patient's home for treatment Exclude current and potential acute or chronic bacterial, fungal and viral infections Treat dental pathology prioritising sources of dental sepsis Discuss antibiotic prophylaxis with cardiology prior to any procedure which manipulates the gingivae (3 g amoxicillin one hour prior or equivalent) Consider admission for overnight observation following dental extractions.	
Following dental treatment	Letter to cardiology stating patient is dentally stable for cardiac surgery If seen within SCD, correspond with patient's GDP to inform them of any treatment provided and encourage regular review	
While on transplant waiting list	Treat any dental pathology quickly and definitively Inform cardiac team if the patient requires dental treatment while on cardiac transplant waiting list Patients on the transplant waiting list should be recalled annually while also attending their GDP, unless clinical indication for more frequent review	

Table 6 Cardiac transplant dental protocol for those on urgent and super urgent cardiac transplant waiting list

Referral	Patient should be seen within two weeks of referral
Assessment	 Patients should be assessed as comprehensively as possible given the likelihood of being bed-bound If the patient is not fit for treatment pre-transplant they should be assessed, treatment requirements noted, and followed-up soon after transplant
Treatment protocol	 Likely to undergo emergency dental care only Consult with cardiology prior to any treatment Treatment should be conservative and avoid invasive dental treatment Screen for oral cancers, pathology and active infections Exclude current and potential acute or chronic bacterial, fungal and viral infections Consider review of patient while on waiting list

Table 7 Cardiac transplant dental protocol for treatment post-transplant				
Review	Six-monthly reviews until two years post-transplant Annual review after two years post-transplant by SCD Patients should continue to attend GDP for routine dental care where appropriate (SCD available for advice as required)			
Treatment immediately post-cardiac transplant up to six months	Emergency dental care only ¹⁰ Consult with cardiology Emergency treatment to be carried out in a hospital setting with cardiology input Avoid invasive dental treatment Ensure recall planned Screen for oral cancers, pathology and active infections			
Dental treatment during rejection (acute or chronic)	Postpone dental treatment Emergency treatment only Liaise with cardiology Conservative management with antibiotics to be considered Treat in hospital setting Ensure recall period in place			
Treatment >6 months post cardiac transplant until stable	If invasive treatment has not been completed prior to transplant, plan in conjunction with cardiology and consider admitting overnight with post operative antibiotics Any outstanding elective and invasive treatment can be completed If corticosteroid supplementation required, consider delaying treatment until course is completed Screen for oral cancers, pathology and active infections Emphasis on prevention Ensure recall period in place			

instructions (OHI) and denture hygiene advice, ten extractions, professional mechanical plaque removal (PMPR) on all remaining lower teeth and construction of a new denture. Treatment was carried out using a staged approach, limiting adrenaline containing local anaesthesia to two cartridges per session, and ensuring a pre-op INR check. While pre-operative antibiotic cover would not usually be advised, in this case, the patient's cardiac transplant team were concerned about the risk of ICD-related endocarditis and specifically requested that cover was given.

Case 2

A 42-year-old was admitted to hospital with heart failure and a new diagnosis of dilated cardiomyopathy. An intra-aortic balloon pump (IABP) was inserted and they were commenced on milrinone and furosemide, before being placed on the urgent cardiac transplant waiting list.

As per local protocol, the patient was referred to the special care dentistry (SCD) team for assessment. As they were attached to an IABP, they were seen on the ward and could not leave the ward for radiographs. They had last attended a dentist nine years ago. Bedside assessment revealed poor oral hygiene with extensive caries in the 36 and 38. They were judged to require a full assessment including radiographs and would then require OHI, scaling and extraction of at least these molars to optimise their oral health before transplant. Unfortunately, the patient's unstable medical status prevented completion of dental treatment as it was felt, following liaison with the cardiac team, that the risks outweighed the potential benefits. In this case, regular dental review was maintained to encourage oral hygiene measures and check for any deterioration in the dental condition.

The patient underwent a cardiac transplantation and were commenced on tacrolimus, mycophenolate mofetil and prednisolone as per the unit's immunosuppression protocol. Additionally, they started alendronic acid for steroid-related bone protection, pravastatin as prophylaxis for graft vasculopathy, furosemide for volume overload, co-trimoxazole for pneumocystis pneumonia prophylaxis, and nystatin.

They experienced a number of postoperative complications, including pressure sores, a chest infection and posterior reversible encephalopathy syndrome.

Several months after transplant, the patient was reviewed in the SCD clinic where they complained of a sore tongue. The pain had been present for two months and was limiting eating. Examination was difficult due to pain, but a large ulcer was seen on the postero-lateral aspect of the tongue which extended to the left



Fig. 1 Dental panoramic tomograph of Case 3

tonsil. Adjacent to this were two grossly carious and fractured teeth. Differential diagnoses included trauma, drug side-effect, or malignancy. Due to its association with oral ulceration, tacrolimus was withdrawn by the medical team and the patient commenced on cyclosporin. Additionally, an incisional biopsy was planned. Histopathology confirmed the ulcer to be a post-transplant lymphoproliferative disorder with the features of a high-grade B-cell lymphoma. Computerised tomography and positron emission tomography scans showed involved nodes in the mediastinum, liver, supra-clavicular regions, tonsil, pelvis, abdomen and colon.

The patient was urgently referred to haematology and started on R-CHOP chemotherapy. They developed neutropenic sepsis during their first and second rounds of chemotherapy and were then treated with a third round as an inpatient as a precaution.

Case 3

A 42-year-old man was referred for pre-cardiac transplant dental assessment to SCD.

His medical history included hypertrophic cardiomyopathy, an ICD *in situ* and worsening heart failure symptoms. Medications included entresto, ezetimibe, bisoprolol, atorvastatin, lansoprazole, dapagliflozin, apixaban and clopidogrel. He was a regular dental attender and had been advised by his GDP that he required a tooth removed following the failure of a crown. Due to concerns regarding his medical history, his dentist was reluctant to proceed with the treatment. On examination, all extra- and intra-oral soft tissues were healthy.

Clinical and radiographic examination with an orthopantomograph (Fig. 1) revealed the upper left first permanent molar (26) to be temporarily dressed, with associated secondary caries. The lower right first permanent molar (46) had been previously root treated with residual apical pathology and minimal supragingival tooth structure, following

previous preparation for an indirect restoration. The 48 displayed an occlusal carious lesion. Tooth surface loss, due to a likely combination of erosion and attrition, affected the palatal and incisal aspects of the upper anteriors, with evidence of fractured composite restorations. Localised calculus deposits were present around the lower anteriors with a basic periodontal examination score of 111/221.

The treatment plan included oral hygiene and diet advice, a prescription of high fluoride toothpaste and mouthwash, and education about the aetiology of tooth wear. Treatment completed included PMPR, extraction of the 46, restoration of the 26 and 48, repair of fractured anterior composites, and provision of a splint.

Conclusion

With increasing numbers of cardiac transplants being carried out, more of these patients will be encountered in a primary care setting. The principles of the cardiac transplant dental protocol should be followed. Post-transplant, any routine dental intervention should be avoided for at least six months, with subsequent care ideally shared by the GDP and an SCD team.

Ethics declaration

The authors declare no conflicts of interest.

Written consent to publish has been obtained for cases where necessary.

Author contributions

Emma O'Donnell, Shazia Kaka, Helen Patterson and Carole Ann Boyle all fulfil the following criteria: substantial contributions to the conception or design of the work, or the acquisition, analysis, or interpretation of data for the work; drafting the work or revising it critically for important intellectual content; final approval of the version to be published; and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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