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Outcomes of microvascular free flap reconstruction for mandibular osteoradionecrosis: A systematic review

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ABSTRACT

Introduction: Osteoradionecrosis of the mandible is a devastating complication of radiotherapy in patients with head and neck cancer. Many cases present at a late stage, from months to years following completion of radiation therapy. When medical treatment fails, surgery may be required with a variety of free flaps available for microvascular reconstructive techniques.
Objective: To conduct a systematic review of the literature investigating the outcomes of free flap reconstruction of the jaw in mandibular osteoradionecrosis and determine the failure rates of different flap tissue.
Methods: A systematic literature search was performed using Medline (Ovid) Pubmed and Embase databases and Google Scholar. Primary outcome measures were flap failures and complications, with donor site complications representing the secondary outcome measure. Analysis of pooled outcomes was undertaken for different flaps.
Results: 333 articles were identified and 15 articles met the final inclusion criteria, detailing 368 primary free tissue flap transfers. There was a flap failure rate of 9.8%. There were 146 post-operative complications (39.7%), the most common being fistula formation (8.4%), hardware plate exposure (7.1%) and flap wound infections (6.5%).
Conclusion: The fibula is the workhorse free flap for reconstruction in mandibular osteoradionecrosis. Evidence to date is largely limited with the need for larger powered multi-institutional prospective studies to determine the ideal flap donor tissue and evaluate patient and treatment predictors of free flap outcomes in order to tailor the best patient-based surgical approach for mandibular osteoradionecrosis.

1. Introduction

Osteoradionecrosis (ORN) is one of the most debilitating complications of radiation therapy in patients undergoing treatment for head and neck cancer. It is defined as exposed irradiated bone that fails to heal over a three-month period in the absence of residual or recurrent tumour (Epstein et al., 1987) and can affect any bony component of the craniomaxillofacial skeleton (Teng and Futran, 2005).

The management of ORN comprises primarily on symptomatic management and prevention of further disease progression. Despite appropriate management, many patients will progress to advanced ORN disease to a stage where tissue may become necrotic and overwhelmed by infection, making it difficult to salvage affected bone (Alam et al., 2009).

With advancements in reconstructive techniques, there is increasing evidence for improved outcomes with microvascular free flap (MVFF) transfer following segmental resection of non-viable bone in osteoradionecrosis. MVFF in reconstructing ORN defects has an advantage over multi-stage reconstructions as it allows simultaneous reconstruction of both hard and soft tissue components of the defect with tissue from a separate site (Buchbinder and St Hilaire, 2006).

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Historically, it has been shown that higher complication rates are experienced when reconstructing tissue previously exposed to radiation treatment (Weaver and Smith, 1973; Margolis et al., 1976; Salyer et al., 1977; Kudo and Fujioka, 1978; Adamo and Szal, 1979; Serafin et al., 1980) with the key challenge in the inherent poor wound healing in irradiated tissue. Radiation exposure compromises the integrity of recipient vessels and negatively affects free flap viability (Krag et al., 1982), with both pre-operative and post-operative radiotherapy associated with an increased flap complication rate (Deutsch et al., 1999).

With advancements in technology and surgical techniques, the rates of flap success have increased to a reported rate of 86–100% (Celik et al., 2002; Store et al., 2002; Ang et al., 2003; Militsakh et al., 2005; Buchbinder and St Hilaire, 2006). Whilst free flap outcome is arguably primarily due to surgical technique, a better understanding of clinical predictors and contributing factors is necessary to help optimise peri-operative and post-operative management. The aim of this systematic review is to present collective evidence from up to date literature and further define factors contributing the flap failure by exploring the outcomes of microvascular free tissue transfer reconstructions in patients with mandibular osteoradionecrosis.

2. Methods

2.1. Study protocol

We followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2009). Relevant articles were identified through a systematic search of the databases MEDLINE, PubMed, Embase, Cochrane databases and Google Scholar through to September 1, 2014. The search used the terms 'Free Tissue Flaps' AND 'Osteoradionecrosis' OR 'Osteoradionecrosis' AND 'Mandibular Reconstruction', which were searched as text word and as exploded medical subject headings where possible. The reference lists of relevant articles were also hand-searched for appropriate studies. Conference proceedings were not examined. No language restrictions were used in either the search or study selection. A search for unpublished literature was not performed.

2.2. Study selection

We included all types of studies that met the following inclusion criteria: (1) Osteoradionecrosis was clearly described by clinical examination and/or confirmed radiologically; (2) the total sample size of the study exceeded 5 free flaps; (3) results examined the outcomes of microvascular free tissue transfer reconstruction; (4) the point estimate was reported as an odds ratio (OR), or the data was presented such that an OR could be calculated; (5) the 95% confidence interval (CI) was reported, or the data was presented such that the CI could be calculated. Two independent reviewers initially screened the titles and abstracts of the search for possible inclusion and the full text of all screened studies were obtained for assessment. Any uncertainty or disagreement was resolved by discussion with a third independent reviewer. We excluded studies that did not meet the inclusion criteria.

2.3. Data extraction

One reviewer (M.L.) performed the data extraction using a standardized data extraction form. Information was extracted on the publication year, study design, number of cases, population type, country, continent, mean age, gender, adjuvant treatment, months of follow-up, flap failure rates and incidence of free flap complications. Quality of the studies was not assessed as all studies found were observational case series. In articles that provided a contact email address, authors were contacted for missing data. Fig. 1.

From the initial literature search, 333 titles were retrieved and after removal of duplicates, screening and exclusion based on criteria, a final 15 articles met the final inclusion criteria (Fig. 1) (Ioannides et al., 1994; Nakatsuka et al., 1996; Curi and Dib, 1997; Santamaria et al., 1998; Chang et al., 2001; Celik et al., 2002; Store et al., 2002; Militsakh et al., 2005; Bozec et al., 2006; Suh et al., 2010; Baumann et al., 2011; Cannady et al., 2011; Chandarana et al., 2013; Sawhney and Ducic, 2013; Hillerup et al., 2014).

2.4. Statistical analysis

Pooled odds ratio estimates and 95% confidence intervals were calculated for risk factors of mandibular osteoradionecrosis using a random effects model (DerSimonian and Laird, 1986). We tested heterogeneity with Cochran's Q statistic, with $P < 0.10$ indicating heterogeneity, and quantified the degree of heterogeneity using the I^2 statistic, which represents the percentage of the total variability across studies which is due to heterogeneity that is not due to chance (Higgins et al., 2003). All analyses were performed with Comprehensive Meta-analysis (version 2.0).

3. Results

3.1. Study characteristics

Table 1 shows selected characteristics of the identified studies (Ioannides et al., 1994; Nakatsuka et al., 1996; Curi and Dib, 1997; Santamaria et al., 1998; Chang et al., 2001; Celik et al., 2002; Store et al., 2002; Militsakh et al., 2005; Bozec et al., 2006; Suh et al., 2010; Baumann et al., 2011; Cannady et al., 2011; Chandarana et al., 2013; Sawhney and Ducic, 2013; Hillerup et al., 2014). Eight studies examined populations from North America, one from South America, four from Europe and two from Asia. Of the 11 studies that reported follow-up periods, the average duration was 35.4 months. Mean age was 57.4 years, and the reported percentage of males was 68% (58%–72%), $I^2 = 37.52$, $p = 0.07$ and smokers 55% (18%–88%), $I^2 = 92.07$, $p < 0.001$. Squamous cell carcinoma comprised the majority of cases, 83% (77%–89%), $I^2 = 0.00$, $p = 0.61$ and the mean radiotherapy dose 67.71 gray (Gy).

3.2. Adjuvant treatment

Of those that reported adjuvant treatment, one quarter received adjuvant chemotherapy (25% (17%–36%), $I^2 = 37.63$, $p = 0.16$) and more than half underwent hyperbaric oxygen therapy (HBO) (53% (40%–65%), $I^2 = 70.83$, $p < 0.01$).

3.3. Free flap donor sites

A total of 368 primary free flaps were performed in 15 different studies. Used donor sites comprised of that from the fibula ($n = 215$), iliac crest ($n = 43$), radial ($n = 31$), scapula ($n = 18$), anterolateral thigh ($n = 18$), latissimus dorsi ($n = 16$), rectus abdominis ($n = 12$), serratus anterior ($n = 10$) and the humerus ($n = 5$).