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How and when in eyelid reconstruction of autologous transplantation

Miotti G *et al.* Transplantation in eyelid reconstruction

Abstract

Reconstructive surgery of the eyelid after tumors excision, trauma or other causes can be challenging, especially due to the complexities of the anatomic structures and to the necessity of both functional and aesthetical successful outcomes. The aim of our minireview was to investigate the use of tissue transplantation in eyelid reconstruction. Surgical procedures are various, based on the use of both flaps - pedicled or free - and grafts, in order to guarantee adequate tissue reconstruction and blood supply, which are necessary for correct healing. Common techniques normally include the use of local tissues, combining non-vascularized grafts with a vascularized flap for the two lamellae repair, to attempt a reconstruction similar to the original anatomy. When defects are too wide, vast, deep and complex, or when no adjacent healthy tissues are available, distant areas tissues need to be recruited as free flaps or grafts and paired with mucosal layer reconstruction. With regards to the anterior lamella, full thickness skin grafts are commonly preferred. With regards to the reconstruction of posterior lamella, there are different graft options, which include conjunctival or tarsoconjunctival, mucosal or palatal or cartilaginous grafts usually combined with local flaps. Free flap transplantation, normally reserved for seldom select cases, include the use of the radial forearm and anterolateral flaps combined with mucosal grafts, which are surgical options currently reported in literature.

Key Words: Eyelid reconstruction; Graft transplantation; Flap transplantation; Eyelid lamella grafts; Cartilage grafts; Dermis grafts; Mucosa grafts

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Core Tip: Transplantation tends to be a viable option in eyelid reconstruction surgery. The most commonly used technique involves the use of grafts for the reconstruction of one or both eyelid structures. The use of free flaps are seldom used and only reserved

for cases of extensive tissue lost. In these cases, favorable flaps considered are those that are anatomically thin and pliable.

INTRODUCTION

Eyelid reconstruction tends to be complex, difficult and can be needed after oncological surgery or trauma. There are also cases, which are not frequent, in which reconstructive surgery is needed to repair damage caused by aesthetic surgery, such as lagophthalmos post-blepharoplasty or scarring eyelid retraction. In patients with invasive and relatively large eyelid tumors, the need to perform complete oncologic excision with margins adapted to tumor type may result in the removal of an important part of this anatomical structure that encompasses both esthetic and functional properties^[1]. The eyelid consists of an anterior and posterior lamella. The anterior portion of the lid is composed of skin and orbicularis muscles, while the posterior portion includes the posterior tarsal plate, retractors (in the lower eyelid) and conjunctiva^[2]. In most eyelid reconstruction surgical procedures, both lamellae need to be replaced. At least one lamella needs to include a functioning blood supply and therefore has to be pediculated, otherwise the reconstructed tissue cannot properly grow and heal, resulting in poor and/or no wound closure^[3]. Several surgical techniques are currently available for lower eyelid reconstruction; the choice of the technique and postoperative results mainly depend on the preference and experience of the surgeon, and on the etiology of the eyelid defect. Most surgical techniques combine different flaps and grafts in order to reconstruct both lamellae. The most commonly used reconstructive techniques are based on local flaps, which are widely described in literature^[4-6], and possible grafts to complete lid reconstruction. The main objectives of surgery include to obtain postsurgical outcomes that reflect the normal eyelid in terms of anatomy, esthetics and function. The aim of our minireview was to present a brief overview of reconstructive techniques based on autologous tissue transplantation for eyelid reconstruction surgery, including the use of grafts and/or free flaps, which have been reported in literature in the past ten years.

MATERIAL AND METHODS

We conducted a search of the literature published between January 1, 2011, to November 1, 2021, using MEDLINE (PubMed). The database was first searched using the key words “eyelid reconstruction, eyelid reconstruction AND grafts, free flaps, tissue transplantation, autologous grafts, autologous tissues”. We considered only studies in English and those referring to humans and with abstract, thus reducing the count to 1473 papers. The reference lists of all retrieved articles were assessed to identify additional relevant studies.

Only articles with abstract were considered. After selection by title and abstract, excluding all works where only local flaps are used for reconstruction, 63 studies were analysed. A quality score was calculated for each article using a check list from the American Society of Plastic Surgeons guideline for therapeutic studies^[7]. Each study was independently assessed by at least two reviewers (Miotti G and Zeppieri M), and rating decisions were based on the consensus of the reviewing authors. The results of the most relevant studies are shown in Table 1.

GENERAL NOTIONS REGARDING RECONSTRUCTIVE EYELID SURGERY

The particular eyelid anatomy must always be considered when reconstructing it. In doing so, we must always remember the presence of two lamellae that constitute the two eyelids. Full thickness defects larger than a third of the eyelid should be reconstructed in two planes, which correspond to the posterior and anterior lamellae. In order to avoid necrosis of the reconstruction, at least one lamella should have an intact blood supply. The association of two grafts is therefore not recommended. The two planes must thus consist of the association of either two flaps or a flap and a graft^[1]. Most studies reported in literature follow this common idea, however, some authors have also proposed the use of only grafts.

The association of two flaps is the safest combination regarding vascular supply and postoperative recovery. However, the use of two flaps can lead to a thick reconstructed

eyelid, which can be limited if each flap is comprised exclusively of the exact missing layer. For this reason, the use of a flap and a graft is the best option for satisfactory aesthetic result. The final choice of the surgical technique depends on several factors, which include: The preference and experience of the surgeon, etiology of the eyelid defect, and the availability flaps and grafts^[8]. The quality of local tissues can also modify this choice. History of radiotherapy, previous or planned in the post-operative period, can guide the reconstruction. By determining a reduction of the vascularization of the treated tissues, well vascularized tissue are preferred to repair the defects^[3,5]. Local flaps certainly represent a common reconstructive choice and are preferable to grafts, especially for previous irradiated sites. The aim of our study, however, was to assess a narrower and more specific field of literature, to concentrate on studies regarding eyelid reconstruction surgery based on tissue transplantation, to include grafts or free flaps.

GRAFT TRANSPLANTATION

Grafts transplantation in eyelid reconstruction is perhaps the most common used procedure in routine clinical setting. Various tissues can be transplanted to complete the eyelid reconstruction. Both lamellae can be restored with grafts, however, the anterior lamella is the most common segment that tends to be repaired. As a basic rule, grafts should be used when there is an adequate vascular bed to enhance post-transplanted survival. Grafts can also be used in irradiated tissues when needed, however, these types of grafts generally need to be associated with local flaps to enhance the vascularization and guarantee graft survival. Radiotherapy on engrafted areas could cause ulceration or delay the wound healing^[9]. Commonly used techniques combine a non-vascularized graft for one lamella with a vascularized flap for the other^[9].

As mentioned above, usually only one lamella can be reconstructed with a graft, but techniques to reconstruct both have also been described. Kakizaki *et al*^[10] reported bilamellar graft reconstruction with orbicularis muscle mobilization between grafted areas (“sandwich flap”), first described by Doxanas^[11] in 1986. The orbicularis oculi

muscle provides an excellent blood supply to grafted tissues in these cases, in addition to enhancing the mobility of the reconstructed lid. In 2020, Bortz *et al*^[12] published a clinical series in which full-thickness lid defects were restored using free tarsal grafts for the posterior lamella and free skin grafts for anterior lamella. The authors reported this method as an alternative to the “classic” Hughes flap for lower eyelid reconstruction, especially when the occlusion of the eye could be a problem (vision deficit, elderly patients, *etc.*). The evidence reported by Tenland *et al*^[13] led the authors to propose this type of reconstruction. The study showed that tarsoconjunctival (TC) tissue survival does not seem to be dependent on a conjunctival flap, and thus free TC grafts or composite grafts might be considered as viable alternatives.

Anterior lamella grafts

Anterior lamella is often reconstructed with a full-thickness skin graft^[10-14]. Other possibilities of tissue transplantation include tissue cultured autograft, tissue cultured allograft, skin bank allograft, acellular dermal replacement and xenograft^[15]. Ideal donor sites include upper and lower eyelid skin and posterior auricular, preauricular or supraclavicular skin. Split-thickness skin grafts should not be used, with exception to cases of extensive burns in which the donor site is limited^[9].

Posterior lamella grafts

Grafts or flaps are viable options for posterior lamellar reconstruction^[10]. Grafts include conjunctival or TC grafts, hard palate (or palate) graft, cartilage (auricular or nasal septal) grafts, mucoperichondrium grafts, dermis fat grafts (DFGs), venous grafts (VGs), galea or pericranium grafts, mucosal membrane (buccal or labial) grafts, temporalis fascia grafts. For lower eyelid reconstruction, for example, single or tandem composite skin muscle tarsus-conjunctival eyelid grafts from the upper lids or contralateral lower lid may be an option^[10].

TC grafts: TC grafts are an excellent choice for posterior lamellar reconstruction considering that this structure reflects the features of a normal eyelid^[9]. Tarsal grafts alone, taken from the fellow healthy eyelids, can be used in association with local flaps for anterior lamella reconstruction^[16]. TC grafts and flaps are essential components of eyelid reconstruction, since these alternatives provide anatomically similar tissues for the inner layer of reconstructed eyelids^[17]. First described in 1918 by Blaskovics^[18] for lower eyelid reconstruction, autogenous TC grafts have found widespread use, as described by Hughes^[19], Leone *et al*^[20] and several others in literature^[21,22]. Hawes *et al*^[17] proposed guidelines for the use of TC flaps and grafts to repair lower eyelid defects.

Free grafts are preferred in most cases in which the defect is from one-third to three-quarters of the eyelid length. TC flaps are advantageous when the defects are large (entire lower eyelid loss) and when poor healing can be expected. Usually, this type of reconstruction is completed by a local flap for the anterior lamella, and is not limited only to lower eyelid. Yazici *et al*^[23] recently described the association of a TC graft with a bilobed local flap for the upper eyelid. Bengoa-González *et al*^[24] described the use of the graft to complete and modify the Cutler-Beard's technique for the upper eyelid. The TC graft gives stability to the new upper eyelid, avoiding retraction caused by scar. From a technical point of view, it is fundamental to avoid complications also in the donor site, that usually heals spontaneously by secondary intention^[9]. Almost 3-4 mm of tarsus must be maintained to allow donor eyelid stability, and Müller's muscle should be conserved. To avoid entropion or ectropion to reconstructed eyelid, tarsal graft should be snug and no wider than the smallest dimension of the defect^[17]. Figure 1 shows an example of our patient that underwent left lower eyelid reconstruction after tumor excision using a TC graft (from the left upper eyelid) for the posterior lamella and a local flap for the anterior one.

Hard-palate mucoperiosteal grafts: Hard-palate mucoperiosteal (HPM) grafts, described for the first time by Siegel^[25] in 1985, can be used to replace the posterior

lamella due to the ability of this graft to provide structural support and mucosal lining^[9]. HPM may be considered the optimal choice for reconstructing the posterior lamella of the eyelids because it has similar histological composition and texture to the tarsoconjunctiva, and an adequately sized graft can easily be acquired^[26,27]. HPM tends to be one of the preferred choices for most lower eyelid reconstructions in routine clinical settings^[26]. The use of HPM in upper eyelid reconstruction is controversial because hard-palate mucosa is composed of keratinized, stratified squamous epithelium, which can irritate the cornea, especially when the defect is adjacent to the middle part of the cornea^[9-28]. Despite this, excellent results without complications have been reported in studies when used in upper eyelid posterior lamellar reconstruction^[28,29].

The reconstruction of the anterior lamella requires the use of flaps. Palatal mucosal grafts provide a good structural support to the eyelid. This is essential for the inferior eyelid, especially when the graft is combined with a heavy flap such as the Mustardé or the orbito-nasogenien flap. The graft is and remains stiff. The shrinkage is minimal, thus providing a stable free eyelid margin and limiting ectropion or entropion^[28]. Limits of this technique, in addition to the aforementioned corneal irritation, is the described pain and delayed healing at donor site observed when periosteum is included in the graft^[30].

Auricular and nasoseptal cartilage grafts: Auricular and nasoseptal cartilage can also be useful alternatives when considering graft tissues for reconstructive surgery^[28,31,32]. In some case, this graft may prove to be too thick and too stiff to match with the eye convexity, thus need to be thinned without compromising the supportive strength. Ear cartilage is useful because it is easy to harvest and fabricate, has suitable flexibility, and provides adequate support^[33]. The spherical surface fits well with the shape of the external bulbar surface^[34]. Chondromucosal grafts from the nasal septum consist of highly supportable tissue. Caution must be taken when harvesting a chondroseptal graft, to avoid damage to the remaining mucosa surrounding the vast perforation. Considering this tissue is composed of hyaline cartilage, however, it lacks softness and

flexibility. This may result in difficulty with fabrication and unsuitable contact with the bulbar conjunctiva. In addition, the harvestable size is limited^[33]. The use of alar or triangular cartilages provides a thinner but smaller sized sample, with good adaptability in eyelid reconstruction but raise the problem of donor site morbidity^[28]. Suga *et al*^[34] in 2016 published a comparison between ear and nasal septum grafts. The study reported that both tissues provide good options for reconstructing an inner layer of the lower eyelid. The authors stress that the main difference lies on postoperative outcomes at the donor site: Ear cartilage tends to have a lower complication rates, while harvesting nose grafts can cause important septal perforation and vast bleeding.

Another option for cartilaginous reconstruction of the posterior lamella of the lower eyelid is a scapha chondrocutaneous graft, first proposed by Yanaga and Mori^[35]. Further studies reported by Uemura *et al*^[36] described interesting results with the use of this graft combined with a local propeller flap. The scapha cartilage graft is an interesting alternative because it has a thin coat of skin, and is round and soft with a shape similar to that of the lower lid. This tissue can provide a good fit with the eye globe and can be harvested quickly without severe complications.

DFGs: DFGs can provide useful replacement tissue for eyelid and orbit reconstruction. The DFG is composed of a dermis button, obtained by removing the overlying epidermis, with the underlying subcutaneous fat. The dermis provides stiffness, additional surface area, and a scaffold. Moreover, the dermis helps with vascularization and decreases fat tissue atrophy. This tissue can be flat or domed shaped^[37]. This graft option tends to be considered primarily for socket reconstruction in the context of anophthalmia, either congenital or acquired^[38]. Secondary indications are eyelid reconstruction, socket contraction, eyelid contraction (used as spacer^[39]) or implant exposure.

VGs: Barbera *et al*^[40] first proposed VGs as a reconstructive possibility in 2008. The study reported that VGs obtained by propulsive venous vessels are the most suitable

for this type of surgical reconstruction because of the tissue thinness, texture, and anatomical structure. Moreover, due to the properties of elasticity, smoothness and concavity, the venous graft conforms to the globe without inducing a chronic inflammatory reaction on the bulbar conjunctiva or on the cornea^[41]. Scevola *et al*^[42] showed that VG is a good technique for palpebral reconstruction because it is safe, fast and easily reproducible, when compared with a chondroseptal graft.

Galea and pericranium grafts: Galea and pericranium grafts represent a secondary choice in eyelid reconstruction. These tissues represent a reconstructive possibility in cases of severe periocular trauma, wide tumor resections or in socket reconstruction^[35]. Ibáñez-Flores *et al*^[43] published a series of cases in which pericranium grafts were used. The authors concluded that pericranial grafts provide a sufficient amount of tissue to cover large defects, thus providing appropriate substitutional volume without painful post-operative healing.

Buccal mucosa graft: Buccal mucosa graft (BMG) is a good lining option^[9]. Oral mucosa has similar biological properties to conjunctiva, thus making it a viable alternative to restore the ocular surface^[44]. This tissue, however, lacks structural integrity, and tend to be too weak and small to support the lower eyelid. Moreover, postoperative shrinking can be substantially during the follow-up period, thus should be used in combination with cartilage^[43,45]. It is important to note that BMG harvesting and post-operative healing tend to be rather painful for most patients.

FLAP TRANSPLANTATIONS FROM DISTANT SITES

When defects are too complex to be reconstructed with local flaps or grafts, or when no adjacent tissues are available, the operation is challenging, and transplantation of tissues from distant areas is necessary. Mechanical support and mobility for reconstructive surgery can seldom be found in tissues from a distant region, combining thin and pliable skin with mucosal layer reconstruction. The flap needs to provide

characteristics that are appropriate both from a functional and esthetic prospective. Free flaps are normally not frequently considered in reconstructive surgery. In addition, reconstructions with free flaps have several possible complications. The effect of a possible RT on the recipient site (which is frequent in advanced tumors) is one of the elements that can determine the failure of autologous microsurgical reconstruction. The harmful effects on tissues and blood vessels are well known. There are only a few studies reported in literature that are based on this surgical option for complete or partial eyelid reconstruction.

One of the first attempts of periocular region reconstruction using free flaps is described by Chait *et al*^[46] who used a neurovascular free flap from the first web space of the foot after exenteration. An alternative distant surgical flap was described in a case report by Yap *et al*^[47] in 1997 in which the eyelids were rebuilt using a free flap based on the second metacarpal artery. Thai *et al*^[48] proposed a free dorsalis pedis flap for the outer lamella and a local conjunctival flap for the inner one for total eyelid surgical reconstruction after deep facial burn in study published in 1999.

One of the main problems in periocular region reconstruction is represented by the extreme thinness of the tissues that compose it. This represents a limit for the reconstructive techniques, due to the thickness of the tissues generally used to cover the defects. This limit is highlighted when the reconstructive choice is a free flap. For this reason, it is quite difficult to find a viable flap that can provide satisfactory surgical reconstruction outcomes. Kushima *et al*^[49] described an entire upper eyelid reconstruction using a free radial forearm flap (RFF) for the anterior lamella and a hard palate graft for the posterior one. This flap, thanks to its flexibility and thinness, is considered the ideal solution. The same flap has been used by Ghadiali *et al*^[50] in a case of upper and lower eyelids total reconstruction in which the patient had an extensive tissue loss of the ipsilateral forehead and temple. In this specific case, there was no local tissues available for reconstruction. The authors used a 5 cm × 11 cm radial flap to reconstruct the entire area, followed by a fenestration of the flap four months after. The tarsal plate of the eyelids was rebuilt by palmaris tenon grafts. As a result, the patient

obtained a visually useful eye, which remained intact after the trauma^[50]. RFF was also used by Iwanaga *et al*^[51] in 2 cases of functional upper eyelid defect reconstruction surgeries. The authors used a free flap elevated with palmaris longus tenon in a fascinating way: The palmaris longus tenon was split into two strips, in which one strip was fixed to the frontalis muscle to achieve the opening function and the second to the medial palpebral ligament and the lateral orbicularis muscle to achieve functioning closing lids.

Another feasible free flap, especially in thin or super-thin forms, is the anterolateral (ALT) flap. In 2008, Rubino *et al*^[52] described a case of upper and lower eyelid unilateral full thickness reconstruction with ALT free flap in a patient with no available adjacent tissues, which had extensive burns, and no possibility of using RFF. In this patient, the blepharoraphy was opened after 3 mo from the first surgery, obtaining good skin coverage but incomplete closure of the eye.

CONCLUSION

Eyelid reconstruction remains extremely complex and fascinating, especially considering that the main aims of surgery include re-establishing the anatomy, providing protection of the eye globe, favoring the sight, and guaranteeing the esthetics of the face. It is clear that each surgical procedure requires experience, careful planning and personalized surgical options tailored for each patient. From the analysis of current literature in this field, it appears significantly advantageous to exploit periocular tissues when possible, however, other options including non-traditional flaps and grafts can prove to be viable alternatives in specific cases, especially when there is extensive damage to the lids and/or neighboring tissues are scarce and not feasible options. Stem cell harvesting and new transplanted autologous tissues can pave the way to future surgical techniques in reconstructive lid surgery.

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