

ORIGINAL PAPERS

Is Vascularized Composite Allotransplantation a Suitable Reconstructive Option for Extensive Defects in Burned Patients? Clinical and Immunological Evaluation Protocol

Andreea Grosu-Bularda¹, Serban Arghir Popescu^{1,2}, Razvan Teodoreanu^{1,2}, Liviu Cojocaru¹, Luana Lazarescu¹, Ioan Lascar^{1,2}

Abstract

Traditional reconstructive methods can fail in achieving a good functional and aesthetic outcome in patients with extensive defects, involving multiple layers of functional tissue, often necessitating numerous, and staged, surgical interventions with unsatisfactory results. Transplantation of vascularized composite allografts (VCA) opened a new, promising era in reconstructive surgery, offering a unique restorative opportunity for those complex situations. VCA transplantation have been performed for life enhancing indications in a selected group of patients under institutional protocols. The controversy of those procedures, having functional benefits and the goal of quality of life restoration, rather than life-saving indications, resides to the life-long required immunosuppressive therapy, with implicit side effects. In order to extend VCA indications, translational studies are needed to develop less toxic immunosuppressive regimens and possibly achieve donor-specific tolerance, the ideal situation in transplantation. Extensively burned patients, especially of the face and cervical region, having severe mutilations and also unilateral or bilateral hand amputations, like after high voltage electric injuries, present functional and aesthetic deficits, with devastating impact on their quality of life and, constituting potential candidates for receiving a vascularized composite allotransplantation, as the only reconstructive solution. With this paper, we discuss the indications and limits, from clinical and immunological perspectives, of the consideration of VCA as surgical option for burn patients with complex tissue defects, impossible to approach by conventional techniques.

Keywords: Vascularized Composite Allotransplantation (VCA), Burns reconstruction, Electric injuries, Sensitization, Eligibility.

Rezumat

În cazul pacienților ce prezintă defecte tisulare extensive, interesând mai multe unități funcționale, metodele reconstructive tradiționale pot să nu fie eficiente în obținerea unui rezultat bun din punct de vedere funcțional și estetic, în ciuda unui tratament chirurgical stadializat, ce include multiple intervenții laborioase. Transplantul alogrefelor vascularizate compozite (VCA) a deschis un nou orizont terapeutic, oferind o oportunitate reconstructivă unică pentru astfel de pacienți. Transplanturile tisulare compozite au fost efectuate urmând protocoale stricte, în instituții acreditate, după o selecție atentă a pacienților, indicația acestor proceduri fiind reconstrucția funcțională și estetică, urmărind redobândirea calității vieții pacientului. Controverse au apărut legat de efectuarea transplanturilor de

¹ Clinic of Plastic Surgery, Aesthetic and Reconstructive Microsurgery, Emergency Clinical Hospital, Bucharest, Romania

² »Carol Davila» University of Medicine and Pharmacy, Bucharest, Romania

Corresponding author:

Andreea Grosu-Bularda

Department of Plastic Surgery, Aesthetic and Reconstructive Microsurgery, Emergency Clinical Hospital, Calea Floreasca no. 8, 014461, Bucharest, Romania.

E-mail: andreeabularda@gmail.com

țesuturi compozite, deoarece acestea nu reprezintă intervenții indispensabile supraviețuirii, necesitând expunerea pacienților la terapie imunosupresoare pentru tot restul vieții, cu efectele adverse legate de administrarea acestora. Pentru a permite utilizarea pe scară largă a acestor proceduri, se impune continuarea cercetării translaționale în domeniu, cu scopul de a dezvolta strategii terapeutice imunosupresoare cu mai puține efecte adverse și posibilitatea inducerii toleranței imunologice donor-specifice, situația ideală în transplant. Pacienții prezentând arsuri severe, mutilante, mai ales la nivelul feței și regiunii cervicale, cât și cei având amputații, unilaterale sau bilaterale, la nivelul membrelor toracice (situație întâlnită după electrocuții cu voltaj înalt), constituie o categorie de potențiali candidați pentru reconstrucția utilizând transplantul vascularizat compozit, ca unică soluție terapeutică, deficitelor lor funcționale și estetice având un impact nefavorabil major asupra calității vieții. Scopul acestei lucrări este evaluarea, atât din perspectiva clinică cât și imunologică, a chirurgiei reconstructive de transplant ca opțiune terapeutică în cazul pacienților arși grav, prezentând deficite funcționale complexe, imposibil de rezolvat utilizând tehnicile chirurgicale convenționale.

Cuvinte cheie: transplantul alogrefelor vascularizate compozite, reconstrucție în arsuri, electrocuții, sensibilizare, eligibilitate.

INTRODUCTION

Vascularized composite tissue allotransplantation (VCA) is a recent reconstructive entity that bases on the restoration of deformity by the allotransplantation of a vascularised tissue unit with more components (skin, muscle, bone, cartilage, bone marrow, tendon, nerve). Since the field emerged with the first hand transplant performed in France in 1998, VCA showed a huge potential in replacement of extensive tissue defects and disfigurements (after burns, severe high energy-trauma like gunshots, congenital facial malformations), offering a viable treatment option for injuries that involve multiple layers of functional tissue, impossible to repair using conventional surgical techniques, permitting restoration of extensive defects in just one stage procedure with good functional and aesthetic results. A significant number of those procedures have been reported worldwide for various anatomic locations including upper and lower extremities, face, tongue, trachea, larynx, abdominal wall, uterus and penis. These procedures are offered for quality of life and functional indications rather than life-saving indications¹⁻⁷.

Limitation in a rapid expansion of vascularized composite allotransplants as standard reconstructive procedures is posed by the side effects of the immunosuppressive drugs that patients must take to prevent rejection and graft loss, those procedures serving for quality of life and functional recovery, rather than life-saving indications. In order to improve VCA outcomes, translational studies are needed to develop less toxic immunosuppressive regimens and possibly achieve donor-specific tolerance (the ideal situation in transplantation)²⁻⁵.

Extensively burned patients may have severe mutilations, especially of the face and cervical region and also unilateral or bilateral hand amputations, like after high voltage electric injuries. Those people, having a poor

quality of life and functional disorders, constitute potential candidates for receiving a vascularized composite allotransplantation, in present days being the most promising and also the only reconstructive solution⁸. VCA is already a recognized reconstructive option for patients with severe facial or upper limb burns, based on clinical worldwide experience⁹.

Almost since the beginning of the VCA programs, burn victims have been considered as immunologically complex patients for these types of procedures, due to possible previous sensitization, which represents in many centers around the world a significant criteria of patient exclusion in composite tissue allotransplantation^{10,11}.

As VCA it seems to become a valid reconstructive option for mutilated burned patients, it becomes very important to familiarize with clinical and immunological challenges posed by those complex procedures, requiring special techniques and permanent interdisciplinary approach for obtaining safe and good clinical outcome.

The current article aims to provide a general overview on current experience with VCA procedures for burn injuries reconstruction, identify the main clinical and immunological problems and propose a comprehensive protocol for evaluation of burns victim as VCA potential recipients, based on current international recommendations and our clinical experience with burns defects assessment and reconstruction using autologous methods.

Current clinical experience in hand and face transplantation

Based on The International Registry on Hand and Composite Tissue Transplantation update for year 2015, for the 51 recipients of hand allotransplants (25 patients with single upper extremity transplant and 26

of them with bilateral upper extremity transplants), 42 were males and 9 female patients, with ages between 17 and 67 years (mean age 33.5 years). Regarding the mechanism of the amputation, explosion was involved for 12 patients, electric injury in 6 patients and burns in 5 patients. Twenty of the hand allotransplants recipients had working accidents, illustrating the impact of such injuries in young, active population¹².

First partial facial transplant was performed in France in 2005 by Devauchelle et al. and world full face transplant took place in Spain in 2010¹³⁻¹⁵. To date, a number of 29 partial and total facial transplants were performed worldwide. The majority of the recipients are men (23 men and 6 women), young (ages ranging between 19 and 59 years, with mean age 34 years) with the cause of deformity dominated by trauma (in 16 cases) and burns (8 cases). The deficit involved in the larger majority of the cases the central part of the face (23 patients having their midface affected, including the nose), severely affecting important functions of swallowing, eating, speaking, 22 of patients having a tracheostomy^{12,16}.

Recipients of vascularized composite allotransplants require life-long immunosuppressive therapy for avoid the rejection and maintain the functionality of the allograft. Standard immunosuppressive protocols include an initial, induction phase followed by the maintenance period. Induction therapy usually consists of infusion of anti-lymphocyte antibodies or anti-T-cell therapy, short after transplant. Triple maintenance therapy usually consists of steroids, Tacrolimus and Mycophenolate mofetil. When rejection episodes are observed, a more aggressive immunosuppressive regimen is temporarily administered^{2,17}.

BURNS PATIENTS AS VCA RECIPIENTS

Clinical considerations

Burns are one of the most severe forms of trauma, responsible for significant morbidity and mortality worldwide, leading to chronic devastating physical sequel and severe impairment of quality of life of the patients, with psychological and socio-professional unfavorable consequences¹⁸.

In United States, there are 486 000 burn victims receiving medical treatment each year, accounting for 40 000 hospitalizations per year. On a ten years selected statistics (2005-2014 Burn Admissions to Burn Centers) performed by *American Burn Association*, the survival rate was 96.8%, males are two times more involved

in burn accidents than females (68% Male, 32% Female) and causes of burn admissions to Burn Centers were distributed as follows: 43% flame injuries, 34% scalds, 9% contact burns, 4% electrical injuries, 3% chemical burns, 7% other mechanism¹⁹.

Among the different types of burns, electrical injuries are the most severe. Electrical burns are an important socio-economic problem, resulting in important complications for the patients. A classification of electric injuries includes: high voltage injuries (>1000 V)-severe lesions, usually more extensive than the visible skin burn, low voltage injuries (<1000 V), flash burn (no electrical current flow through the body of the patient) and burns caused by lightning. High-voltage injury causes damage at the contact point and deeper structures, resulting in a large area of necrosis. Electrical injuries requires complex reconstructive procedures, including microsurgical techniques for obtain the coverage of extensive tissue loss, if possible with best functional outcome. Electrical burns are associated with important complications (myoglobinuria, cardiac, renal complication, compartment syndrome) making the acute phase more difficult to manage therapeutically and devastating sequels which compromise the later functional, social and professional performance of the patient^{20,21}.

Extensive burns, covering more than 40% total body surface area (TBSA) affects nearly every organ system, are typically followed by a period of stress, inflammation and hypermetabolism and have significant morbidity and mortality. Sepsis and multi-organ failure are the main mortality causes²².

Progresses made with therapeutic strategies, including advances in resuscitation, early coverage of burned wound, better support of hypermetabolic response, improved infection control and sustained treatment of inhalation injury, have significantly improved the clinical outcome of the patients with severe lesions²². Despite the efforts in burn recovery, there are some patients, survivors of burns injuries, which present major deformities and are not able to regain their previous social life and activities. This category of patients, with mutilating injuries, constitute the subject of discussion related to the indication of vascularized composite allotransplantation as only possible reconstructive method²³.

Facial allotransplantation is indicated in severely disfigured burned patients, involving cutaneous and osseous tissue, affecting the functional structures (perioral and peri-orbital disruption), when other surgical option have failed. Usually, disfigured patients having only skin affection, may be resolved by means of tra-

ditional surgical techniques, depending on the grade of functional impairment. Careful selection of patients is mandatory: appropriate surgical indication, absence of comorbidities, compliance, psychological stability, adequate social support and good understanding of the procedure with all the clinical and immunological implications are implicit characteristics for transplant potential recipient^{11,24}.

As reconstructive method, facial allotransplantation has the advantage of restoring very complex structures and functions in a single reconstructive procedure, for the complete functional result being necessary an intensive postoperative rehabilitation program. In transplanted patients facial function were satisfactorily regained, including: eyelids open and closure, nasal function, chewing, swallowing, drink and eat ability, speech recovery, possibility to smile and kiss¹². After face transplantation procedures which restored also the upper airway, clinical benefits were revealed on patient respiration, increasing of airway volumes, good nose breathing, allowing the remove of tracheotomy tubes²⁵.

Hand and upper extremity transplantation is the most commonly performed type of reconstructive transplantation and, for properly chosen recipients, shown the capacity to greatly enhance quality of life and function. Hand allotransplantation should be performed only by centers performing hand/limb replantation in collaboration with the organ transplantation team to ensure adequate expertise to promote best outcomes and limit patient risk as much as possible. After adequate recovery, good functionality of the hands/upper limbs was observed for both unilateral and bilateral transplanted patients¹². Allotransplantation can be an optimal solution for patients having bilateral upper limb amputation after burns. Those situations can occur in electric injuries with deep and extensive tissue loss²⁶⁻²⁹.

In burned children, the VCA procedures are not recommended in present, awaiting, based on ongoing research, for amelioration of immunosuppressive regimens in order to reduce their serious side-effects and possibility of developing strategies for inducing transplantation tolerance^{2,11}.

Immunological considerations

The principal factor limiting the extent of clinical application in reconstructive allotransplantation is the necessity for lifelong immunosuppressive therapy, with its complications and side effects, in context of those procedures that are not considered life-saving³⁰.

Hand and face transplantations consist of histological different tissues, expressing different antigenicity,

including skin, mucosa, connective tissue, muscle, bone, bone marrow, tendons, nerves, and blood vessels, that form a single functional unit transplanted based on its vascular pedicle. From all the components of a vascularized composite allograft, skin is considered the most antigenic tissue^{31,32}.

The immune response in composite tissue transplantation is primarily T-cell mediated. The cytotoxic activity of T-cells is donor specific. The rejection of VCA in sensitized recipients is mostly cell mediated and it differs by mechanism from that of solid organ transplantation. The preponderance of the T-cell response during VCA rejection could explain the efficiency of the usual triple therapy approach used in the majority of VCAs (steroids, tacrolimus, mycophenolate mofetil), which mainly targets the T cell response³⁰.

An intricate medical history that includes trauma and blood transfusions with consequent sensitization is probable in patients qualifying for VCAs. In transplantation, sensitization represents the acquired ability of the immune system to respond to allogenic human leukocyte antigens (HLA), producing anti-HLA antibodies and subsequently developing memory cells¹⁰. In renal transplant, patients have been transplanted against positive complement-dependent cytotoxicity (CDC) cross-matches with lengthy pre- and post-transplant immunosuppression. It is still unknown whether similar approaches may also apply in VCAs. VCAs have mainly been followed closely for donor-recipient cross-matches comparable to the approach in solid organ transplantation. So far, there have been very few reports of either antibody mediated rejection in VCA, circulating donor-specific antibodies, or the displacement of the complement product C4d in VCA recipients. It is known that donor-specific HLA antibodies (DSA), like in ABO incompatibility, represent a major risk factor for hyper-acute and acute rejection of the transplanted graft. The degree of sensitization in solid organ and VCA recipients is generally tested using pre-transplant panel reactive antibody (PRA) scores. The score grants a relative estimate with a 100% PRA predicting a positive cross-match against any given donor^{10,26,30}.

Burned patients with extensive lesions, usually deep second and third degree burns on more than 40% TBSA (total body surface area), require long-term intensive-care, during this time accumulating a series of risk factor for sensitization like multiple blood transfusions or vital functions support with assisting devices^{10,33}.

Klein et al.¹⁰ identified a list of causes of sensitizations in burned patients, as it is shown in Table 1.

Table 1.

Cause	Observations
Pregnancy	HLA sensitization The sensitization risk increases with the number of pregnancies of the woman
Blood transfusions	Extensive burned patients require multiple transfusion session
Previous transplant	Previous organ transplant VCA re-transplantation in case of transplant failure
Human skin allografts(homografts)	Frequently used for temporary coverage of extensive burns, when autologous sources are not available or autologous coverage is not possible due to local or sistemic factors
Assist devices	VAD (ventricular assist devices) ECMO (extracorporeal membrane oxygenation) Dialysis there is controversy in representing a risk factor for sensitization
Proinflammatory situations	HLA-unrelated immune stimulation Infections, sepsis

In order to increase the probability of finding a suitable donor, desensitization protocols have been established to remove both anti-HLA and anti-A/B blood group antibodies. These protocols combine different techniques meant to either dispose of circulating antibodies and/or prevent their synthesis and secretion. Techniques like plasmapheresis and immunoabsorption can be used for removing pre-existent antibodies. Also other procedures are recommended as splenectomy, application of Rituximab antibodies or intravenous administration of immunoglobulins targeting indirectly anti-HLA antibodies¹⁰.

Recent advances in transplant immunology are shifting the focus from immunosuppression to immunoregulation, making composite tissue allotransplantation with novel and less potent immunosuppressive regimens a possibility².

OUR CLINICAL EXPERIENCE

We analyzed the burned patients admitted in our service in order to identify severe injuries, affecting functional areas and representing potential challenges for optimal reconstruction using conventional techniques, having in mind the perspective for using a vascularized composite allograft as ultimate reconstructive solution for selected patients.

Between October 2011 and December 2015, 181 burnt patients were admitted in our clinic: 127 (70.2%)

male and 54 (29,8%) female patients, with ages between 18 and 88 years(mean age 44,24 years).

There were 42 patients with more or equal to 40% TBSA burn lesions (23.30%), from total number of patients. We evaluated burns interesting functional areas, focusing on upper limbs and cephalic extremity. Upper limbs were affected in 136 (75.13%) patients and 92 (50.82%) patients presented cephalic extremity involvement.

Table number 2 illustrates more detailed clinical data.

In 5 male patients it was imposed performing upper limbs amputation: 3 patients after high voltage electrocutions (right arm level in two patients and bilateral arm amputation in one patient) and two patients after thermal burns (upper right limb at wrist level in one patient and distal third of left forearm in another patient).

Nine patients (7 men and two women) necessitated amputation of the fingers, at different levels, 7 of them after thermal burns and 2 after electrocutions.

Skin allografts were used for temporary coverage in 17 patients with extensive burns, when autologous resources were limited or for patients having severe general status, which not permit autografting after excision of burn lesions. Skin allografts are applied after a previous expansion (1:3 rate). In 3 patients we observed integration and long-term persistence of allografts (for more than 21 days).

Table 2.

	Total number of patients	Electrocutions (Number of patients/ percentage)	Right upper limb	Left upper limb	Cephalic extremity involvement	Upper airway
Admitted burned patients	181	18 (9.94%);	109 (60.22%)	105 (58.01%)	92 (50.82%)	38 (20.99%)
Patients with ≥40% TBSA burn lesions	42 (23.30%)	11 (26.19%)	42 (100%)	34 (80.95%)	38 (90.47%)	21 (50%)

Administration of blood and derivatives was necessary in all extensively burned patients and also sustained intensive care measures are required for support vital functions in those patients.

The images below illustrates some clinical cases with severe tissue affectation after burn injuries.

First two cases are two men with severe upper limb injuries after electrocutions, with ischemic lesions ne-

cessitating bilateral arm amputations in first case and partial hand amputation in the second one. Third case is represented by a woman with severe third degree thermal burns of the facial region, in the context of extensive deep burns on 50% of body surface. The fourth case shows skin homografts applied for temporary coverage of thoracic region after severe electrical burns interesting 60% TBSA.

Case 1:



Case 2:



Case 3:



Case 4:



DISCUSSION

Burns are severe lesions affecting predominantly young people, men being more exposed to such accidents than female patients.

A special group of patients is represented by the extensive, deep second and third degree burns, covering more than 40% TBSA, requiring intense support in acute phase of the burn and having difficult recovery, with risk of developing severe complications even long-term after the injury. Burns of the upper airways are unfavorable situations, increasing the severity of lesions. Good systemic support and early burn excision and grafting are essential elements influencing the outcome of the patient with extensive burns.

Based on the international reported data, the anatomical regions most commonly affected by burn injuries are upper extremities (70%) and head and neck region (50%), leading to long term morbidity²³. We observed similar percentages in our admitted patients, with those functional areas primary affected, emphasizing the importance of following well established protocols, in order to obtain a accurate evaluation of the lesions and select the appropriate treatment for best functional and aesthetic outcome.

The large majority of cases can be resolved using conventional surgical reconstructive techniques, including a large panel of procedures, from simple to complex: skin grafts, permanent skin substitutes, tissue expansion, local or regional flaps, free tissue transfers, flaps obtained using prefabrication and prelaminarion techniques.

For many patients having the upper limbs amputated, using prosthesis can be an acceptable solution for social reintegration, but for some cases satisfaction cannot be obtained, despite using advanced prosthetic devices. Also for patients with extensive, mutilating facial injuries, even complex microsurgical methods using autologous tissue reconstruction can fail in restore loss functions and ensure psycho-social recovery.

Vascularized composite allotransplantation is in present time the only surgical option for restore optimal functionality in those categories of patients.

There are some particular aspects to take into consideration when think at VCA as reconstructive option in burned patients:

- Need for interdisciplinary team and complex transplant program with adequate institutional support.
- Careful selection of the recipients: general concepts regarding selection criteria for VCA applies, but also with burned patients some problems

may occur, impairing with the final outcome of the procedure: due to extensive lesions, in burned patients modification of tissue architecture is often a problem, resulting after initial injury and also after multiple previous reconstructive procedures; in this situation anatomy is changed, structures may be disrupted and vascular pedicles impaired. Venous drainage is also affected in burn injuries.

- In electric injuries with high voltage, massive tissue loss is common, with involvement and disorganization of multiple anatomic structures including muscles, nerves, blood vessels, resulting sometimes in an inappropriate recipient site for microsurgical procedures. Also lost of muscle and nerves on long areas determine a poor functional prognosis even after transplantation. An accurate preoperative imagistic assessment is mandatory, using technologies like Angio-CT or Angio-IRM for visualization of vasculature, its anatomical reports and tridimensional aspect of the region.
- Evaluation of systemic status is mandatory for a burned patient.
- Other deficits can be observed: neurologic, sensorial, psychological, making the rehabilitation program more difficult to follow after transplantation. For optimal result cortical reintegration is very important.
- Moment of transplantation: usually VCA are elective procedures, effectuated after a good medical and institutional preparation. In burned patients, the lesions have to benefit from a dynamic evaluation if the injury is recent and wait for obtain a stabile local situation with good systemic status. The seriate assessment of lesions is made in order to evaluate the results of conventional surgical techniques if those are proposed to the patient. From the moment of accepting the patient in the transplant program, the waiting period depends of the possibility to find a suitable donor.
- Adequate surgical preparation and good coordination of medical teams during the procedure (in burns patients a laborious dissection is required).
- Adequate post-operative rehabilitation program
- Immunological aspects: the most important thing is to prevent rejection of the allograft.
- The immune status of the patient is important for the success of VCA. Immune system is affected in extensively burned patients. In acute period following the injury a systemic immuno-

suppressive status is described²³. This is the motif of skin allografts integration and long-term persistence, aspect observed also in 3 of our patients.

- Transfusion of blood and derivates in severe burns is mandatory; it can be associated with increased risk of sensitization. As we seen earlier there are multiple causes which can lead to sensitization in burnt patient.
- HLA sensitization must be avoided, if possible, to keep open the option for vascularized composite allotransplantation in indicated cases. But, in the acute phase of extensive burn injury, priority is clearly immediate survival and effective coverage³⁴.

Predictive criteria could help to optimize the later use of VCA after burn injuries. Multiple parameters have to be noted, including the total burn surface area, the affected body areas, and blood transfusion. The risk

of sensitization is justified by the need for coverage of tissue defects, aspect that is important for patient survival^{34,35}.

A solution may be represented by the development of skin substitutes and tissue engineered products, able to provide effective coverage during the acute phase of burn injury without causing HLA sensitization³⁴.

The long-term goal in transplantation is to induce donor-specific tolerance in order to avoid the toxicity of immunosuppression, an essential aspect for burned patients, many of them presenting different degrees of organ dysfunctions (renal, hepatic), even long term after burn injury.

Evaluation protocol:

We propose the following general protocol for patients evaluated as candidates for reconstructive allotransplantation:

Support structure/follow up:

Institution with experience in transplantation

Multidisciplinary team

Safe established protocol

Adequate support for medication(lifelong immunosuppression planned regimens), therapy and follow-up program,

Infection prophylaxis/immunization regimen is needed and has to be provided

Approvals by institutional review boards; Legal approvals



Evaluation of potential recipients:

Considerations:

-Lesion severe enough to justify transplant,

-Sufficient remaining tissue for stability, range of motion, extrinsic muscle-tendons units, nerve supply, vessels;

-Benefit analysis in upper limb transplantation- bilateral vs unilateral/ dominant vs non-dominant/amputation level/ time passed since amputation

-Return of function: realistic expectation of return of meaningful function: existence of cortical representation, no proximal nerve damage

-Improvement in current quality of life: potential for independent living before and after transplant, realistic patient goals for functional improvement following transplant

-Age (recommended >18 years and <65 years)

-Other injuries(additional amputations, vision impairment, burns)

-Co-morbidities:

Higher surgical risk(cardiac diseases, diabetes, coagulopathies, collagen vascular diseases)

Functional recovery: neurologic disorders

Immunological complications: highly sensitized recipients, multiple transfusions, prior transplant

Systemic problems that interfere with immunosuppression:

Ongoing/latent infections: HIV, Hep B, C, CMV, osteomyelitis, MRSA, fungal

Malignancy: active, metastatic, past history

Already immunosuppressed: solid organ transplant, immunocompromised
Compatibility between recipient and donors (ideally, the matching of: gender, age, race, blood type, and HLA – Human Leukocyte Antigen- type)



Training: technical feasibility, and applicability (flap dissection, microsurgery, logistics);



Ethical, social, psychological, and psychiatric issues

Ability to inform consent
Ability to comply with recovery program and immunosuppressive therapy
No serious coexisting psychosocial problems including alcoholism, drug abuse, no tobacco use.

CONCLUSIONS

Despite the initial skepticism about its applicability, due mainly to ethical and technical reasons, the previous worldwide cases and their associated positive outcomes, including acceptable immunosuppressive regimens, excellent aesthetic and functional results, and good psychological acceptance by the recipient, enable the conclusion that composite tissue allotransplantation has become a viable therapeutic area in the reconstructive surgery. A careful selection strategy is imposed when proposing VCA as reconstructive option in

burned patients, due to the clinical and immunological particularities found in this group of patients.

Further research in VCA field is needed for standardization of surgical procedures, eligibility criteria and resolve the immunological challenges for reducing the risk from lifetime immunosuppression therapy. Ideal, the problem can be solve by developing strategies of transplant tolerance induction, allowing a vast reconstructive armamentarium for extensive, mutilating defects, including for burns victims.

Conflict of interests: none declared.

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