Fresh osteochondral allografts—procurement and tissue donation in Europe

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A B S T R A C T

Fresh osteochondral allografts are a well-established treatment for large, full-thickness cartilage defects. The clinical outcome for carefully selected patients is very favorable, especially for the young and active and graft survival up to 25 years has been described in the literature. Furthermore, patient satisfaction rate has been reported, but the biggest obstacle to overcome is the availability of tissue for transplantation. Large fresh bone allografts for cartilage damage repair only can be harvested from organ donors following organ removal or cadaveric donors, preferably in the setting of an operation room to minimize possible contamination of the tissue. Apart from the logistic challenges this entails, an experienced recovery team is needed. Furthermore, the public as well as medical staff is much less aware of the possibility and requirements of tissue donation than organ donation and families deceased are rarely approached for bone and cartilage donation.

This review aims to highlight the current situation of organ and tissue donation in Europe with special focus on the processing of bones and possible safety and quality concerns. We analyze what may prevent consent and what might be done to improve the situation of tissue donation.

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Introduction

Bone allografts have a long history in the treatment of skeletal defects [1,2], aiming to initiate a healing response in the host. Nowadays, patients requiring joint replacement are heavier, more active and live up to 25% longer than several decades ago, challenging modern medicine to provide more durable and long-living treatments [3].

Different techniques have been introduced to tackle this task, concentrating either on preservation or replacement. Most techniques such as abrasion arthroplasty, subchondral drilling, fragment fixation, microfracture, autologous chondrocyte implantation (ACI) or osteochondral autografts are not suitable to treat large defects. Fresh osteochondral allografts (OCA) are a viable treatment option for a wide variety of pathologies (e.g. osteochondritis dissecans with lesions >3 cm² and 1 cm in depth, osteonecrosis, posttraumatic defects or for reconstruction after tumor resection) with favorable clinical outcome [4–6].

For young very active patients the return to daily life activities and previous sport level has been shown to be similarly good between osteochondral autografts and OCA and higher when comparing OCA treatment with ACI or microfracture [7].

Graft survival rate has been reported up to 95% after five years, 91% after ten years, 84% after 15 years, 69% after 20 years and 59% after 25 years, contributing to high patient satisfaction [8]. OCA transplantation uses mature hyaline cartilage (restoring a very natural joint structure and function), live chondrocytes (contributing to graft survival) and can treat large defects as well as underlying osseous defects. In general, fresh autologous grafts are considered the ‘gold standard’. They provide all desired properties of graft material needed to promote healing and long lasting treatment solutions: osteoinduction, osteogenesis and osteoconduct [9]. However, this technique is indicated for the treatment of smaller defects due to limited material that can be harvested from the donor site. Usage of fresh allografts has been shown to be a viable alternative. The clinical outcomes are similar to osteochondral autografts [10,11] and it also prevents donor site morbidity compared to autografts [12]. Human leucocyte antigen (HLA) and AB0-matching is not necessary, allogenic cartilage transplants are immunological privileged tissues similarly to the original cartilage. The intact cartilage matrix provides a protective barrier between allograft and host antibodies. While HLA-specific
antibodies in fresh allograft recipients have been described in literature, they were never identified as cause for graft failure or graft rejection [7,13].

Despite all these advantages, availability is the greatest concern for its use. While femoral heads from living donors that underwent hip arthroplasty are readily available bone allografts for other purposes and may even exceed the demand in some cases [14], large fresh bone allografts needed for the treatment of large cartilage defects can only be harvested from organ donors and cadaveric donors. Additionally, storage time is limited since the allografts should be transferred within 14–28 days after procurement for maximum chondrocyte viability [12].

Processing of musculoskeletal tissue and safety/quality concerns

Despite all therapeutical possibilities allogenic grafts offer, they also may pose a risk to human health when not handled properly. Transmission of several pathogenic organisms and diseases to tissue transplant recipients has been described, such as Clostridium spp., Elizabethkingia meningoseptica, Candida albicans and molds, Epstein-Barr virus (EBV), human immunodeficiency virus 1 (HIV-1), Hepatitis C virus (HCV), tuberculosis, rabies and group A streptococci [15–18].

To minimize the risk associated with allografts, a stringent donor selection is recommended, involving a careful screening of the available medical data of potential donors as well as an interview with the family to exclude risk factors that render the tissue unsuitable for transplantation (e.g. previous diseases, high risk behavior, travel to or residing in areas with transmissible endemic diseases) [19,20]. Table 1 shows a general overview of generic and tissue specific contraindications, regulated by different authorities and law.

Before starting the procurement procedure, a physical examination needs to be done by trained personnel to check for contraindications, indications of high risk behaviour, bone or joint deformities and signs of high contamination risk such as open [9]. The donor should be washed and after thorough pre-operative disinfection the procurement should be done under strictly aseptically conditions within 24 h after cardiac arrest if the body has been refrigerated after death or within 15 h if not [19]. This includes sterile drapes, gowns and gloves, face shields, glasses or protective masks [9]. While the procedure can be handled by personnel other than physicians, the staff needs extensive education, training and significant anatomical knowledge. It is also highly recommended to keep the procurement team as small as possible and to define specific functions for the different members to minimize cross-contamination risk [9]. Every additional person, prolonged post mortem time prior to tissue recovery and a previous organ donation might increase the contamination risk [19,21,22].

Reconstruction of the deceased donor is the last step of bone procurement and should be handled with the same care and respect for the donor as the procurement itself since the integrity of the body and possible disfigurement are recurring themes for reluctance towards donation (see below). Wooden or plastic replacements might be used; the skin should be sutured similar to normal surgery to achieve a look as close as possible to the original [9].

The procurement does not necessarily need to take place in an operation room. European regulations mostly allow the recovery in the morgue, but studies show that while the absolute number of organisms detected is higher with tissue recovered in operation theatres, the number of pathogens is lower [19].

For transport to the processing tissue bank, the tissue should be double-packed or triple packed in air-tight packages or sterile drapes as well as sterile containers. They should be sent at hypothermic conditions and should arrive within 24 h [9].

Processing should take place in environments with Grade A air quality (as defined by European Union Good Manufacturing

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Contraindications for bone donation according to the European Directorate for the Quality of Medicines &amp; Health Care of the Council of Europe [9].</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generic contraindications</td>
<td>• Active systemic infection (bacteria with multidrug-resistance, viruses, fungi, parasites)</td>
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<td></td>
<td>• Hematological malignancies (present or history)</td>
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<td>• Risk of transmission of diseases caused by prions e.g. Patients with diagnosed or suspected Creutzfeld-Jakob-disease</td>
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<td>• Patients with rapid progressive dementia or dementia without confirmed primary cause</td>
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<td>• Degenerative or demyelinating disease</td>
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<td>• Disorders of unknown aetiology involving the central nervous system transfused in the UK recipients of hormones derived from the human pituitary gland and recipients of tissues or cells of cornea, sclera and dura mater</td>
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<td>• Recent history of vaccination with a live attenuated virus</td>
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<td>• Transplantation with organs</td>
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<td>• Intoxication with cyanide or heavy metals (e.g. gold, mercury, lead)</td>
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<tr>
<td>Specific contraindications for musculoskeletal tissue</td>
<td>• Diffuse connective tissue</td>
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<td>• Metabolic bone diseases (e.g. severe osteoporosis, Paget disease)</td>
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<td>• Radiation exposure at the location of the tissue intended to donated</td>
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<td>• Evidence of trauma (e.g. open fractures) at the procurement site</td>
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<td>• Iatrogenic, degenerative tears or lesions detected during procurement</td>
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<td>• For cartilage tissue: age &lt;15 years and &gt;55 years</td>
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