

Bone Graft as an Adjunctive Treatment for Delayed Union and Non-Union of Fractures in Dogs: Systematic Review

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1. Abstract

The cases of non-union or delayed union are the main diagnoses related to complications of orthopedic fractures within the veterinary surgery of companion animals, mainly dogs. Bone graft transplantation is a growing competence as an adjuvant treatment in these cases. The study reveals its use through the evaluation of the data obtained in an advanced research on the topic referring to the main scientific databases, resulting in a systematic review, in addition to proving its means of extraction and conservation. Although there is the possibility of performing autograft and xenograft, among other substitute materials, a choice on the part of the veterinarian must make a tiny assessment of each case. However, this therapeutic approach requires greater professional, structural and, consequently, financial investment by veterinarians and hospital doctors. As well as, the realization of scientific works with the objective of contributing to the evolution of this method of associated treatment

and bringing more and more benefits to the orthopedic patient.

2. Keywords: Bone Graft; Union Delay and Nonunion; Canine.

3. Introduction

Orthopedic traumas are part of the clinical routine of pets in veterinary medicine, among common for this treatment. However, the intention to reestablish a function of the evolve limb cannot be caused, due to complications, such as delayed union or non-union, mainly in the canine species. That is, when the healing time exceeds the expected bone healing process time [1]. Thus, studies are being followed alternative and adjuvant procedures to obtain greater success from surgical procedures for the treatment of fracture

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complications in dogs.

Along with surgical fracture reduction, the use of bone grafts as in adjuvant treatment is increasing every year. It is estimated that during 2006 worldwide, the number of bone grafts exceeded 2.2 million [2]. Since, the results obtained are satisfactory and often this is the right bet for cases with a history of several unsuccessful surgical procedures.

The union delay and the non-union bone have a multifactorial cause, but by definition it is considered as the partial of complete cessation of the reparative processes of bone healing [3]. The probable causes cited are: bone instability due to the proposed treatment method and vascular injury, that compromises the healing process [4]. Temporal, clinical and radiological parameters are used to diagnose in define the condition. The American Food and Drug Administration (FDA) defines the condition as “established when a minimum period of nine months has passed since the injury and the fracture shows no visible progressive sign of healing for three months”. However, there are marked temporal variations about this parameter in the literature [5,6]. As regarding to the situation of non-union, it is classified in two aspects, viable and non-viable, according to the osteogenic capacity and characteristic of vascular supply [6]. Characterized as viable non-unions, which competes for biologically active fractures with varying degrees of proliferative bone activity, with interposed cartilaginous and fibrous tissue. In addition, they can be subclassified according to the position of theses tissues: hypervascularity – when there are no reductions in adequate rotation forces and excess bone callus formation occurs. Moderately hypervascularity – associated with fixation instability processes through the use of plates and screws, with moderate formation of bone callus; Oligotrophic – provides absence or very low amount of bone callus formation, despite being considered active. In turn, viable processes are divided between: dystrophic - when the

intramedullary canal closes; Necrotic or comminuted – when there are loose bone portions; By defects – considerable spacing between bone portions; And finally, atrophic - bone portion that undergoes a responding process [6]. Despite the different classification factor, non-union cases are not independent on subjective influence for the diagnosis, since the evaluation of the painful process of the fracture site during movement at the clinical examination depends on the professional’s sensitivity. Still, the sum of the clinical, radiographic and temporal discretion provides variations regarding the consensus on diagnostic definition [7].

The bone graft, in addition to being used to treat fractures with non-union or delayed union, is in option as in adjunctive treatment for the correction of bone loss due to neoplastic involvement, arthrodesis and as in inducer of bone filling after removing plates and screws, in which says orthopedic surgery. Furthermore, due to the versatility of its therapeutic application, it has also been used in veterinary dental procedures [3-6].

According to the origin, the bone grafts is classified as: Autogenous, a portion of bone tissue extracted from one location and transplanted into another, by the same individual. Homologous, when the transplant is carried out between different individuals of the same species. Or even heterologous, when performed between different animal species [8,9]. The choice of the type of graft to be used must be evaluated on a case-by-case, essential considering material availability, combability, immunogenicity, morbidity and costs. Thus, so-called autografts (autogenous) do not induce rejection due to immunological compatibility. However, they have reduced availability. In the case of xenografts (homologous and heterologous), several procedures are performed aiming at the safety of their use, decreasing antigenicity through irradiation, freezing, autoclaving or chemical preservation. In addition, bone grafts can also be classified according to their

morphological structure, being: Spongy – formed by trabecular bone and normally extracted from the internal portion of the diaphysis of long bones, it is porous and has high cellularity. Cortical – it is moderately acellular due to its constitution of compact and dense bone. Finally, Spongy cortical – which confers the union of both types described, extracted from the rib or wing of the ilium [5,6]. However, the bone graft often consists of material from different sources to obtain a larger sample volume [6].

Given the context of the estimated casuistry of orthopedic fractures that need surgical approach or not, as well as the related complications. Prioritizing the delay in the union or non-union of fractures, due to its therapeutic complexity. The objective of this systematic review is to approach viability of the bone graft through the study of its compatibility, processing and conservation methods, main clinical and surgical approaches and the best choice for cases that include fractures in dogs, based on the veterinary medical literature, available in indexed databases.

4. Materials and Methods

This systematic review was carried out through a bibliographic survey of original articles, review articles and cases reports obtained from the NCBI, Science Direct, BIREME and Scielo databases. The Keywords used to carry out the research were: Bone grafts, bone non-union, bone union delay, dogs.

The following filters were used as inclusion criterion: Languages: English and Portuguese;

Species: dogs;

Types of articles: originals, reviews and case reports;

Period of publication of articles: 2010 – 2020.

The research was carried out using the advanced search feature of the databases, where 2.390 publications were found. Of these, there are at least two of the keywords according to the purpose of the review, which were: bone grafts and dogs; covering the synonymous terms: bone and canine transplantation. However, 41 articles were used owing to exclusion criteria. These being:

Duplicate articles in the databases;

Non-original articles, reviews and case reports;

Articles in languages other than Portuguese in English;

Articles that contain less than four keywords;

Articles published before 2010.

Another refinement was made after Reading and evaluating the abstract of the remaining publications, excluding with did not need the theme based on the criterion already mentioned. Therefore, were left 5 articles consistent with the objective or the review.

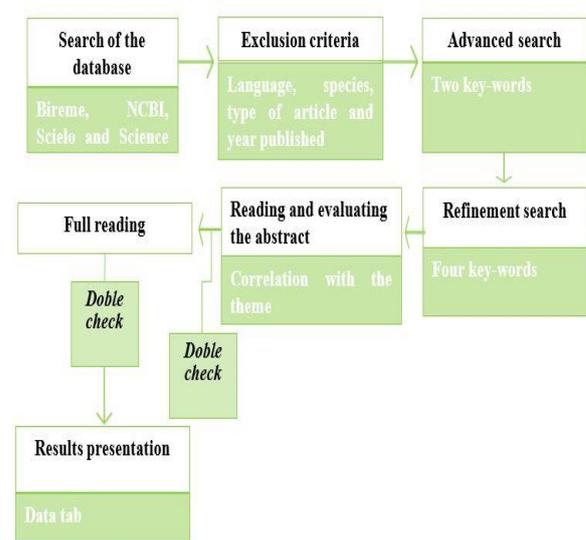


Figure 1: The flowchart of the scientific methodology

At first, 2.390 publications were found, to which 41 articles were included for reading abstracts. In a second stage, 36 articles were excluded because they did not meet the search refinement criteria, at least four keywords. From this stage, 5 articles were read in full that fit the objective of this review, that is, addressing the use of bone graft as an adjuvant treatment for cases of delayed union and non-union in dogs. Thus, table 1 shows the reference, publication objective, corresponding results and conclusion, which contributed to the construction of this work.

Table 1: Characterization of the scientific publications found in the databases, to highlight the use of bone graft as an adjuvant treatment in cases of delayed union and non-union in dogs.

Author	Objective	Results	Conclusion
Déjardin et al (2012) [10]	Verify the effectiveness of MIPO in cases of non-union or delayed fracture union in canine patients	Describe 15 different cases where MIPO was performed and among the is some, bone transplantation was chosen as adjuvant treatment	The use of bone graft proved to be inappropriate when associated with MIPO
Machado (2016) [11]	Evaluated the application of bone graft in orthopedic surgery for pets	Considers the individual assessment of cases when opting for bone transplantation, since its effectiveness is related to the type of condition	Bone graft can be considered an alternative to the use of plaque in fractures of the pelvis in dogs. Proposes the creation of bone graft banks
Zacher et al (2013) [12]	Discuss the progress of oral and facial maxillary orthopedic surgeries in pets	Describe 21 different cases that contemplate the objective of the study, where in some it was opted for the use of bone graft	Establish the definitive diagnosis before any treatment, evaluated multiple simultaneous problems and only then apply the surgical principles. In addition, to promote appropriate monitoring patient. Bone transplantation proved to be effective when combined with in external fixator for caudal jaw fractures treatment
Bhatt et al (2012) [13]	Evidence bone transplantation and substitutes materials according to their effectiveness	Describes the use of xenograft, autograft and various substitutes materials	Autografting is preferred and considered the gold standard as a choice for bone transplantation. Substitutes materials undergo substantial advances in their use. Making the choice of the professional difficult. Emphasizes the importance of fracture alignment and stabilization, as well as maintaining adjacent soft tissues
Palmer (2012) [14]	Discuss the use of external fixators in MIPO is small animals	Describe MIPO and the use of external fixators, showing when it is indicated, contraindicated and what are the possible complications	The use of external fixators should be evaluated, due to its complications. In cases of delayed union or non-union autologous bone transplantation using a minimally invasive technique has proven effective

5. Results and Discussion

The bone graft proved to be inefficient through its application along with a minimally invasive surgical procedure [10], since the authors report only the invasive method for bone transplantation. Thus, its

application did not correspond with the objective of the work. However, PALMER et al [14] describe a minimally invasive technique for the application of bone transplantation, which consists of the traditional extraction of cancellous bone, that is, the collection of

a portion of tissue from the metaphyseal region of the humerus and proximal tibia or the crest iliac. This material together with associated blood is placed in a 1-3cm³ syringe, percutaneous bone marrow aspiration is performed and subsequent application of the syringe content to the fracture line through the access to MIPO. According to the authors, this method is desirable in cases where bone healing delay occurs, proposing the approach even after the surgical procedure if necessary, clarifying the need for intense sedation or short anesthetic episode. PALMER and his collaborators [14] showed in their study that use of bone graft by means of a minimally invasive technique associated with MIPO brought success to the cases evaluated [10,15].

The search for substitute materials for bone grafting has provided veterinarians with several options, currently materials such as minerals, cements, bioactive glass and bone morphogenic proteins are a reality in veterinary medicine worldwide. Each of these materials has its own characteristics and behave differently “in vivo”.

As for example, Hydroxyapatite, which is a basic component of the bone mineral phase and its structure allows ion exchange, its composition fluctuates between the precursor mineral salt of calcium phosphate and calcium phosphate three. Its porous nature makes this material a good osteoconductive and osteointegrative agent, acting as a scaffold to induce fibrovascular growth that will serve as a margin for bone-producing cells that will be deposited in its structure. However, it lacks osteoinductive and osteogenic aptitude. Among the minerals, there is Coralline HA, derived from a marine coral that has a regular porous characteristic, resembling trabecular bone. This material goes through several processes to ensure its application and is often used in combination with the autograft. In the article published by Bhatt et al [13], indicates that it has osteoinductive growth proteins, although when compared to the exclusive use of autogenous graft, it

did not show a superior result. It has good resistance to compression, but low resistance to tensile strength, showing fragility. In addition to being questionable its potential for bone remodeling, since it does not present good osteoclastic resorption. Several materials, such as hydroxyapatite and Coralline HA, are being studied and although most of these substitute materials demonstrate low resorption rate, require several processes to make the material viable and still often out of financial reach, these prove to be a valid alternative as substitutes for autologous bone graft, due to its greatest availability, a highly porous and interconnected characteristic, allowing it to serve as a structure to direct fibrovascularization and eventual bone replacement [13,16].

Allograft (Homologous) is an option give the choice of many veterinarians, seen that many times is accepted by tutors when offered opposite as substitute options for bone grafting. The collection of this material from individuals who died is shown to be quite efficient and convenient to the needs of veterinary clinics and hospitals that board bone graft as an adjunctive treatment for orthopedic surgical repairs. Being indicated until the creation of bone graft banks. As far as their characteristics are allowed with the patient's receiver, although processes are necessary for their viability, which are the osteogenic cells, such as osteoblasts unavailable in their composition. Still, it has a compatible architectural structure to promote osteoconduction and attraction of cells required for bone development [11].

The authors Machado [11], Bhatt and Rozental [13] address an arsenal of options regarding bone graft transplantation, but some cases, as demonstrated by Zacher and Marreta [12] The use of autogenous graft is the most discussed, mainly due to the simplicity of obtaining it and in some cases it is the only method available or accepted by tutors. However, only Machado [11] addressed the complications of this option, which depict the recurrent painful process of collection that can extend throughout the patient's

life. An extremely important point regarding animal welfare, considering that the state of pain affects the quality of life [11-13].

Another aspect that must be taken into consideration is the preservation method to keep the bone graft material viable, regardless of its origin, be it allogeneic or exogenous. This factor was punctually approached in the work of Machado [11], stating that the fresh material does not have a satisfactory result compared to those that undergo some conservation process. Mainly because of the immunological compatibility and ability to include the material in the recipient. Therefore, processes such as freezing drying, which is freezing the sample after repeated immersion baths with alcohol and chloroform solution for degreasing. Freezing which allows you to store the material for more than 30 days, if kept at a temperature of less than 80 °C [17] Glycerin 98% consists of keeping the material for at least 28 days in this solution, performing exchange after 7 days. Honey is a simple procedure that allows you to conserve the material effectively and has a notable antimicrobial property. Ethylene oxide is a gas with antiseptic properties and as the lyophilization process the sample must go through a degreasing process, in addition to dehydration in absolute alcohol for 48 hours. All these conservation methods make possible and are pointed out as the key to the success of the transplant [11,17,18,19].

Future perspectives direct the field of orthopedic surgery for pets to create bone graft banks. However, the scientific literature emphasizes means of processing and conservation, characteristic of natural and synthetic materials, applicability in orthopedic routine, among other, indications and contraindications. In contrast, the report on the use of this associated treatment is scarce and even experimental, considering that no articles were found that clearly addressed the use of the technique. Only articles were found that included surgical procedures within the scope of veterinary orthopedics and that

occasionally addressed bone graft transplantation as an adjuvant treatment in some cases.

6. Conclusion

This article highlights the wide range of valid efficiency alternatives that contribute to the use of bone transplantation in orthopedics within the veterinary medicine of pets. Assigning visibility to methods of obtaining, processing and conservation. As well as, therapeutic applicability of these methods. However, the topic suffers neglect from literary content regarding clinical studies and results of its use. It is proposed that this fact is due to the lack of knowledge on the part of the professionals or the disregard for proposing the treatment for the client, no effectively clarifying doubts about the use of bone graft as an adjuvant treatment and its application.

When compared to the procedure applied to orthopedic surgery within human medicine, bone transplantation undergoes a notable discrepancy in a veterinary medicine, whether in its use in medical routine or in the production of studies and literature. Despite of knowledge of all procedures that include the technique by the veterinarian, the financial factor related to cost and investment by both, the establishment that intends to offer the treatment and the client. On the other hand, according to data extracted from the Pet Brazil Institute (IPB), the country is the second largest consumer of the pet market in the world, in 2018 the pet sector handled around 34.4 billion, where the veterinary medical segment (general and specific services) add up to more than 30%. This data shows that in fact there is an unpreparedness, even regarding the management and marketing of the service to be offered.

The therapeutic contribution of bone transplantation, whether autograft or xenograft, is undeniable as a treatment associated with surgical maneuvers to correct orthopedic trauma and their complications, in particular union and non-union delay. The need for specialized labor, creation and investment of structure is indispensable. Since it is approached in a favorable

way, it will bring positive results to the patient and the veterinary medical establishment. Therefore, dedicating oneself to carrying out studies related to the theme, is an important point for promoting bone transplantation in veterinary medicine for pets.

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