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RADIOGRAPHIC EVALUATION OF THE USE OF XENOGENEIC GRAFT IN THE TREATMENT OF SCOLIOSIS

AVALIAÇÃO RADIOGRÁFICA DO USO DE ENXERTO XENOGÊNICO NO TRATAMENTO DA ESCOLIOSE

EVALUACIÓN RADIOGRÁFICA DEL USO DE INJERTO XENOGÉNICO EN EL TRATAMIENTO DE LA ESCOLIOSIS

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ABSTRACT

Objective: To evaluate the radiographic results obtained using a bone substitute of xenogeneic origin as an adjunct to consolidation in a sample of patients diagnosed with scoliosis and undergoing surgical treatment in a tertiary hospital. Methods: The total sample consisted of 12 female patients, with an average age of 13.5 years. There was a predominance of the single posterior approach (83.3%) In all cases, 30g of the xenogeneic graft was used. Results: The average Cobb angle of the main curve was 85.5 degrees and of the minor curve was 49.2 degrees. We obtained a mean main curve correction of 48 degrees or 56%, which remained in the measurements 6 months postoperatively. The analysis of arthrodesis consolidation demonstrated a predominance of cases classified as Molinari Grade 2, n= 7, (58.7%) at 3 months and at 6 months, n= 8, (66.7%), associated with three Molinari cases Grade 1 (25%) noting a total of 91.7% consolidation of the arthrodesis. Conclusion: The use of the xenogenic graft of bovine origin Bonefill Mix from the company Bionnovation^{R} demonstrated a good consolidation rate, being a consolidation adjuvant that can be used to treat these patients. ***Level of Evidence IV; Prospective Case Series.***

Keywords: Allograft; Spinal Fusion; Xenograft; Tissue Banks.

RESUMO

Objetivo: Avaliar os resultados radiográficos obtidos com a utilização de um substituto ósseo de origem xenógena, como adjuvante da consolidação em uma amostra de pacientes com diagnóstico de escoliose, submetidos ao tratamento cirúrgico em um hospital terciário. Método: A amostra total foi de 12 pacientes, todos do sexo feminino, com idades médias de 13,5 anos. Houve predomínio da abordagem posterior única, (83,3%) Em todos os casos foi utilizado 30g do enxerto xenógeno. Resultados: O ângulo de Cobb médio da curva principal foi de 85,5 graus e da curva menor de 49,2 graus. A correção da curva principal, em média foi de 48 graus ou 56%, que permaneceu nas medidas com 6 meses de pós-operatório. A análise da consolidação da artrodese demonstrou predomínio de casos classificados como Molinari Grau 2, n= 7, (58,7%) aos 3 meses e aos 6 meses, n= 8, (66,7%), associado a três casos Molinari Grau 1(25%) notando um total de 91,7% de consolidação da artrodese. Conclusão: A utilização do enxerto xenógeno de origem bovina Bonefill Mix da empresa Bionnovation^{R} demonstrou boa taxa de consolidação, sendo possível a sua utilização. ***Nível de Evidência IV; Série de Casos Prospectivas.***

Descritores: *Aloenxerto; Artrodese Vertebral; Xenoenxerto; Banco de Tecidos.*

RESUMEN

Objetivo: Evaluar los resultados radiográficos obtenidos con el uso de un sustituto óseo de origen xenogénico como coadyuvante de la consolidación en una muestra de pacientes diagnosticados de escoliosis sometidos a tratamiento quirúrgico en un hospital terciario. Material y método: La muestra total fue de 12 pacientes, todas mujeres, con una edad media de 13,5 años. Hubo un predominio del abordaje posterior único (83,3%). Se utilizaron 30 g de xenoinjerto en todos los casos. Resultados: El ángulo de Cobb medio de la curva principal fue de 85,5 grados y el de la curva menor de 49,2 grados. La corrección media de la curva principal fue de 48 grados o 56%, que se mantuvo en las mediciones a los 6 meses del postoperatorio. El análisis de la consolidación de la artrodesis mostró un predominio de casos clasificados como Grado 2 de Molinari, n= 7, (58,7%) a los 3 meses y a los 6 meses, n= 8, (66,7%), asociados a tres casos de Grado 1 de Molinari (25%), dando un total de 91,7% de consolidación de la artrodesis. Conclusión: La utilización del xenoinjerto de origen bovino Bonefill Mix de la empresa Bionnovation^{R} mostró una buena tasa de cicatrización, posibilitando su utilización. ***Nivel de Evidencia IV; Serie de Casos Prospectivos.***

Descriptores: *Aloinjerto; Fusión Vertebral; Xenoinjerto; Bancos de Tejidos.*

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INTRODUCTION

Adolescent idiopathic scoliosis (AIS) is characterized by a deformity in the frontal plane of the spine, greater than 10 degrees, according to the Scoliosis Research Society (SRS), and its exact etiology remains unknown.[1] Numerous theories are proposed to explain its etiology and pathogenesis, including genetic theories.[1,2] The Cobb angle[3] is used to quantify and assess the progression of the deformity in standard posteroanterior radiographs, with less radiation exposure to breast tissue compared to anteroposterior radiographs.[4] Surgical treatment is generally recommended when the angle is greater than 45 or 50 degrees, associated with skeletal maturation criteria.[5,6]

The purpose of the surgery is to improve shoulder and flank asymmetry, usually observed during physical examination, by halting the progression of the deformity and promoting spinal fusion. In addition to improving self-esteem, body image, and quality of life for patients.[7]

The success of posterior arthrodesis depends on patient-related factors, such as smoking, systemic diseases, and nutritional status, and also on local factors related to the arthrodesis bed[8] and the type and amount of bone graft. The local dried bone is usually used as the base of this graft; however, it becomes insufficient, especially in long fusion segments, as in AIS surgery.

There are descriptions in the literature of multilevel posterolateral fusion rates using autogenous iliac crest grafting, which is currently the gold standard, with pseudarthrosis rates below 5%. However, graft harvesting, additional surgical site aggression, intra- and postoperative morbidity, increased surgery time, and blood loss, as well as often insufficient quantity taken from the iliac crest, motivate surgeons to seek alternatives.[9-11]

The pillars of bone regeneration are already well established, osteogenesis, osteoinduction, and osteoconduction. Osteogenesis consists of synthesizing new bone cells derived from the graft or patient. The process of osteoinduction occurs with the recruitment of mesenchymal cells, with consequent differentiation of chondroblasts into osteoblasts, with these newly formed osteoblasts being responsible for bone formation.[12,13]

Osteoconduction is the process by which capillaries, perivascular tissue, and mesenchymal cells form a structure around the bone resulting in the graft fusing with the patient's bone structure.

The use of allograft as an adjunct to autologous graft shows satisfactory fusion results.[9,10,12] However, there are concerns regarding the efficacy of frozen or lyophilized allograft, potential immunogenicity, and the risk of microbial contamination. In our midst, this is compounded by the difficulty of accessing tissue banks, in addition to the scarcity of bone donors, something still not widely known.[14,15] Alternatively, we can use the xenogeneic graft, which characterizes the performance of bone transplantation between species.[14]

Although the use of bovine grafts has been reported since the 1990s, especially in dentistry, the literature lacks indications for its use as an adjunct in posterolateral vertebral fusion.[16]

The Table 1 demonstrates the main advantages/disadvantages of the xenogeneic graft and autologous.

The rate of bone consolidation is directly related to the success of the vertebral arthrodesis procedure. The present study aimed to evaluate the rate of radiographic consolidation in scoliosis surgeries using as an adjunct to consolidation the deproteinized bovine xenograft, *Bonefill Mix*, from the company Bionnovation[R].

MATERIAL AND METHOD

The study was conducted from October 2021 to June 2022 in a tertiary university hospital, being a prospective cohort study. The sample was for convenience, following the indications of arthrodesis for the treatment of scoliosis, of the cases treated on an outpatient basis, totaling 12 patients. (Table 2)

All cases of deformity in the coronal plane, with an angular value greater than 50 degrees, male or female gender, who agreed to undergo surgical treatment, were included.

The analysis of bone consolidation was performed through imaging exams at 3 and 6 months of treatment by 2 independent examiners, both spine surgeons, with titles from the Brazilian Spine Society, following Molinari's radiographic criteria[17] (Table 3). In all images we also evaluated the presence of signs of implant loosening and Cobb angle.

In this study, the xenogeneic graft *Bonefill Mix* from the company Bionnovation[R] (Figure 1), of bovine origin, whose mineralized

Table 1. Advantages and disadvantages of autologous vs. xenogeneic graft.

Bone graft	Advantages	Disadvantages
Autologous	osteogenesis / osteoinduction and osteoconduction.	approach surgical additional.
	biological safety.	scars/ pain at the donation site.
	absence of risk of reaction immunological.	
Xenogene	architecture and similar geometry.	risk potential of transmission of diseases.
	literature support.	absence of viable cells and biological components.
	bioavailability slow, preserve the bone volume.	variable rate of reabsorption.

Table 2. Identification of the etiology of scoliosis, classification, and variation of the Cobb angle in the pre and postoperative periods. 1- Cerebral palsy / 2- Hemivertebra at T10 / 3 – Marfan syndrome.

	Diagnosis	Pre/Post-Surgical Cobb Angle – Minor Curve	Pre/Post-Surgical Cobb Angle – Main Curve	Lenke Classification	Early Onset Classification
1	Neuro-muscular[1]	90.8 / 73.8	123.9 / 80.3	-	15 M3 (n) P1
2	Idiopathic	38.7 / 14.3	76.4 / 26.1	5CN	-
3	Idiopathic	46.4 / 35.1	140.2 / 58.8	2C+	-
4	Idiopathic	69.2 / 35.4	83.5 / 44.3	3BN	-
5	Idiopathic	41.6 / 2.5	52.5 / 8.1	6CN	-
6	Idiopathic	66.7 / 40.4	99.6 / 61.7	3CN	-
7	Idiopathic	56.1 /14.3	72.8 / 19.3	1CN	-
8	Idiopathic	28.3 / 7.8	70.4 / 18.8	2BN	-
9	Congenital[2]	39.2 / 16.7	79.2 / 54.4	-	13 C3 (+) P0
10	Neuro-muscular[1]	22.7 / 7.4	80.4 / 36.6	-	13 M3 (n) P1
11	Neuro-muscular[3]	57.4 / 21.6	65.3 / 22.9	-	13 S3 (n) P0
12	Idiopathic	33.7 / 6.4	58.2 / 13.4	1BN	

Table 3. Radiographic classification of Molinari.

	Radiographic Classification of Molinari
Stage I	Bilateral fusion with trabeculation present in the transverse process
Stage II	Unilateral fusion, with difficulty visualizing the other side
Stage III	Suspicious radiolucency or defect in the fusion area
Stage IV	Graft resorption with instrumentation fatigue

Figure 1. Xenogeneic graft Bonefill Mix from the company BionnovationR[R].

inorganic bone matrix has a macro and microporous structure similar to human cortical and cancellous bone, was used, favoring osteoconduction.

At the end of the osteosynthesis, all levels were decorticated, making the bed favorable for the placement of the granulated graft (Figure 2), associated with the local autologous graft (Figure 3), always distributed in the posterolateral region, as shown in Figure 4, following the proposal described by Moe,[8] and in the two cases where the anterior approach was performed, after the discectomy, the site was filled with xenogeneic graft. In all cases, 1 g of vancomycin powder was added and mixed with the granulated graft before its placement in the arthrodesis bed. The surgical approach used was posterior, anterior, or combined.

We used radiographic images of the entire spine in front and side views to measure the Cobb angle of the main curve and smaller curves, as well as thoracic kyphosis, as shown in Figure 5. The evaluation of arthrodesis levels, amount of graft used, and complications such as implant loosening, breakage of rods or screws, and the need for surgical revision were also evaluated.

The study design was conducted prospectively for case selection. Due to the difficulty of using autologous grafts from a tissue bank, a control group was not obtained. Approval was obtained from the institution's ethics and research committee with the number CAAE:57514821.2.0000.5479.

Figure 2. Clinical image of the xenogeneic graft Bonefill Mix from the company Bionnovation[R].

Figure 3. Clinical image of the local autologous bone graft.

Figure 4. Example of distribution of autologous and xenogeneic graft placement during intraoperative.

RESULTS

The total sample consisted of 12 cases undergoing surgery, all female, with an average age of 13.5 years (±1.6 years). There was a predominance of the single posterior approach, n=10 cases (83.3%), followed by the double approach, n=2 cases (16.7%), and in no case was the anterior approach performed alone. In all cases, 30g of the xenogeneic graft *Bonefill Mix* from the company Bionnovation[R] was used. (Table 4)

Evaluating the preoperative full spine radiographic images, the mean Cobb angle of the main curve was 85.5 degrees (±25.9), while the postoperative was 37 degrees (±22.6). Regarding the mean preoperative Cobb angle of the minor curve, the value found was 49.2 degrees (±19.5), and in the postoperative period, it was 22.9 (±20.3). (Table 5)

The measurement of the main curve found in the immediate postoperative evaluation was 37 degrees, noting a correction of the average main curve of 48 degrees or 56%. This correction remained in the measurements six months postoperatively, with no statistical difference.

There was a case where proximal hook release occurred, whose main Cobb value was 68 degrees in the preoperative evaluation and 39.3 degrees in the immediate postoperative period. With implant

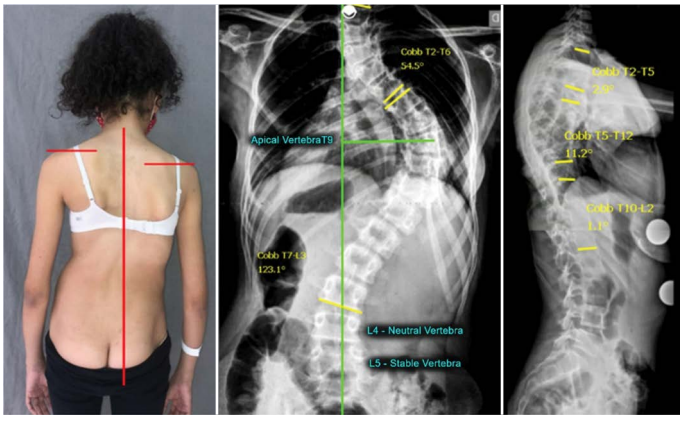

Figure 5. Example of preoperative clinical and radiographic evaluation of curves using the Cobb method.

Table 4. General demographic data of our sample.

Descriptive Data	Total
Sample Size	12 (100%)
Age	13.5 years (±1.6)
Sex	
Female	12 (100%)
Diagnosis	
Scoliosis	12 (100%)
Access Roads	
Posterior	10 (83.3)
Double track	2 (16.7%)
Graft Quantity	30 g
Implant Release	
No	9 (75%)
Yes	3 (25%)

Table 5. Measurement of the Cobb angle.

Cobb angle	Total
Smaller Curve	N total (12)
Preoperative	49.2 (±19.5)
Postoperative	22.9 (±20.3)
Main Curve	N Total (12)
Preoperative	85.5 (±25.9)
Postoperative	37 (±22.6)

release at three months, it returned to the initial value of 62 degrees, considered the same due to measurement divergence already described in the literature of up to five degrees in the angular value measured by Cobb.[3]

In two cases, we had signs of loosening of a screw, identified by the presence of lysis around the screw, without migration of the same, being two screws at the apex of the curve and one in the last vertebra instrumented distally, without clinical repercussions, totaling two patients, rod breakage was not observed. In another patient, a surgical re-approach was necessary due to proximal operative wound dehiscence, followed by the loosening of two proximal hooks. In this case, the bipolar technique had been used.

The analysis of the consolidation of the arthrodesis showed a predominance of cases classified as Molinari Stage 2, n= 7, (58.7%) at three months and at six months, n= 8, (66.7%), associated with three cases of Molinari Grade 1 (25%), noting a total of 91.7% consolidation of the arthrodesis. Only one case remained as grade 3 in the radiographic evaluation at three and six months postoperatively, the same one in which the proximal hooks loosened and required reoperation.

Statistical analysis involved quantifying descriptive data through mean and standard deviation for continuous variables and using percentages for categorical variables using SPSS Statistics 21 software.

DISCUSSION

The use of xenogeneic grafts may involve risks such as disease transmission (especially by retroviruses), activation of the recipient's immune response, absence of viable cells, and reduction of osteoinductive properties during the manufacturing process.[10] However, just like hydroxyapatite, there is no residual organic material or protein residues, and its potential for bone regeneration has been documented in vitro through high permeability to cells and fluids. This allows rapid formation of new bone without foreign body reaction, that is, with low immunogenic potential.[15]

The use of posterior instrumentation, using pedicle screws, has led to pseudarthrosis rates reported in the literature below 3%, regardless of graft selection. Kirzner et al,[18] in a recent meta-analysis, did not demonstrate a statistically significant difference in posterolateral fusion rates in the surgical approach to scoliosis, regardless of graft choice, reporting 100% consolidation rates. In our sample, despite the limited number of cases and the six-month postoperative evaluation period, we noticed a consolidation rate of 91.7%, very similar to the data in the literature.

Using grafts with lower osteoinduction potential does not interfere with the final consolidation, since the immature skeleton in scoliosis may have a higher fusion potential, in addition to the local stability provided by the instrumentation, which seems to favor consolidation. In one case, there was a failure of proximal fixation, with the loosening of the hooks and consequent halt in the consolidation process, Molinari Stage 3, which indicates that mechanical stability favors consolidation. However, in this case, we still had surgical re-approach, which leads to greater devitalization of the arthrodesis bed. Nevertheless, intraoperatively, a consolidation bed was observed, as shown in Figure 6.

Another factor related to the low rate of pseudarthrosis is the difficulty in assessing consolidation due to the presence of the metal implant, which may interfere with the evaluator's analysis. Despite this consideration, there is a low reported re-approach rate, with indices of 2%. In our sample, only one case was readdressed, obtaining a rate of 8.3%. In the literature, other factors are still considered for determining pseudarthrosis, related to pain or curve progression, regardless of whether there was a total or partial consolidation.[11,12]

Despite this report, we know that consolidation is crucial for the mechanical strength of the implant and a favorable clinical outcome. Loosening and failure of the implant can lead to prominence of the synthesis material, pain, and local ulceration, requiring re-approach. Hence, the importance of seeking adjuvant solutions for consolidation.

The autogenous graft remains the gold standard.[19,20] Still, chronic pain at the donor site can be present in up to 10% of cases when the posterior iliac crest is harvested, also associated with the need for drains and longer surgical time and bleeding, compared to the use of xenogenous graft or other biomaterial.[14,16,21] Especially in the surgical approach to scoliosis, the presence of an immature skeleton leads to a smaller amount of available autologous graft and a risk of physical injury during its removal, so using grafts from other sources is always recommended.[18]

The option for use without adjuvants, only the local autogenous graft, tends to lead to higher rates of loss of correction in the literature, despite shorter surgical time and bleeding.[22] The largest release of soft tissues, necessary to obtain a sufficient amount of local graft, seems to be related to this loss of gradual correction. However, scientific production with a longer follow-up time is still necessary to corroborate this hypothesis.

In our study, we obtained an initial correction that was maintained during the minimum follow-up period of six months, always performing the combination of the local autogenous graft taken only from the levels of arthrodesis in combination with the xenogenous graft *Bonefill Mix* from the company Bionnovation[R]. Furthermore, the preparation of the graft bed has always been carried out at the end of the procedure, with extensive decortication, as initially recommended by Moe.[8]

A small sample (n=12), varied etiology of the operated scoliosis cases (idiopathic, neuromuscular, and congenital), absence of a control group, and an initial follow-up of only six months were considered limiting factors of the study and identified by the authors during the study's preparation.

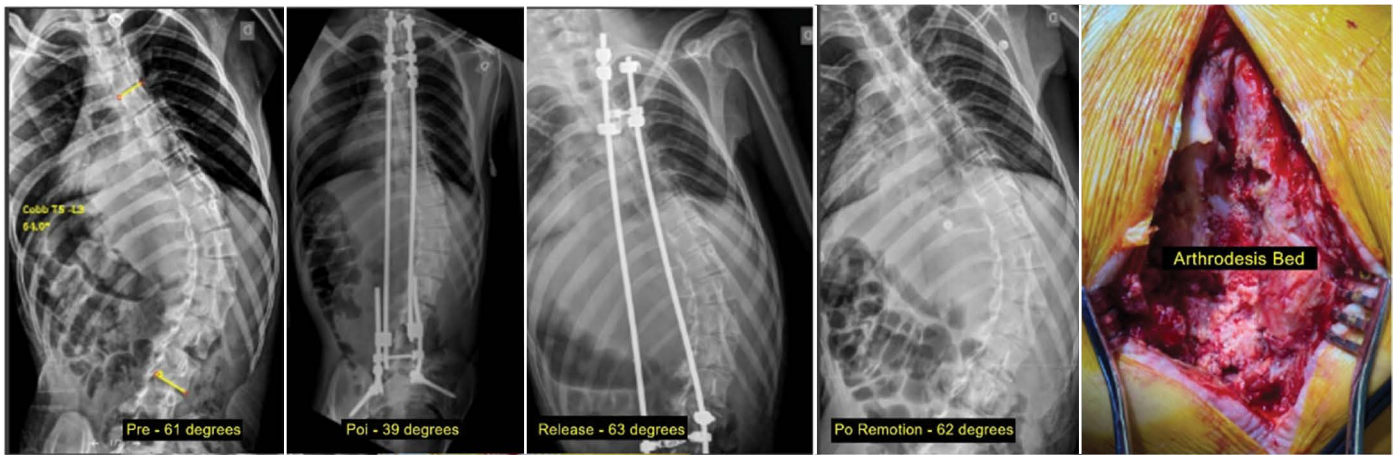

Figure 6. Release of the implant and arthrodesis bed showing consolidation at 11 months postoperatively.

CONCLUSION

The use of bovine-derived xenograft Bonefill Mix from Bionnovation[R] did not show an increase in the incidence of infection, local inflammatory reaction, implant failure, or pseudoarthrosis in the minimum follow-up of six months. It can be safely used as an adjunct in the bone consolidation process in cases where the goal is posterolateral fusion and maintenance of the correction obtained during this period.

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All authors declare no potential conflict of interest related to this article.

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