

USE OF XENOGRAFT AS AN ADJUVANT IN SPINAL ARTHRODESIS CONSOLIDATION: A CASE SERIES

UTILIZAÇÃO DO ENXERTO XENÓGENO COMO ADJUVANTE NA CONSOLIDAÇÃO DA ARTRODESE VERTEBRAL: SÉRIE DE CASOS

USO DE XENOINJERTO COMO ADYUVANTE EN LA CONSOLIDACIÓN DE LA ARTRODESIS ESPINAL: SERIE DE CASOS

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ABSTRACT

Objective: To evaluate the radiographic fusion rate and safety of a deproteinized bovine-derived xenograft as an adjunct in spinal arthrodesis. **Methods:** A prospective case series study (n=35) was conducted on adult patients undergoing instrumented spinal fusion. Radiographic fusion was assessed at 6 months using the Molinari classification. Descriptive and inferential statistical analyses (Fisher's Exact Test, Mann-Whitney U, Kruskal-Wallis) were performed to investigate associations between demographics, etiology, and the outcomes of fusion and complications. **Results:** The overall fusion rate (Molinari grade I or II) was 88.6% (31/35). There was no statistically significant association between etiology, sex, or age and the fusion outcome ($p > 0.05$). The complication rate was 11.4% (4/35), consisting of superficial wound infections. The occurrence of complications was significantly associated with deformity patient group ($p < 0.001$). **Conclusion:** The deproteinized bovine xenograft proved to be a safe and effective adjunct for spinal arthrodesis, with a high and consistent radiographic fusion rate (88.6%) across different pathologies. Complications were associated with the surgical magnitude of the underlying disease rather than the graft material itself. **Level of Evidence IV; cross-sectional study.**

Keywords: Spinal Fusion; Bone Transplantation; Heterografts; Survival Analysis; Postoperative Complications.

RESUMO

Objetivo: Avaliar a taxa de consolidação radiográfica e a segurança do enxerto ósseo xenógeno de origem bovina desproteinizado como adjuvante na artrodese da coluna vertebral. **Métodos:** Estudo prospectivo de série de casos (n=35) em adultos submetidos à artrodese vertebral instrumentada. A consolidação óssea foi avaliada radiograficamente aos 6 meses pela classificação de Molinari. Foram realizadas análises descritivas e testes de associação (Teste Exato de Fisher, Mann-Whitney U, Kruskal-Wallis) para investigar a relação entre variáveis demográficas, etiológicas e os desfechos de fusão e complicações. **Resultados:** A taxa de fusão global (graus I ou II de Molinari) foi de 88,6% (31/35). Não houve associação estatisticamente significativa entre a etiologia, sexo ou idade e o sucesso da fusão ($p > 0,05$). A taxa de complicação foi de 11,4% (4/35), consistindo em infecções superficiais de ferida. A ocorrência de complicações esteve significativamente associada ao grupo de pacientes com deformidade ($p < 0,001$). **Conclusão:** O enxerto ósseo xenógeno bovino demonstrou ser um adjuvante seguro e eficaz, com elevada e consistente taxa de fusão radiográfica (88,6%) entre diferentes patologias. As complicações estiveram associadas ao porte cirúrgico da doença de base, e não ao material em si. **Nível de evidência: IV; estudo transversal.**

Descritores: Artrodese vertebral; Enxerto ósseo; Xenoenxerto; Análise de sobrevida; Complicações pós-operatórias.

RESUMEN

Objetivo: Evaluar la tasa de fusión radiográfica y la seguridad de un xenoinjerto bovino desproteinizado como adyuvante en la artrodosis espinal. **Métodos:** Se realizó un estudio prospectivo de serie de casos (n=35) en pacientes adultos sometidos a fusión espinal instrumentada. La fusión radiográfica se evaluó a los 6 meses mediante la clasificación de Molinari. Se efectuaron análisis estadísticos descriptivos e inferenciales (prueba exacta de Fisher, U de Mann-Whitney, Kruskal-Wallis) para investigar asociaciones entre los datos demográficos, la etiología y los resultados de fusión y complicaciones. **Resultados:** La tasa global de fusión (grado I o II de Molinari) fue del 88,6% (31/35). No se observó asociación estadísticamente significativa entre la etiología, el sexo o la edad y el resultado de la fusión ($p > 0,05$). La tasa de complicaciones fue del 11,4% (4/35), consistiendo en infecciones superficiales de

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la herida. La aparición de complicaciones se asoció significativamente con el grupo de pacientes con deformidades ($p < 0,001$). Conclusión: El xenoinjerto bovino desproteínizado demostró ser un adyuvante seguro y eficaz para la artrodesis espinal, con una tasa de fusión radiográfica alta y consistente (88,6%) en diversas patologías. Las complicaciones se relacionaron con la magnitud quirúrgica de la enfermedad subyacente más que con el material del injerto en sí. **Nivel de evidencia III; estudio de corte transversal.**

Descriptor: Fusión Espinal; Injerto Óseo; Xenoinjerto; Análisis de supervivencia; Complicaciones Posoperatorias.

INTRODUCTION

Spinal fusion is a standard procedure for treating various conditions that cause instability or refractory pain¹. Achieving solid bone fusion is crucial for clinical success, being directly influenced by the type of bone graft used².

Bone consolidation in arthrodesis depends on multiple factors, including the patient's systemic conditions (such as smoking, diabetes mellitus, osteoporosis, and malnutrition), as well as local factors related to the fusion bed and the type of bone graft employed³. In this context, the graft acts as a central biological element, directly influencing osteointegration and pseudarthrosis rates.

Iliac crest autograft is the gold standard, but its harvesting is associated with significant morbidity, including chronic pain, infection, hematoma, nerve injury, and increased operative time, along with limited availability in certain patient profiles⁴. Allograft eliminates donor site morbidity but comes with higher costs and lower osteoinductive capacity⁵.

In light of this, bone substitutes such as xenografts have gained interest. Bovine-derived materials, when processed to remove antigenic components, offer a biocompatible osteoconductive scaffold⁶. The use of xenografts is well established in other areas, such as dentistry, where they have been used for decades with high success rates⁶. Despite this, experience in spinal surgery, with its high biomechanical demands, remains limited and requires rigorous validation⁷.

Therefore, this study aims to evaluate the radiographic consolidation rate and the safety profile of the deproteinized bovine-derived xenograft (Bonefill® Mix, Bionnovation) when used as an adjunct in spinal fusion in a tertiary care service.

METHODS

Study Design and Selection of Patients

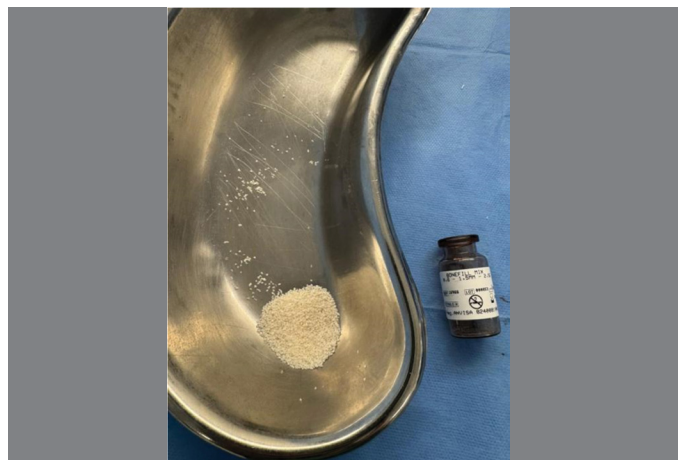
A prospective and observational case series study was conducted at a single center between September 2021 and September 2024. Thirty-five consecutive adult patients undergoing instrumented spinal fusion were included. All participants provided written informed consent and were followed for a minimum period of six months. Patients diagnosed with vertebral infections, such as spondylodiscitis or tuberculosis, and those with primary or metastatic tumors in the spine were excluded from the study. Exclusion criteria also included the need for revision surgery in the same segment during follow-up, the use of unconventional instrumentation, such as isolated anterior fixations, and the presence of osteogenesis imperfecta or other severe bone dysplasias. Patients with inadequate radiographic documentation, loss of clinical follow-up, or who refused to participate in the study were also excluded. Patients were categorized into three groups according to the etiology of the condition that led to surgery: degenerative (spondylolisthesis, stenosis, discopathies), deformities (scoliosis, hyperkyphosis, Scheuermann's disease), and traumatic (unstable vertebral fractures, fracture-dislocations). (Figures 1-3).

Graft Preparation

In all procedures, the bone graft was prepared using 5 to 30 grams of crushed xenograft, combined with local autologous graft obtained during surgical decompression (e.g., laminectomy or osteotomies). A small amount of local blood was added to the mixture to enhance the biology of fusion.

Radiographic Evaluation and Outcomes

The evaluation of the fusion consolidation was performed through simple radiographs at the sixth month post-operation. The images



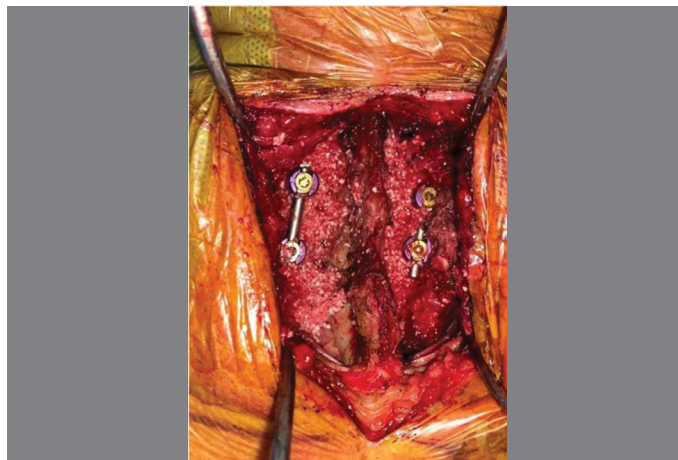
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Figure 1. Crushed xenograft in a kidney dish.



Source: Own authorship.

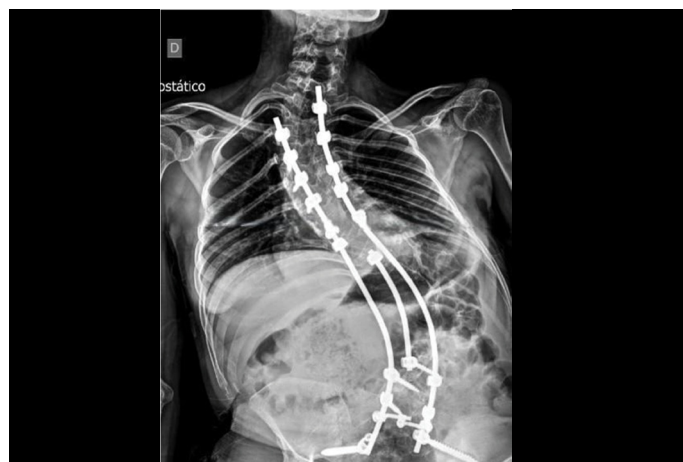
Figure 2. Mixture of xenograft and autologous graft.



Source: Patient database from the Spine Surgery Group – Brotherhood of Santa Casa de Misericórdia of São Paulo.

Figure 3. Placement of the graft mixture in the lumbar spine after insertion of the fusion screws during the intraoperative period.

were independently analyzed by three spine surgeons who were unaware of the patients' clinical data. For the classification of fusion, the criteria of Molinari et al. were used, which stratify the outcome as success (grades I and II) (Figure 4) or failure (grades III and IV – nonunion). The recording of postoperative complications was carried out systematically. The data were collected on the REDCap platform and the images analyzed in the Xero Viewer system.



Source: Patient database from the Spine Surgery Group – Brotherhood of Santa Casa de Misericórdia of São Paulo.

Figure 4. Radiograph of the spine of a patient classified as Molinari I.

Statistical Analysis

The statistical analysis was performed using R software (version 4.1.2). Categorical variables were presented as frequencies and percentages, while continuous variables were described by mean and standard deviation (SD) or median and interquartile range (IQR), according to the data distribution. The association between categorical variables was evaluated with Fisher's Exact Test, and the comparison of age medians between groups was conducted using Mann-Whitney U or Kruskal-Wallis tests. The level of statistical significance was set at $p < 0.05$.

Ethical Aspects

This study was conducted in compliance with the principles established in Resolution No. 466/2012 of the National Health Council. The project received approval from the Research Ethics Committee of the Brotherhood of Santa Casa de Misericórdia of São Paulo, under opinion number 5.515.147 (CAAE: 57514821.2.0000.5479).

RESULTS

Sample Characteristics

The sample consisted of 35 patients, with 21 (60.0%) being female. The overall average age was 48.2 ± 19.3 years. The etiological distribution included 15 (42.9%) cases of deformity, 13 (37.1%) of degenerative disease, and 7 (20.0%) of trauma (Table 1). A statistically significant difference was observed in the median age among the etiological groups ($p < 0.001$), with 64 years for the degenerative group, 36.5 years for the trauma group, and 17 years for the deformity group.

Bone Consolidation and Association Analysis

Bone consolidation of the fusion was achieved in 31 of the 35 patients, resulting in an overall fusion rate of 88.6%. Among the successful cases, 17 (48.6%) were classified as grade I and 13 (37.1%) as grade II, according to Molinari's criteria. Five patients (14.3%) experienced fusion failure (nonunion), being classified as grade III.⁸ (Table 2)

The analysis of associations did not demonstrate a statistically significant relationship between the occurrence of nonunion and

Table 1. Clinical-demographic characteristics of patients undergoing the use of a mixture of xenograft and autologous graft after spinal fusion surgery.

Variable	Value
Age (years)	
Mean $\pm$ SD (Range)	34.3 $\pm$ 20.6 (11 – 73)
Gender	
Female, n (%)	20 (57.1)
Male, n (%)	15 (42.9)
Primary Etiology	
Deformity, n (%)	15 (42.8)
Degenerative disease, n (%)	13 (37.1)
Trauma, n (%)	7 (20.0)

Table 2. Analysis of bone consolidation based on Molinari's criteria.

Molinari Grade	Description	Number of Patients (n)	Percentage (%)
I	Bilateral fusion with present trabeculation	17	48.6%
II	Unilateral fusion, with difficulty in visualization	14	40%
III	Suspicious radiolucency or defect in the fusion area	4	11.4%
IV	Graft reabsorption with instrumentation fatigue	0	0.0%
Total		35	100%

the studied variables. The observed fusion rates were 100% in the degenerative group, 93.3% in the deformities group, and 42.8% in the trauma group ($p = 1.00$). Similarly, there was no significant difference between genders ($p = 1.00$), with consolidation rates of 100% for females and 73.3% for males. The median age of patients who achieved successful fusion was 31 years, compared to 18 years in the nonunion group ($p = 0.25$).

Postoperative Complications

The overall complication rate was 11.4% (4/35), consisting exclusively of superficial infections of the surgical wound. A statistically significant association was identified between etiology and the occurrence of complications ($p < 0.001$). All four adverse events occurred in patients from the deformities group, corresponding to a complication rate of 26.7% (4/15) in this subgroup, in contrast to 0% in the degenerative and trauma groups.

DISCUSSION

This study demonstrated a radiographic fusion rate of 88.6% with the use of bovine xenograft, a robust and clinically relevant result. These findings are consistent with the results obtained in previous studies that document fusion rates using autologous or mixed grafts between 80 and 95%.⁹⁻¹¹ Similarly, it demonstrates that the performance of the xenograft is comparable to other sources, as shown by Chiang et al., who achieved rates of 100% by using xenograft.¹² Furthermore, Durigan et al., in a series of 12 cases of scoliosis in children treated with a combination of bovine xenograft and autograft, found fusion rates of 91.7%.¹³

When analyzing fusion rates by etiology, the lowest rates were found in the trauma subgroup (42.8%). Although this finding did not present a statistically significant relationship ($p = 1.00$), it may have clinical relevance. This suggests that the adverse conditions presented by the patient during a trauma scenario (bone loss, local osteonecrosis, systemic condition, or presence of local hematoma) affect the osteogenic potential and biological stability, which may compromise osteointegration.^{14,15}

In the age analysis, no statistically significant relationships ($p = 0.25$) were found between this variable and the fusion rates.

Notably, there is a median age of 31 years in the fusion cases compared to a median age of 18 years in the pseudoarthrosis cases. This is consistent with previous studies that mention that age alone is not an influencing factor in the success of a fusion, but that there are other more important factors, such as the mechanical stability achieved and the quality of fixation.^{16,17}

Regarding complications in the present study, 4 superficial infectious processes were found in the evaluated patient group. No adverse events related to pain processes, rejection, or additional morbidity were found. This is within the expected ranges documented in the literature, where Campbell et al. and Lee et al. document complication rates between 5-10% in infectious processes.^{18,19} This allows us to assert that the use of xenografts as adjuncts is quite safe in spinal surgery and that their use does not imply an increase in postoperative complications.

Another important factor is that, when performing the differential analysis, a strong association was found between complications and the group of patients with deformity ($p < 0.001$), with all four infections occurring in this subgroup. Upon reviewing the literature, it was found that Charosky et al. reported that complication rates in such cases can reach up to 39%.²⁰ Akintürk et al. conducted a study with over 25,000 patients, finding complication rates of up to 34.5%, with 3.6% in infections.²¹ This suggests that the complications presented in these patients may not be directly related to the use of the graft, but to the complexity of the procedure performed.

Rejection by the host, disease transmission, or loss of osteoinductive properties are negative factors to be considered when using

xenografts. However, in this study, a quite satisfactory fusion rate is observed, and no type of graft rejection or signs suggesting disease transmission have been found so far. This is consistent with the findings of Kubosch et al., who conducted a study comparing autologous grafts with xenografts, showing that there were no organic or protein residues in the material with good permeability to cells, which demonstrated a good in vivo capacity for bone formation with good biocompatibility (low risk of host response).²²

This study also presents some limitations. First, there is no control group to monitor the results, in addition to a short follow-up (6 months). On the other hand, as identified by Buser et al., randomized studies with larger samples are needed to make better decisions.²³ Finally, it is necessary to conduct a subgroup analysis to try to differentiate the behavior of the intervention according to each specific case.

CONCLUSION

The deproteinized bovine-derived xenograft demonstrated to be a safe and effective biomaterial with a high and consistent radiographic fusion rate (88.6%) across different pathologies. Our series suggests that the complications were associated with the inherent risks of the procedures, and not associated with the biomaterial used.

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CONFLICT OF INTEREST

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

CONTRIBUTIONS OF THE AUTHORS

Each author contributed individually and significantly to the development of this article. Boldorini R., Parente R. and Fortunato D. assisted with data collection. Aily J. assisted with data maintenance and data entry into the collection platform. Trincado R., Durigan J., and Garcia T. reviewed the article. Goes R. and Gotfryd A. contributed to methodology and supervision. Caffaro M. and Meves R. contributed to formal analysis and data curation. Parente R., Fortunato D., Boldorini R., Lee T., Filho T., Quebradas J., and Filho E. contributed to validation and writing — review and editing.

DATA AVAILABILITY DECLARATION

The underlying contents of the research text are contained in the manuscript.

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