



Original Article

Evaluation of the effectiveness of platelet-rich plasma in the bone consolidation of patients submitted to lumbar arthrodesis[☆]



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ABSTRACT

Objective: To determine whether the use of autograft associated with platelet-rich plasma (PRP) increases bone healing in patients undergoing lumbar fusion.

Method: This was a prospective, descriptive, and comparative study, which included 40 patients undergoing lumbar fusion, who were divided into two groups: group I, autograft only, and group II, autograft associated with PRP. After surgery, patients were followed-up on the first, third, and sixth month. The Molinari radiographic classification and Glassman tomographic classification were used as criteria to analyze the bone consolidation.

Result: Comparing the group I with group II, according to the criteria of Molinari, bilateral fusion was observed in 27.5% of the patients in group I in the first month after surgery. In group II, the rate of bilateral fusion was 25.0% and 20% in the third and sixth months, respectively. The results of computed tomography scans performed at six months after surgery indicated, according to the criteria of Glassman, a rate of bilateral solid fusion of 15.0% and 10.0% in groups I and II, respectively.

Conclusion: The use of PRP showed no significant difference in bone healing in cases of lumbar arthrodesis.

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Avaliação da eficácia do plasma rico em plaquetas na consolidação óssea de pacientes submetidos a artrodese lombar

R E S U M O

Palavras-chave:

Dor lombar
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Objetivo: Analisar se o uso de enxerto autólogo associado a plasma rico em plaqueta (PRP) aumenta a consolidação óssea em pacientes submetidos à artrodese lombar.

Método: Estudo prospectivo, de caráter descritivo e comparativo, com 40 pacientes submetidos à artrodese lombar, que foram divididos em dois grupos: grupo I, somente enxerto autólogo, e grupo II, enxerto autólogo associado a PRP. Após o procedimento cirúrgico, o acompanhamento foi feito no primeiro, terceiro e sexto mês. Os critérios de classificação radiográfica de Molinari e tomográfica de Glassman foram usados como padrão para analisar a consolidação.

Resultado: Na comparação do grupo I com o grupo II no primeiro mês de pós-operatório, de acordo com os critérios de Molinari, 27,5% dos pacientes apresentaram fusão bilateral no grupo I. No terceiro e sexto mês, observou-se uma taxa de fusão bilateral de 25% e 20% para o grupo II. O resultado das tomografias feitas no sexto mês de pós-operatório indicou, de acordo com os critérios de Glassman, uma taxa de fusão sólida bilateral de 15% e 10% nos grupos I e II, respectivamente.

Conclusão: Observou-se que o uso do PRP não apresentou diferença significativa na consolidação óssea nas artrodeses lombares.

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Introduction

Low back pain has been considered a frequent cause of morbidity and disability in the general population, presenting a higher prevalence among females and those aged 40–80 years.¹ Vertebral instability, whether or not associated with disk disease, is an important etiological factor in this pathology. In cases refractory to conservative treatment, and after careful and accurate diagnosis of instability, stabilization of the affected segment (vertebral arthrodesis) is indicated.

When vertebral arthrodesis is performed, it is necessary to use some type of graft and/or bone substitute at the osteotomy site in order to accelerate the process of bone consolidation. The most commonly used one for this purpose is the autologous graft.²

The use of the autologous graft is the gold standard for arthrodesis, due to its osteogenic (osteoblastic cells derived from the medulla and pre-osteoblasts), osteoconductive (collagen and mineral matrix), and osteoinductive properties (growth factors), in addition to the fact that it does not trigger immune response and infectious diseases. In turn, it presents several limitations, such as: exhaustible sources, which limits its use in children and in surgical revisions; frequent presence of morbidity at the donor site; and the fact that its quality depends on the age and general condition of the individual.³

The first lumbar arthrodesis was described in 1911 by Russel Hibbs and Fred Albee; the procedure, which was done *in situ* with autologous graft, was indicated for the prevention of progressive spinal deformity.⁴⁻⁶ In the 1970s,

Roy-Camille popularized the use of pedicle screws in vertebral arthrodeses,^{7,8} which greatly contributed to the reduction of the nonunion rate, a complication still very much feared by spine surgeons.⁹

Considering the importance of adequate bone healing for the success of vertebral arthrodesis surgery and the various existing limitations for the use of autologous grafts, an increase in the number of studies with the use of bone substitutes associated with hydroxyapatite (HA), bone morphogenetic proteins (BMP), and platelet-rich plasma (PRP) has been observed. Among the aforementioned materials with osteoinductive properties, the literature describes PRP as one of the most used and researched.²

PRP is obtained from autologous blood centrifugation; its application at the surgical site releases several naturally occurring growth factors, such as platelet-derived growth factor (PDGF), transforming growth factor beta (TGF- β), and vascular endothelial growth factor (VEGF). It is comprised of these growth factors and clot-forming cells. These, in turn, serve as the carrier of said growth factors. This property differentiates it from recombinant growth factors, such as BMPs and HA, allowing it to promote and stimulate the differentiation of stem cells from the mesenchymal system into osteoblasts and accelerate the bone healing process.²

This study aimed to analyze whether the use of autologous grafts associated with PRP enhances bone consolidation in patients who underwent lumbar arthrodesis due to degenerative diseases, as it presents characteristics very close to those of autologous grafts. As it is a natural source of growth factors, it does not trigger immune reactions and the transmission of infectious and contagious diseases.¹⁰

Materials and methods

This is a retrospective, descriptive, and comparative study with 40 randomized patients. Sample size was calculated based on bibliographic reviews, for convenience, in patients who were attended to at the Department of Degenerative Pathologies of the Spine Group of the Hospital Santa Casa de Misericórdia de Vitória, from August of 2013 to August of 2015. The study was approved by the Research Ethics Committee under no. 009632/2013 and CAAE 12039813.3.0000.5065.

Through a careful selection, the sample comprised only of patients with degenerative pathologies who underwent arthrodesis of up to two lumbar levels (comprising the levels between L3-L4, L4-L5, and L5-S1), older than 18 years, who were attended to at the Department of Degenerative Pathologies of the Spine Group of the Hospital Santa Casa de Misericórdia de Vitória, in the aforementioned period, and who signed the informed consent. Patients with tumor pathologies and infections, surgical revisions, traumas, and those under 18 years of age were excluded.

A sheet with patient data included variables such as age, gender, diagnosis, participant group, level of surgery, and follow-up duration. The groups were divided in the preoperative period by a member of the orthopedic group who was not among the authors of the study, through a simple paper draw in which 40 cards were placed in a box, 20 labeled as group I and 20 as group II. In group I, patients received only autologous graft; in group II, they received autologous graft associated with PRP. After each draw, the card removed from the urn was discarded.

During surgery, the autologous graft was removed from the spinal process, laminae, and articular facets during decompression of the vertebral canal at the level in question. Subsequently, this graft was prepared in thin sections, leaving only cancellous bone. The graft was placed in the intertransverse space to finish the lumbar arthrodesis only with autologous graft.

For lumbar arthrodesis with autologous graft associated with PRP, in first place it was necessary to prepare the PRP: the patient's own blood was collected, followed by centrifugation and separation of the plasma. The patient's blood was placed in 3.6 mL vacuum tubes with ACD (citric acid, sodium citrate, and dextrose) anticoagulant. The material collected in the ACD tubes was centrifuged for platelet concentration, at a speed of 1800 rpm, for eight minutes. After centrifugation, the upper portion, about 80% plasma, was removed from the ACD tubes. This portion corresponds to the platelet-poor plasma (PPP). The remaining 20% corresponded to PRP; 0.5–1 mL of this PRP were collected above the buffy coat. For PRP activation, 10% calcium chloride was added at the rate of 0.1 mL for each 1 mL PRP to be used; the preparation was placed in a warm water bath for 15 min.¹¹ This concentrate was then added to the initial autologous graft and applied to the intertransverse space of the lumbar spine.

The postoperative evaluation of the consolidation was performed at three moments (one, three, and six months) by master surgeons and by radiologists specialized in musculoskeletal imaging who were not aware of the group to which the patient in question belonged. During the analysis of bone

Table 1 – Molinari radiographic classification.

Grade	Description
I	Bilateral fusion with presence of the trabeculae in the transverse process
II	Unilateral fusion, with difficulty to visualize the other side
III	Suspected radiolucency or defect in the fusion area
IV	Reabsorption of the graft with instrumentation fatigue

Table 2 – Glassman tomographic classification.

Grade	Description
I	Absence of fusion
II	Partial unilateral fusion
III	Partial bilateral fusion
IV	Solid unilateral fusion
V	Solid bilateral fusion

fusion in the lumbar spine, the sides were not evaluated separately, as there is no currently validated classification to compare them. In view of this, the criteria of the Molinari radiographic classification (Table 1) were used as standard.¹² A single postoperative tomographic evaluation was performed at six months, following the Glassman classification criteria (Table 2).¹²

A descriptive statistical analysis was performed, using mean and standard deviations for the variable of age. The chi-squared test was used to verify the association between the qualitative variables and the association of significance in the two groups. The level of significance was set at $p < 0.05$. Excel 2010 and SSPS v. 23 were used for data analysis.

Results

The study assessed 40 patients from August 2013 to August 2015. The mean age of the study population was 49.18 years \pm 10.02 (SD), with a predominance of females (65%). The inclusion diagnosis were hernia with instability ($n = 5$), spondylolisthesis ($n = 12$), and hernia with stenosis ($n = 23$).

Radiological findings

Based on the radiographs obtained in the first postoperative month, according to the Molinari criteria, in groups I and II the rate of bilateral fusion was 27.5% and 22.5%; of unilateral fusion, 12.5% and 10%; and of defects in the fusion area, 5% and 12.5%, respectively. The rate of graft resorption was 5% for both groups ($p = 0.660$; Table 3).

In groups I and II, in the third postoperative month, the rate of bilateral fusion was 20% and 25%; unilateral fusion, 17.5% and 7.5%; defects in the fusion area, 7.5% and 10%; and graft resorption, 5% and 7.5%, respectively ($p = 0.539$; Table 4).

In groups I and II, in the sixth postoperative month, the rate of bilateral fusion was 15% and 20%; unilateral fusion, 17.5% and 5%; defects in the fusion area, 12.5% and 17.5%; and graft resorption, 5% and 7.5%, respectively ($p = 0.308$; Table 5).

Table 3 – Classification of the lumbosacral radiograph on the first postoperative month.

	Group I	Group II	Total
Molinari – first month			
<i>Bilateral fusion</i>			
Number	11	9	20
% of the total	27.5%	22.5%	50.0%
<i>Unilateral fusion</i>			
Number	5	4	9
% of the total	12.5%	10.0%	22.5%
<i>Defect in the fusion area</i>			
Number	2	5	7
% of the total	5.0%	12.5%	17.5%
<i>Graft resorption</i>			
Number	2	2	4
% of the total	5.0%	5.0%	10.0%
Total			
Number	20	20	40
% of the total	50.0%	50.0%	100.0%

Source: The authors.

Table 4 – Classification of the lumbosacral radiograph on the third postoperative month.

	Group I	Group II	Total
Molinari – third month			
<i>Bilateral fusion</i>			
Number	8	10	18
% of the total	20.0%	25.0%	45.0%
<i>Unilateral fusion</i>			
Number	7	3	10
% of the total	17.5%	7.5%	25.0%
<i>Defect in the fusion area</i>			
Number	3	4	7
% of the total	7.5%	10.0%	17.5%
<i>Graft resorption</i>			
Number	2	3	5
% of the total	5.0%	7.5%	12.5%
Total			
Number	20	20	40
% of the total	50.0%	50.0%	100.0%

Source: The authors.

Table 5 – Classification of the lumbosacral radiograph on the sixth postoperative month.

	Group I	Group II	Total
Molinari – sixth month			
<i>Bilateral fusion</i>			
Number	6	8	14
% of the total	15.0%	20.0%	35.0%
<i>Unilateral fusion</i>			
Number	7	2	9
% of the total	17.5%	5.0%	22.5%
<i>Defect in the fusion area</i>			
Number	5	7	12
% of the total	12.5%	17.5%	30.0%
<i>Graft resorption</i>			
Number	2	3	5
% of the total	5.0%	7.5%	12.5%
Total			
Number	20	20	40
% of the total	50.0%	50.0%	100.0%

Source: The authors.

Table 6 – Classification of the lumbosacral computed tomography on the sixth postoperative month.

	Group I	Group II	Total
Glassman			
<i>Absence of fusion</i>			
Number	0	2	2
% of the total	0.0%	5.0%	5.0%
<i>Partial unilateral fusion</i>			
Number	3	2	5
% of the total	7.5%	5.0%	12.5%
<i>Partial bilateral fusion</i>			
Number	6	4	10
% of the total	15.0%	10.0%	25.0%
<i>Solid unilateral fusion</i>			
Number	5	8	13
% of the total	12.5%	20.0%	32.5%
<i>Solid bilateral fusion</i>			
Number	6	4	10
% of the total	15.0%	10.0%	25.0%
Total			
Number	20	20	40
% of the total	50.0%	50.0%	100.0%

Source: The authors.

Tomographic results

Based on the results of the computed tomography scans performed in the sixth postoperative month in groups I and II, according to Glassman criteria, the rate of absence of fusion was 0% and 5%; unilateral partial fusion, 7.5% and 5%; bilateral solid fusion, 15% and 10%; solid unilateral fusion, 12.5% and 20%; and solid bilateral fusion, 15% and 10%, respectively ($p = 0.499$; Table 6).

Discussion

The search for the development of techniques and materials that allow bone replacement is a necessity for orthopedic surgery. Bone fusion is of fundamental importance in the postoperative stabilization of spinal arthrodeses. Therefore, it is essential to use graft materials that favor bone neoformation that suffered vertebral segment osteotomy during surgery.²

Autologous bone is an ideal graft material due to three main properties: the presence of osteogenic cells, its osteoconductive structure, and its osteoinductive matrix. Autologous graft implies greater operative morbidity in order to obtain a small amount of graft. Hence the need to search for biomaterial options that favor bone fusion in arthrodeses.¹³ One option is HA, a porous synthetic bone that is used as a non immunogenic complementary graft of unlimited quantity; however, it only has osteoconductive properties. To overcome this limitation, a combination with an osteoinductive material, such as BMP, is recommended.¹⁴ Another option is the use of PRP, which is the most used source of growth factors in bone grafts; it provides two of the main growth factors involved in bone repair: PDGF and TGF β . The former acts in chemotaxis of macrophages

and fibroblasts, fibroblastic proliferation, angiogenesis, and fibroblast and osteoblast mitosis. The latter has a mitogenic action on fibroblasts, chondroblasts, and osteoblasts; it also has chemotaxis, collagen synthesis, and osteoblastic functions, and acts in the synthesis of other factors and in the differentiation of undifferentiated mesenchymal cells.¹⁵

Some studies have demonstrated the use of PRP for the treatment of other musculoskeletal diseases, describing the results in cartilage, bone, muscle, tendon, and ligament, although this aspect has not been widely documented in the literature.¹⁶

Lenza et al.,¹⁷ in a review study, demonstrated that autologous bone grafts combined with PRP showed positive results in accelerating bone healing in animal models.

Marx et al.¹⁸ observed promising results regarding bone formation in the treatment of mandibular defects. When PRP was used, radiographic bone maturation was 1.62–2.16 times faster. In the present study, no significant differences were observed in bone healing between the two groups in the first, third, and sixth postoperative months. It was observed that the use of PRP in lumbar arthrodeses did not present a significant difference in the tomographic evaluation in the sixth postoperative month. The six month postoperative follow-up did not harm the patients.

A great difficulty in evaluating the effectiveness of a bone substitute in promoting consolidation is the large number of variables present in the procedures in which the substitute was applied. There is some evidence that the more advanced the age of the patient, the more ineffective the consolidation process.⁸ However, in the present study, in which the mean age of group I was 48.7 years and of group II was 49.6 years, no significant differences were observed in the results of bone maturation. Osteoporosis is an important pathology that negatively influences this process; it is assessed through bone mineral density in women aged over 65 years and men over 70 years.¹⁹ As the mean age of the present study population was 49.18 years, this pathology was not investigated.

In light of the aforementioned results, it is noted that the true potential of this blood derivative still requires further studies and substantial trials prior to an indiscriminate application of PRP in lumbar arthrodesis.²⁰

Conclusion

Based on the present results, it was observed that the use of PRP did not present a significant difference in the bone consolidation process of lumbar arthrodeses. However, due to the true potential of this blood derivative, further studies are needed in order to draw better conclusions regarding its efficacy.

Conflicts of interest

The authors declare no conflicts of interest.

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