

NEW APPROACHES TO TREATMENT OF PATIENTS WITH COXOVERTEBRAL SYNDROME

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ABSTRACT.

The aim of the study was to develop an algorithm for choosing a rational tactics for surgical treatment of patients with coxo-vertebral syndrome. Material and methods. The study included 175 patients with coxo-vertebral syndrome who underwent total hip arthroplasty from 2009 to 2016. The results of surgical treatment were studied at an average time of 9 months. (from 8 to 10 months) after surgery in 134 patients. Their average age was 54.4 ± 12.7 years. The patients were divided into the main group (74 patients) and the comparison group (60 patients). In the comparison group, standard approaches to hip arthroplasty were used, implying restoration of the anatomical center of rotation and the length of the lower limb. The study group used the developed algorithm for choosing the optimal surgical tactics. Clinical and functional data were assessed using the Harris and Oswestry scales. Radiographic assessment was performed on radiographs of the spine-pelvic complex in a standing position, functional radiographs, CT and MRI. The significance of differences in the groups was assessed using the Mann-Whitney U-test and the McNemar test. Results. The use of the developed surgical approaches made it possible to increase the proportion of patients with good clinical and functional results (the main group - 82.4%, the comparison group - 26.7%) and to achieve higher indicators of the functioning of the hip joint and the quality of life of patients in the postoperative period. Excellent results on the Harris scale in the main group were obtained in 53.2% of patients, in the comparison group - in 9.7%. The proportion of patients with complaints of pain in the lumbar region, lameness and the need to use a cane, preserved after hip arthroplasty, was lower in the study group than in the comparison group.

Keywords: coxo-vertebral syndrome, hip arthroplasty, preoperative planning.

INTRODUCTION

The urgency of the problem of surgical treatment of patients with a combination of degenerative-dystrophic pathology of the hip joint (HJ) and the spine is beyond doubt [1, 10, 19]. It is determined by a significant proportion of such patients both among persons with a predominance of coxarthrosis phenomena (22–95%) and among patients with a prevalence of symptoms of lumbar osteochondrosis (10–15%), as well as a variety of clinical forms and degrees of severity of degenerative-dystrophic manifestations in the considered segments [2, 6, 11].

Until now, the subject of scientific discussions are the features of the pathogenesis of coxo-vertebral syndrome, which determine the tactics of treating patients of this profile. A number of researchers believe that the root cause of its development is the pathology of the spine, leading to the formation of coxarthrosis [14], while other authors describe the emergence and progression of osteochondrosis phenomena against the background of the existence of deforming arthrosis of the hip joint [19]. At the same time, most scientists agree on the dominant role in the development of coxo-vertebral syndrome of the spatial location of the pelvis [4, 12, 14].

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To date, no clear recommendations have been formulated on the surgical technique depending on the results of a comprehensive examination of the spine and pelvis [8], and the criteria for justified correction of relationships in these segments have not been determined. The choice and planning of hip arthroplasty, positioning of implants, as well as the degree of correction of the shortening of the lower limb is often based on the surgeon's personal experience and is carried out by highlighting one leading factor without taking into account the complex nature of biomechanical relationships in the spine-pelvic complex, the stage and manifestations of the disease, the degree of dysfunction, features of the morphology of degenerative-dystrophic diseases of the spine (DDS) and its compensatory capabilities.

The aim of the study is to improve the results of treatment of patients with coxo-vertebral syndrome by developing an algorithm for choosing a rational tactics of surgical treatment.

MATERIAL AND METHODS

The study included 175 patients (98 men and 77 women) who underwent total hip arthroplasty for combined degenerative-dystrophic pathology of one or two hip joints and lumbosacral spine with prevalence of grade III coxarthrosis. The criterion for inclusion in the study was the presence of pain in both the hip joint (s) and the lumbosacral spine. Exclusion criteria: pain syndrome caused only by the pathology of the spine; degenerative-dystrophic lesion of the hip joints without pain in the spine; all variants of dysplastic scoliosis and spondylolisthesis; Scheuermann's disease - Mau; spinal injury; any inflammatory diseases in the hip

joints and spine; tumors; dysplasia and anomalies in the development of the spine, which can cause its deformation or pain syndrome.

The patients were divided into two compared groups in accordance with the applied surgical tactics. In the comparison group formed by continuous selection (81 patients), standard approaches to hip arthroplasty were used, in the main group (94 patients) - the developed algorithm for choosing surgical tactics. In the comparison group, there were 49 males (60.5%), and 32 females (39.5%). A similar gender distribution was also typical for the main group - 49 men (52.1%) and 45 women (47.9%). The age of the subjects in the comparison group averaged 55.5 ± 12.5 (from 25 to 85) years, in the main group - 53.5 ± 12.6 (from 27 to 78) years.

The distribution of patients in the compared groups according to the etiology of deforming arthrosis also indicated their homogeneity.

The general condition of patients was assessed on the basis of data from clinical neurological and laboratory studies, and when studying the orthopedic status of patients with coxo-vertebral syndrome, a diagnostic algorithm was used, which also included methods of additional instrumental examination [8].

Particular attention was paid to the study of radiological parameters of the global sagittal and frontal balance of the trunk. In this case, the frontal parameters measured on the radiographs of the spinal pelvic complex in the standing position were the angle of the pelvic misalignment - pelvic obliquity (PO), scoliotic deformity of the lumbosacral spine - Cobb angle (CA) and the angle of misalignment of the sacrum relative to the pelvis - sacral obliquity (SO). The sagittal pelvic parameters were the pelvic incidence (PI); sacral slope - sacral slope (SS) and pelvic deviation - pelvic tilt (RT). Also, the pelvisacral angle (PA) was additionally measured; pelvic tilt - pelvic lordosis (PL) and sacrum position (L). Sagittal vertebral parameters: lumbar lordosis - global lumbar lordosis (GLL), measured by the Cobb method; the top of the lumbar lordosis - apex of lordosis (AL); upper arch of lumbar lordosis - upper arc of lordosis (UA); lower arch of lordosis - lower arc of lordosis (LA); the highest point of lumbar lordosis (the place of its transition to thoracic kyphosis) - inflection point (IP); as well as deviation of lumbar lordosis - lordosis tilt (LT).

Also, in order to assess the severity, localization and nature of changes in the lumbosacral spine, five parameters of degenerative changes were studied: osteophytes of the vertebral bodies, arthrosis of the facet joints, the height of the intervertebral foramen, the height and wedge shape of the intervertebral discs.

The height of the intervertebral disc in mm was determined by the formula:

$$H = (A+B+C)/3$$

The wedge shape of the intervertebral disc was calculated in mm using the formula:

$$W = C/A \times 100.$$

There were no statistically significant differences in the numerical characteristics of the considered parameters in the compared groups ($p > 0.05$), which also indicates the relevance of the samples.

A control study of patients was carried out on average 9 months (from 8 to 10 months) after hip arthroplasty. Communication with 41 patients was lost, as a result, the comparison group was 60 people, and the main group - 74. The study included a comprehensive clinical and X-ray examination, an assessment of the subjective satisfaction of patients with the treatment results, as well as an assessment of the function of the hip joint and the quality of life of patients according to the Harris and Oswestry questionnaires.

The results of clinical, neurological and X-ray examinations were compared between groups, the significance of differences in relative values in the related samples was assessed, and correlations between the initial parameters and the achieved treatment results within the compared groups were searched. Statistical processing of the results was carried out using the Statistica 8.0 software package.

When analyzing the data obtained, we solved such problems as describing the studied parameters in groups, checking the significance of the difference in quantitative and qualitative indicators in groups, assessing the relationship between indicators. During the study, the following procedures and methods of statistical analysis were used:

1. Estimation of the numerical characteristics of variables.
2. Testing the hypothesis about the significance of differences in quantitative indicators in independent samples using the Mann-Whitney U Test.
3. Testing the hypothesis about the significance of differences in quantitative indicators in related samples using the Wilcoxon Matched Pairs Test.
4. Testing the hypothesis about the significance of the difference in the relative frequency values in independent samples by the two-sided Fisher exact test, in linked samples - by the McNemar Chi-square test.
5. Assessment of the degree of influence of the qualitative factor on the variance of quantitative indicators using the ANOVA Kruskal-Wallis H-test dispersion rank method (with more than two groups).
6. Evaluation of the strength and direction of the relationship between quantitative characteristics was carried out using the Spearman Rank Order Correlation - r_s . Statistical data processing was carried out in accordance with the recommendations for processing the results of biomedical research [5, 9].

RESULTS

The analysis of the subjective assessment of patients in the comparison group of the outcomes of surgical treatment indicated the prevalence of satisfactory results - 28 (46.6%) patients; Harris scale - 71 ± 14 points, Oswestry scale - $21 \pm 20.6\%$. Sixteen (26.7%) patients rated the achieved results as good and another 16 (26.7%) - as unsatisfactory (Harris 82 ± 11 points, Oswestry $5.8 \pm 4.67\%$ and Harris 68 ± 19 points, Oswestry $22, 6 \pm 16.7\%$, respectively). A detailed study of

each clinical observation made it possible to determine six options for the prerequisites for the achievement of unsatisfactory outcomes of arthroplasty in patients with coxvertebral syndrome, associated with the peculiarities of their spinal-pelvic relationships:

- 1) diagnostic errors - 2 (3.3%) patients;
- 2) decompensation of DDS with its rigid deformity - 4 (6.6%);
- 3) decompensation of DDS with hypermobility of the spinal motion segments (VMS) - 4 (6.6%);
- 4) cranialization of the endoprosthesis cup in patients with non-rigid spinal deformity - 1 (1.7%);
- 5) lengthening of the lower limb in persons with rigid deformity of the spine - 4 (6.6%);
- 6) refusal to restore normal spinal-pelvic relationships in patients with dysplastic coxarthrosis with the ability of the spine to compensate - 1 (1.7%).

In addition to a detailed analysis of the reasons that led to the achievement of certain outcomes of surgical treatment in the comparison group, a correlation nonparametric analysis of the relationships between the results of hip replacement, assessed using the Harris and Oswestry questionnaires, with different baseline characteristics of patients was carried out. It was found that the achieved indicators had a correlation with the baseline levels of the functioning of the hip joint and the patient's quality of life, studied using the same scales ($r_s = 0.251$, $p = 0.05$ and $r_s = 0.537$, $p < 0.001$, respectively). A correlation was also revealed between the initial levels of the functioning of the hip joint (Harris scale) and the patient's quality of life (Oswestry questionnaire) and the increase in these indicators, assessed as the difference between their final and initial values and reflecting the degree of improvement of the considered parameters as a result of surgical treatment ($r_s = -0.479$, $p < 0.001$ and $r_s = -0.659$, $p < 0.001$, respectively).

A statistically significant effect of the duration of pain in it on the outcome of hip arthroplasty and a statistically significant trend towards the dependence of the achieved results on the duration of pain in the lumbar region ($r_s = -0.269$, $p = 0.039$ and $r_s = -0.254$, $p = 0.05$, respectively). Another parameter that influenced the outcome of surgical treatment of patients was the height of the intervertebral disc in the L5-S1 segment ($r_s = -0.645$, $p = 0.032$). The revealed correlation meant an improvement in the quality of life according to the Oswestry questionnaire with higher values of the height of the intervertebral disc of the spinal motion segment under consideration.

Prognostically unfavorable were such clinical signs as Trendelenburg gait, positive straightened leg elevation test (STL), pain on palpation of spinous processes and paravertebral zones, neuropathy, and inability to use public transport ($p < 0.05$).

There was no statistically significant effect of the etiology of coxarthrosis, as well as the severity and nature of degenerative-dystrophic changes in the

lumbosacral spinal motion segments (except for the height of the intervertebral disc L5-S1) on the outcome of treatment.

The analysis of the outcomes of surgical treatment of patients in the comparison group, as well as the study of the prerequisites for the achievement of certain results made it possible to develop an algorithm for choosing a rational tactics for surgical treatment of patients with combined degenerative-dystrophic pathology of the hip joint and spine and to conduct its clinical testing in treatment patients of the main group. The developed algorithm assumes an assessment of the compensatory capabilities of the spine of patients with coxo-vertebral syndrome, carried out using a complex of clinical neurological and additional techniques [8], the results of which determine further surgical tactics.

In case of prevalence in the clinical picture of DDSD phenomena with signs of progressive neurological deficit, patients are referred for consultation with an orthopedic vertebrologist (neurosurgeon). If conservative treatment is ineffective in such patients, the first stage should be decompression or decompression-stabilizing surgery on the spine, and the second - hip arthroplasty.

If the manifestations of coxarthrosis dominate in patients with non-rigid deformity of the spine and the preservation of its compensatory capabilities, it is advisable to perform standard hip arthroplasty with restoration of the anatomical center of rotation, the length of the lower limb and offset as the first stage. In patients with a prevalence of pathology of the hip joint and pronounced manifestations of osteochondrosis with rigid, usually long-term deformity of the spine and the absence of compensation opportunities from the latter, it is advisable to perform arthroplasty, which allows maintaining the existing "usual" spinal-pelvic relationships. For this, depending on the specific type of static deformity of the spine-pelvic complex [8], it is permissible to use such techniques as implantation of the acetabular component above the anatomical center of rotation, lengthening of the lower limb, as well as shortening osteotomy of the femur (with old complete dislocation of the hip).

If the patient has a competing pathology of the hip joint and spine (grade III coxarthrosis in combination with DDS, accompanied by neurological deficit, segmental hypermobility, vertebrogenic pain syndrome), the first step is to perform hip arthroplasty with restoration of the anatomical center of rotation and length of the lower limb. It is advisable to perform decompression or decompression-stabilization surgery on the spine as the second stage. When planning the latter, the sagittal pelvic parameters achieved as a result of hip arthroplasty should be taken into account. To calculate the magnitude of lumbar lordosis (Global Lumbar Lordosis - GLL), the formulas $GLL = PI + 9^\circ$, $GLL = 0.5 \times PI + 27^\circ$ and $GLL = SS + 15^\circ (\pm 1.2^\circ)$ can be used [15, eighteen].

The effectiveness of the proposed algorithm for choosing a rational surgical tactics was confirmed by comparing the results of treatment of patients in the compared groups, obtained during a follow-up examination after an average of 9

months. after arthroplasty. Analysis of the distribution of patients with subjective manifestations of the pathology under consideration confirmed statistically significant intergroup differences in the number of observations with pain in the area of the operated hip joint and in the lumbar region, as well as with complaints of lameness and the need to use a cane in the main group ($p < 0.01$). The proportion of patients experiencing pain in the lumbar region from intense to moderate was significantly higher in the comparison group than in the main group - 42 (70%) and 25 (33.8%) clinical observations, respectively ($p < 0.001$). No significant differences in the frequency of occurrence of patients with limited movement in the lumbar region and a sensation of shortening or lengthening of the lower limb were found in the compared groups ($p > 0.05$).

At the control clinical examination, 100% of the patients of the compared groups were absent or insignificantly expressed (mainly the rotational component) contracture of the hip joint, the symptoms of Fabere, Thomas and Trendelenburg were negative. Also, none of the clinical observations revealed Trendelenburg gait. All patients in both groups were able to independently climb stairs and were able to use public transport.

The results of the control neurological examination of the patients of the groups under consideration indicated a lower frequency of occurrence of the studied symptoms in the patients of the main group. Thus, the proportion of patients who noted pain on palpation of the spinous processes of the lumbar vertebrae and paravertebral zones in the main group was five times lower than in the comparison group - 4 (5.4%) and 16 (26.7%), respectively ($p < 0.001$). Four times less often than in the comparison group, among the patients of the main group, there was a positive PVI test - 4 (5.4%) and 13 (21.7%), respectively ($p < 0.001$) and radicular syndrome - 3 (4.1%) and 11 (18.3%), respectively ($p = 0.006$).

The results of a comparative assessment of pain, deformity, as well as the achieved functions and range of motion in the hip joint in patients of the compared groups invited to the clinic for a control examination, analyzed using the Harris questionnaire, testified to the prevalence of the best outcomes in the main group. The average value of the parameter under consideration was 82 ± 16 points, while the same result for the control group was 76 ± 16 points ($p = 0.052$).

When studying the achieved quality of life according to the Oswestry questionnaire, the patients of the main group showed greater satisfaction with the results of surgical treatment, which was manifested by relatively low average indicators (the higher the results, the worse the quality of life): 7.6% in the main group and 13.0% in the group comparisons.

The analysis of the subjective assessment of the achieved results of surgical treatment indicates that the number of patients satisfied with the outcome was 74 (100%) in the main group, and 44 (73.3%) in the comparison group. The distribution of patients in the compared groups according to the achieved results

was as follows. Among the patients of the main group, good results were achieved in 61 clinical observations (82.4%), and satisfactory - in 13 (17.6%). There were no unsatisfactory outcomes in the study group. In the comparison group, the number of good and unsatisfactory results was equal - 16 patients each (26.7%), while there were 28 patients with satisfactory surgical treatment outcomes (46.6%).

DISCUSSION

Comparative results of primary and control X-ray examination of the spine-pelvic complex in patients of the comparison group revealed statistically significant differences in such X-ray parameters as pelvic deviation (PT) ($p = 0.019$), pelvic misalignment (PO) and scoliotic deformity (SA) ($p < 0.001$). The data obtained indicate that, as a result of total hip arthroplasty, in most clinical cases, it was possible to restore the frontal vertebral-pelvic balance.

Comparative analysis of the results of the primary and control X-ray examinations in the main group also revealed statistically significant ($p < 0.05$) differences in the values of frontal X-ray parameters: pelvic misalignment (PO), sacral misalignment (SO), and scoliotic deformity (SA). At the same time, the assessment of the significance of the differences in most of the sagittal spine-pelvic parameters measured in this group before the operation and during the follow-up examination made it possible to reveal statistically significant differences in the values of the pelvic inclination (PL) ($p < 0.001$) and sacrum (SS) ($p = 0.006$), as well as the lower arch of the lumbar lordosis (LA) ($p = 0.006$). The data obtained demonstrate changes in the sagittal spinal-pelvic relationships achieved as a result of hip arthroplasty, leading to the restoration of the sagittal spinal-pelvic balance in patients with excessive compensatory lumbar lordosis by reducing the anteversion of the pelvis and the magnitude of the lumbar lordosis. A detailed analysis of these changes, carried out in each patient subjected to a control examination, indicated their dependence on the severity of degenerative-dystrophic manifestations in the lumbosacral spinal motion segments and the mobility of the spine in question.

CONCLUSIONS

In our opinion, all examined patients with a combination of degenerative-dystrophic pathology of the hip joint and spine after hip arthroplasty should be classified as a risk group due to the possibility of obtaining unsatisfactory results of surgical treatment due to DDSD decompensation. This coincides with the data of G.I. Herzen with co-authors and V.M. Vakulenko et al, describing the potential for aggravation of the patient's condition after arthroplasty of the hip joint due to the progression of symptoms of damage to the spinal motion segments [1, 2]. In our study, a negative effect on the state of the spine occurred during decompensation of its pathology associated with a change in the "usual" spatial orientation of the pelvis in elderly patients with long-standing rigid static deformity of the lumbosacral spine, as well as in those with signs of hypermobility of the SMS.

The reason for the diagnostic errors in patients with coxo-vertebral syndrome is the lack of due attention to the interpretation of the clinical and neurological picture, as well as the refusal of additional examination of the spine, including X-ray of the spine-pelvic complex in a standing position, functional radiography, as well as CT and MRI.

Thus, a comprehensive analysis of indicators, including a subjective assessment, the results of the use of specialized questionnaires, as well as the clinical and neurological characteristics of patients after hip arthroplasty indicate the prevalence of good treatment outcomes in patients after the use of the developed algorithm for choosing a rational tactics for surgical treatment of patients with combined degenerative - dystrophic lesions of the hip joint and spine.

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REFERENCES

1. Vakulenko V.M., Khudobin V.U., Bublik L.A. Degenerative-dystrophic lesions of the hip joints and spine. // *Travma [Trauma]*. 2000;1(1):24-26 (in Russian).
2. Gertzen G.I., Dibkaluk S.V., Ostapchuk N.P. Treatment of degenerative disease of the spinal segment at lumbar-hip syndrome. // *Litopys travmatolohiyi ta ortopediyi [Chronicle of Traumatology and Orthopedics]*. 2003;(1/2):75-78 (in Russian).
3. Denisov A.O., Shilnikov V.A., Burns S.A. // Hip-spine syndrome and its significance in hip arthroplasty (review). *Travmatologiya i ortopediya Rossii [Traumatology and Orthopedics of Russia]*. 2012;(1):121-127 (in Russian).
4. Prodan A.I., Radchenko V.A., Hvisyuk A.N., Kutsenko V.A. Laws of formation of the vertical posture and spinal parameters of sagittal pelvic balance in patients with chronic sciatica and lumbago. // *Khirurgiya pozvonochnika [Surgery of Spine]*. 2006;(4):61-69 (in Russian).
5. Rebrova O.U. Statistical analysis of medical data. Application software package Statistica. // M. : MediaSphera; 2003. 312 p. (in Russian).
6. R.M. Tikhilov, V.M. Shapovalov. Hip arthroplasty guide // St. Petersburg, 2008. 324 p. (in Russian).
7. Sazonova N.V., Shchrova E.N. Influence of complex conservative therapy on the dynamics of the intensity of pain in hip-spine syndrome. // *Khirurgiya pozvonochnika [Surgery of Spine]*. 2008;(3):48-51 (in Russian).
8. K hominets V.V., Kudyashev A.L., Shapovalov V.M., Miroevski F.V. Modern approaches to diagnostics of combined degenerative-dystrophic pathology of hip joint and spine. // *Travmatologiya i ortopediya Rossii [Traumatology and Orthopedics of Russia]*. 2014; (4):16-26 (in Russian).
9. Unkerov V.I., Grigorjev S.G., Rezvancev M.V. Mathematical and statistical processing of data for medical research. // SPb. : MMA; 2011. 318 p. (in Russian).
10. Ben-Galim P., Ben-Galim T., Rand N. et al. Hip-spine syndrome: the effect of total hip replacement surgery on low back pain in severe osteoarthritis of the hip. // *Spine (Phila Pa 1976)*. 2007;32(19): 2099-2102.
11. Burns S.A., Burshteyn M., Mintken P.E. Sign of the buttock following total hip arthroplasty. // *J Orthop Sports Phys Ther*. 2010;40(6):377.
12. Doring J., Goudfrooij H., Keessen W. et al. Toward standards for posture. Postural characteristics of the lower back system in normal and pathologic conditions. // *Spine (Phila Pa 1976)*. 1985;10(1):83-87.
13. Abdullaeva U.K., Shadjanova N.S. Using the OLGA system in chronic atrophic gastritis // *New day in medicine, № 2 (30) 2020, Bukhara, Uzbekistan, P. 9-12.*

14. Abdullaeva U.K., Sobirova G.N., Karimov M.M., Aslonova I.J. The prevalence and possibilities of prevention of noncardial gastric cancer in the Bukhara region // American journal of medicine and medical sciences, 2020, 10(9), P. 679-681.
15. Sobirova G.N., Abdullaeva U.K., Nosirova M.S., Aslonova I.J. Evaluation of the gastrointestinal mucosa by the OLGAsystem in chronic atrophic gastritis // Journal of critical reviews, Kuala Lumpur, Malaysia, Vol. 7, Iss. 2, 2020, P. 409-413.
16. Karimov M.M., Sobirova G.N., Abdullaeva U.K., Aslonova I.Zh., Tulyaganova F.M. Possibilities of serological diagnosis of atrophic processes of the gastric mucosa // European Journal of Molecular & Clinical Medicine Vol. 7, Iss. 11, 2020, P. 2955-2960.
17. Sobirova G.N., Abdullaeva U.K., Mirzaeva D.B., Ismitdinova N.S. Immunopatogenesis of chronic gastritis and its role in carcino genesis // ACADEMICIA An international multidisciplinary research journal, affiliated to Kurukshetra university, Kurukshetra, India. Vol.8, Iss.12, 2018, P. 32-40.
18. Abdullaeva U.K. Predicting the risk of atrophic transformation in chronic gastritis using serum pepsinogen // World journal of pharmaceutical research, Faculty of Pharmacy Medical University, Bulgaria, Vol. 8, Iss. 13, 2019, P. 219-228.
19. Sobirova G.N., Abdullaeva U.K. Chronic gastritis and carcinogenesis issues // electronic journal of actual problems of modern science, education and training, Urganch, Uzbekistan, 2019-I, P. 159-172.