

## Mid-Term Outcomes of Primary Hip Replacement in Patients with End-Stage Chronic Renal Disease


A.N. Tsed, A.K. Dulaev, N.E. Mushtin, K.G. Iliushchenko, A.V. Shmelev


*Pavlov First Saint Petersburg State Medical University,  
St. Petersburg, Russian Federation*

### Abstract

**Purpose** – to evaluate mid-term outcomes of primary hip replacement in patients with end-stage chronic renal disease and to develop an algorithm for selection of surgical tactics and perioperative treatment. **Materials and Methods.** The authors evaluated outcomes of primary hip replacement in 45 patients receiving renal substitution therapy and 47 patients without chronic renal disease. Patients with end-stage chronic renal disease (CRD) were divided into two groups: group I included 30 (66.6%) patients receiving chronic hemodialysis (CH) and group II included 15 (33.4%) patients after renal transplantation (RT). Group III of 47 (51.1%) patients without any signs of CRD who underwent hip arthroplasty within relevant period of time was established to evaluate the effectiveness of primary hip replacement. Blood serum  $Ca^{2+}$  and  $P^{5+}$  levels as well as levels of parathyroid hormone (PTH) and 1.25-dihydroxyvitamin D were measured to determine the rate of calcium- phosphoric metabolism disturbance. Multi-spiral CT scans of hip joint were performed to identify bone mineral density and the mean Hounsfield (HU) value was calculated for which the data was obtained from five various points on the proximal femur and acetabulum. Beta-2 microglobulin (B2M) blood test was performed to confirm amyloid bone disease. **Results.** The authors did not observe statistically significant differences for arthroplasty outcomes in patients of group II and III. Patients receiving long-term hemodialysis demonstrated significantly lower parameters of Harris score and Barthel's index of social adaptation after hip replacement as compared to groups II and III: patients of group I demonstrated outcomes improvement at 19.55%, in group II – at 13.03%, in group III – at 10.15% as compared to preoperative status. Decrease of 1.25-dihydroxyvitamin D below 20,0 mcg results in resorption of cancellous bone in proximal femur and acetabulum along with myopathy of gluteus muscles. Sharp increase of parathyroid hormone level (over 600 pcg/ml) was accompanied by inhibition of osteoblasts proliferation and differentiation resulting in substantial impairment of mineralization. **Conclusion.** According to the algorithm suggested by the authors the key parameters that need to be evaluated in preoperative period are parathyroid hormone (PTH) and 1.25-dihydroxyvitamin D. Five-fold increase of PTH (>600 pcg/ml) demands parathyroidectomy as the first stage of treatment to decrease risk of early aseptic loosening of hip prosthesis and development of periprosthetic fracture.

**Keywords:** hip replacement, hemodialysis, chronic renal disease, vitamin D.

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 *Aleksandr N. Tsed*; e-mail: [tsed@mail.ru](mailto:tsed@mail.ru)

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## Background

Chronic renal disease (CRD) and especially its end-stage with lifelong hemodialysis results in changes of bone tissue morphology (renal osteodystrophy, osteofibrous dysplasia, amyloid bone disease) [1, 2, 3]. Renal transplantation unfortunately doesn't provide significant improvement in bone quality while stipulates lengthy immunosuppressive and hormone medication. Decreased mineral bone density and para-articular pathological alterations lead to increased risk for femoral neck fracture [4, 5] and to degenerative changes in the hip joint [6, 7, 8]. Total hip replacement in patients with end-stage CRD is a complex task, first of all due to many complications (deep periprosthetic infections, periprosthetic fractures, dislocations, etc) [9, 10, 11], as well as low bone quality (osteomalacia, osteopenia, renal osteodystrophy resulting from accumulation of uremic toxins [12], all of above, in turn, extend average hospital stay [13]. Many studies report high bleeding risk and high postoperative mortality [14, 15, 16]. At the same time, there is also a high risk of complications in patients after renal transplantation [17, 18].

Literature demonstrates insufficient coverage of primary hip replacement issues for patients with end-stage CRD and no perioperative management algorithms for such pathology are proposed.

**Purpose** — to evaluate mid-term outcomes of primary hip replacement in pa-

tients with end-stage CRD and to develop an algorithm for selection of surgical tactics and perioperative management.

## Material and Methods

The authors evaluated outcomes of primary hip replacement in 45 patients receiving renal substitution therapy and 47 patients without chronic renal disease in the period from 2014 till 2018.

Research inclusion criteria: osteoarthritis, femoral neck necrosis of various etiology, pathological changes in the proximal femur and acetabulum of degenerative-dystrophic and trauma origin along with renal osteodystrophy or amyloid bone disease in cases of chronic hemodialysis and in cases of renal transplantation. Research exclusion criteria: local or systemic infection in postoperative period, concomitant diseases of cardiovascular, respiratory and central nervous system at decompensation stage, as well as mental disorders.

There were 52 (56.5%) female patients and 40 (43.5%) male patients. Mean age was 67 (55; 75) years. Patients with end-stage CRD were divided into two groups: group I included 30 (66.6%) patients receiving chronic hemodialysis (HD), group II — 15 (33,4%) patients after renal transplantation (RT). Group III consisting of 47 (51.1%) patients without any signs of CRD who underwent hip arthroplasty within relevant period of time was established to evaluate the effectiveness of primary hip replacement (Table 1).

Table 1

### Grouping of patients, key statistical parameters

Research group	Gender		Age (25,75 percentiles)	Bed-day	Type of fixation	
	M	F			Cemented	Uncemented
Group I (HD) <i>n</i> = 30	13 (43%)	17 (57%)	58.5 (1,1)	19.5 (0,4)	19 (63%)	11 (37%)
Group II (RT) <i>n</i> = 15	8 (53%)	7 (47%)	40.0 (49.3; 44.5)	11,0 (12.0; 11.0)	9 (60%)	6 (40%)
Group III (no CRD) <i>n</i> = 47	19 (40%)	28 (60%)	74.3 (0,7)	12,0 (11.0; 13.0)	26 (55%)	21 (45%)
<i>P</i> — variance between groups	$P_{1-2}, P_{1-3}, P_{2-3} > 0.017$		$P_{1-2}, P_{1-3}, P_{2-3} < 0.017$	$P_{1-2}, P_{1-3} < 0.017;$ $P_{2-3} > 0.017$	$P_{1-2}, P_{1-3}, P_{2-3} > 0.017$	

HD — hemodialysis; RT — renal transplantation; CRD — chronic renal disease.

To obtain comparable results the authors performed a mid-term (from 1 to 4 years follow up) representative sampling based on etiological attribute of the main diagnosis (primary arthroplasty after deep infection in hip joint were excluded), based on quality of bone mineral composition (patients in the group III of the study were of elderly age with osteoporosis signs), as well as based on type of prosthesis fixation (only cemented implants, or hybrid fixation prostheses were used).

Preoperatively the authors evaluated laboratory and instrumental parameters of changes in osteoarticular system of patients in all study groups. Blood serum  $Ca^{2+}$  and  $P^{5+}$  levels as well as parathyroid hormone (PTH) and 1.25-dihydroxyvitamin D were measured to determine the rate of calcium-phosphoric metabolism disturbance. Mean parameters of total calcium and phosphorus in blood serum of patients receiving chronic hemodi-

alysis were measured based on average value of three tests: prior and after hemodialysis according to dialysis record and on the day between dialyses at the stage of preparing for surgery.

Multi-spiral CT scans of hip joint were performed to identify changes in the bone mineral density and then the mean Hounsfield (HU) value was calculated, for which data was obtained from five various points on the proximal femur and acetabulum (greater and lesser trochanter, anterior and postero-superior aspects of acetabulum, femoral intramedullary cavity in the metaphysical area). To confirm amyloidosis of osteoarticular system the authors performed  $\beta$ -2 microglobulin (B2M) blood test while in patients with long history of hemodialysis; this protein is accumulated in the body and deposits on meta-epiphyseal area of joints and on myofibrils. Hemoglobin and hematocrit were measured to evaluate anemia of patients (Table 2).

Table 2

**Results of laboratory and instrumental preoperative examinations**

Criteria	Group I (HD) (25,75 percentiles)	Group II (RT) (25,75 percentiles)	Group III (no CRD) (25,75 percentiles)	P – variance between groups
Ca <sup>2+</sup> (serum) N: 2,3–2,8 mmol/l	1.6 (1.5; 1.7)	2.1 (1.5; 2.2)	2.4 (2.3; 2.4)	$P_{1-2}, P_{1-3}, P_{2-3} < 0.017$
P <sup>5+</sup> (serum) N: 0,7–1,6 mmol/l	2.8 (2.6; 3.0)	1.95 (0.03)	1.5 (1.5; 1.5)	$P_{1-2}, P_{1-3}, P_{2-3} < 0.017$
Hb (hemoglobin) N: 120–160 g/l	101.5 (0.8)	123.0 (101.3; 126.5)	129.0 (126.5; 131.5)	$P_{1-2}, P_{1-3}, P_{2-3} < 0.017$
Ht (hematocrit) N: 0,361–0,443	0.305 (0.004)	0.375 (0.009)	0.403 (0.007)	$P_{1-2}, P_{1-3} < 0.017;$ $P_{2-3} > 0.017$
$\beta$ -2-microglobulin macroglobulin N: 1,0–2,4 mg/l	18.2 (0.1)	9.8 (0.2)	2.1 (2,1; 2.2)	$P_{1-2}, P_{1-3}, P_{2-3} < 0.017$
HU (Hounsfield index) N: 30–230 HU for cancellous bone	19.1 (17.9; 21.9)	49.1 (0.9)	47.0 (42.0; 49.0)	$P_{1-2}, P_{1-3}, P_{2-3} < 0.017$
1,25(OH)2D (vitamin D <sub>3</sub> ) N: 20–40 mcg	14.7 (12.9; 26.2)	36.7 (0.9)	63.5 (0.4)	$P_{1-2}, P_{1-3}, P_{2-3} < 0.017$
PTH (parathyroid hormone) N: 9,5–117 pcg/ml	608.5 (324.3; 638.8)	317.3 (12.7)	72.0 (65.5; 78.5)	$P_{1-2}, P_{1-3}, P_{2-3} < 0.017$

As one can see from the table over the patients receiving substitution renal therapy demonstrated significant anemia in preoperative period which required additional preparation for replacement [20, 21]. Comparison of data for patients after renal transplantation and patients without CRD did not reveal statistical differences in preoperative level of blood hematocrit. Preoperative chronic anemia in patients receiving HD is related to the deficit of erythropoietin produced by kidneys [22].

The authors observed an interesting fact when comparing bone mineral density using Hounsfield index. This parameter was reported at the lower limit of the norm (47.5 (43.3; 49.0) HU) in patients without CRD and after renal transplantation which was related to senile osteoporosis in patients of group III (especially in women), and in patients of group II was related to the mechanism of development of renal osteodystrophy and secondary hyperparathyroidism which evolves in several years after surgery despite renal transplantation. In patients receiving chronic HD the mean Hounsfield index value was within range from -80 up to +30HU which is characteristic for adipose and pulmonary tissues.

Some other parameters in patients of groups II and III demonstrated statistically significant differences, however, the parameters started to return to normal which was considered by the authors as the recovery after substitution therapy.

Pathological femoral neck fractures and their consequences, like atrophic pseudoarthrosis, prevailed — 14 (46.6%) cases — in the diagnosis structure used to identify indications for hip joint replacement in patients receiving chronic hemodialysis. Avascular necrosis of femoral neck and manifestations in form of secondary coxarthrosis were observed more often in groups II and III — 40 (64.5%) cases. Femoral neck fractures were less observed in patients without CRD (group III) and in patients after RT (group II) — 10 (16,1%) cases overall (Table 3). Diagnosis of osteoarticular  $\beta$ -2 microglobulin amyloidosis which was not the reason for primary hip joint replacement was reported only in patients of groups I and II.

All surgeries were performed by the same surgical and anesthesiology teams from Harding approach with patient positioned in lateral decubitus on healthy side. In the majority of cases the spinal-epidural anesthesia was used, excluding patients receiving chronic HD who needed insertion of a central venous catheter and, in cases of intraoperative complications, the authors had to switch to endotracheal anesthesia with pulmonary ventilation.

### *Statistical analysis*

Descriptive statistics was used for the measured values of the mean value and the error of the arithmetic mean consistent with the normal. Shapiro-Wilk test was used to

*Table 3*

### **Структура предоперационных диагнозов в группах исследования**

Diagnosis	Group I (HD), n = 30	Group II (RT), n = 15	Group III (no CRD), n = 47
Dysplastic hip arthritis	2	0	7
Protrusion hip arthritis	8	1	4
Idiopathic hip arthritis	1	6	16
Femoral head avascular necrosis	5	7	11
Femoral neck medial fracture	5	1	5
Femoral neck pseudoarthrosis	9	0	4

Hip arthritis due to  $\beta$ -2-amyloidosis was in 17 patients of group I, in 5 patients of II group, in group III it was not found.

verify normality. In case the random distribution was not consistent with normal, median was recorded with 25 and 76 percentiles. Testing of hypothesis for differences or effects was made by Student's criterion (and its varying dispersion model in case such were identified by Fisher criterion) in case of normal compared distributions or Mann-Whitney U test in other cases. Testing of hypothesis for dependent samples was made by paired Student's test for normal samples and paired Wilcoxon test for others. Descriptive statistics for qualitative data was represented by the presence share of each attribute in the group. Groups' comparison was performed using Fisher's exact test. In all cases of testing hypotheses between the three groups, the critical level of significance, taking into account the Bonferroni adjustment, was taken as equal to 0.017.

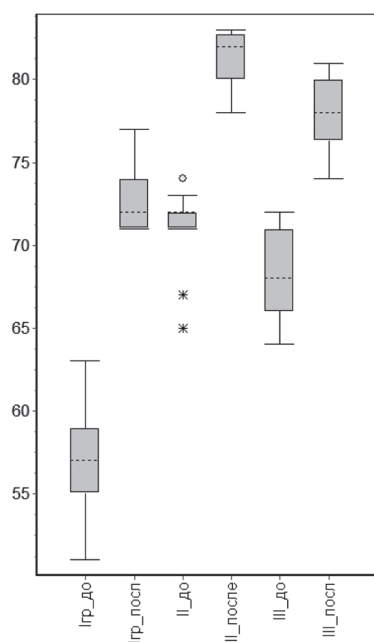
Spearman's rank correlation coefficient  $r_s$  was applied to find relationship between quantitative values while in the present work the values were not consistent with normal distribution.

Statistical calculations were made using Statistica 5.0 (Statsoft, USA) and Cytel Studio 8 (Cytel, USA).

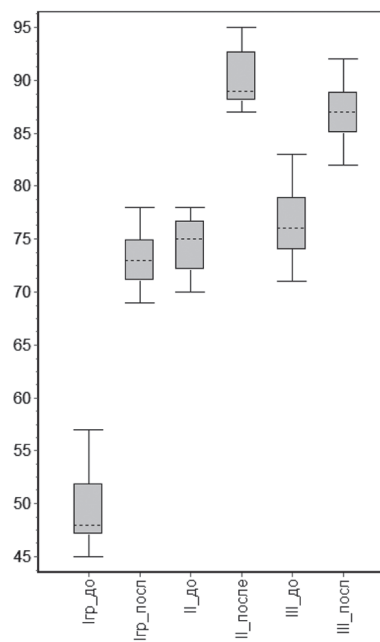
## Results

The authors evaluated results not earlier than in one year after primary hip replacement. First of all functional status on Harris score, social adaptation and independence by Barthel's score were evaluated. Multi-spiral CTs were made to identify changes in the structure of bone mineral density around acetabular and femoral components and Hounsfield index was measured in dynamics. Blood tests were used to monitor changes in calcium-phosphorous metabolism, anemia severity,  $D_3$  vitamin deficit. The authors assessed complications rate and structure after primary hip replacement especially in patients with end-stage CRD.

Figures 1 and 2 demonstrate functional outcomes according to Harris and Barthel scores. There is no statistically significant variances in outcomes for patients of groups II and III. However, patients with lengthy



**Fig. 1.** Functional assessment on Harris score in preoperative period and in one year after hip replacement



**Fig. 2.** Social adaptation score on Barthel index prior to surgery and in one year after hip replacement



hemodialysis demonstrated significantly worse functional parameters on Harris score and social adaptation on Barthel's index after hip replacement as compared to patients in groups II and III. It should be noted that in patients with chronic hemodialysis the preoperative Harris scores and Barthel's index were initially lower as compared to patients after renal transplantation and patients without CRD. Thus, the authors calculated improvement of parameters in percentage within each group and did not record statistically significant differences between the groups. In group I parameters improved at 19.55%; in group III — at 10.15% as compared to preoperative status. It can be concluded that the major effectiveness of surgical treatment was achieved in patients with chronic hemodialysis. The authors obtained satisfactory and good outcomes in all groups as compared to preoperative status.

Considering changes in calcium-phosphorous metabolism and reduced mineral density of bone tissues in all examined patients in preoperative period, the authors prescribed high dose of oral active vitamin D<sub>3</sub> (400 IU/day) to all patients postoperatively up to 6 months. In cases when preoperative parathyroid hormone exceeded mean age norm 5–7 times the patients underwent par-

athyroidectomy to normalize calcium and phosphorous blood content and to terminate renal osteodystrophy.

The authors examined complications rate and structure after primary hip replacement in patients of all three groups as well as revision rate depending on complication features (Table 4).

Majority of complications were observed in group I — patients on chronic HD (66.7%). The most frequent complication in this group was intraoperative bleeding (23.3%) related to specifics of hemodialysis procedure with administering of high doses of anticoagulants. It should be noted that three patients demonstrated several various complications during one hospital stay. Five (16.6%) of 30 patients in group I required revision surgery of varying complexity depending on complication pattern. Patients after renal transplantation demonstrated the best outcomes in terms of complications rate as well as revision rate. Such fact is most likely related to small patient sample (only 15 patients). Besides, normalization of calcium-phosphorous metabolism and increased bone mineral density after renal transplantation significantly contributed to successful outcome of primary hip replacement.

Таблица 4

**Structure of complications after primary hip replacement in research groups**

Complication	Group I (HD), n = 30		Group II (RT), n = 15		Group III (no CRD), n = 47	
	Number of cases	Number of revisions	Number of cases	Number of revisions	Number of cases	Number of revisions
Dislocation	3 (10%)	2 (6.6%)	0	0	1 (2.1%)	0
Periprosthetic fracture	5 (16.7%)	1 (3.3%)	0	0	3 (6.3%)	1 (2.1%)
Early aseptic loosening	1 (3.3%)	1 (3.3%)	0	0	1 (2.1%)	1 (2.1%)
Superficial infection	0	0	1 (6.7%)	0	1 (2.1%)	0
Deep periprosthetic infection	2 (6.6%)	1 (3.3%)	0	0	0	0
Bleeding	7 (23.3%)	0	0	0	0	0
Lethal outcome	2 (6.6%)	0	0	0	0	0
Total	20 (66.7%)	5 (16.7%)	1 (6.7%)	0 (0.0%)	6 (12.8%)	2 (4.3%)

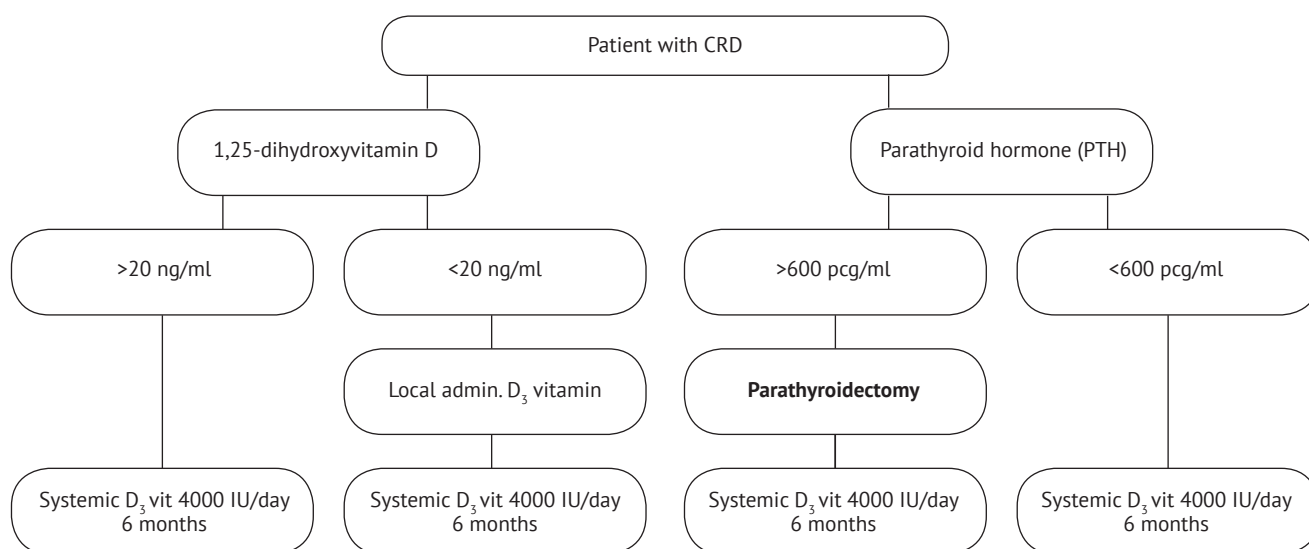
The authors report 2 (6.6%) cases of mortality in patients with chronic HD in one year postoperatively. Causes of lethal outcomes were not related to surgery on the hip joint.

Thorough analysis, especially in group I, revealed negative correlation ( $r_s = -0.75$ ,  $p < 0.001$ ) between preoperative vitamin D<sub>3</sub> values in blood serum and level of parathyroid hormone (PTH): decrease of vitamin D<sub>3</sub> in proximal femur. In such circumstances the risk of periprosthetic fracture significantly increases and stability of component fixation significantly reduces. Thus, according to the authors, relative risk of complications (RR) with vitamin D<sub>3</sub> deficiency and increased parathormone in patients on hemodialysis, compared with patients who do not have kidney disease, is 5.2 times higher (the lower limit of 95% CI – 2.372, the upper limit of 95% CI – 11.495, sensitivity of the method – 0.769, specificity – 0.804).

With a decrease in 1.25-dihydroxyvitamin D values less than 30.0 ng/ml (lower limit of the norm) result in cancellous resorption in

proximal femur and acetabulum as well as in myopathy of gluteus muscles manifested by thinned myofibrils and decreased elasticity of muscular fibers. Simultaneously with such pathological processes in cases of sharp increase of PTH (>600 pcg/ml) the authors observed inhibition of osteoblasts proliferation and differentiation, finally resulting in substantial impairment of bone mineralization in proximal femur. In such circumstances the risk of periprosthetic fracture significantly increases and stability of component fixation significantly reduces. Thus, according to the authors, relative risk of complications with vitamin D<sub>3</sub> deficit and increased PTH in patients with chronic hemodialysis is higher at 5,2 times (lower limit 95% CI – 2.372, upper limit 95% CI – 11.495) as compared to patients without renal disorders.

Based on the performed study the authors developed an algorithm of primary hip replacement as well as perioperative management for patients with chronic hemodialysis (Fig. 3).



**Fig. 3.** Algorithm of perioperative management of patients on long-term hemodialysis

According to the algorithm the key parameter that needs to be evaluated in preoperative period is parathyroid hormone (PTH) and 1.25-dihydroxyvitamin D. Five-fold increase of PTH (>600 pcg/ml) demands parathyroidectomy as the first stage of treatment to decrease risk of early aseptic loosening of hip prosthesis (irrespective of fixation type) and development of periprosthetic fracture. 20 ng/ml was taken as the minimal threshold value of D<sub>3</sub> vitamin. At decrease of D<sub>3</sub> values up to the minimal value and below bone and muscular tissues demonstrate resorption that also increases the risk of postoperative complications. Patients receiving long-term hemodialysis with low values of D<sub>3</sub> vitamin in blood serum and high values of PTH demonstrated the best outcomes of hip replacement in cases of cemented implants fixation. However, in cases of normal laboratory values of D<sub>3</sub> vitamin, PTH, calcium, phosphorous and β-2 microglobulin uncemented fixation of acetabular component is feasible.

The authors suggest local administration of oral active form D<sub>3</sub> vitamin for 6 months postoperatively in patients receiving chronic hemodialysis (patent of Russian Federation 2672370). The method features intraoperative introduction into cancellous bone of alphacalcidol solution at a concentration of 50:1 as well as supplementary ultraviolet irradiation of surgical wound including bone, muscles, fascia, subcutaneous fat and skin during 2 minutes prior to prosthesis insertion. Such method allows to decrease rate of such complications like periprosthetic fractures and early aseptic loosening.

Long-term oral administration of active D<sub>3</sub> vitamin (cholecalciferol) in a dose of 4000 IU/day (corresponding to 2.5 mcg or 10 drops of watery solution) in postoperative period (up to 6 months) is a key part of suggested algorithm irrespectively of preoperative values of PTH and 1.25-dihydroxyvitamin D.

## Discussion

There are few publications in literature dedicated to hip joint replacement in patients with end-stage of chronic renal disease. This fact is related to big number of unsatisfactory outcomes irrespectively of used implants, their fixation methods, patients' compliance, surgeon's skills or hospital equipment. K.E. Ponnusamy et al and P.K. Cavanaugh et al report large multicenter studies on results of hip and knee joints replacement (overall 41242 patients in two studies) in patients with end-stage of CRD [10, 11]. Obtained outcomes were compared to the hip and knee joint replacement outcomes in 978378 patients of general population. Mean hospital stay was twice longer in patients with hemodialysis. Number of blood transfusions was significantly higher ( $p < 0.0001$ ) among patients with end-stage of CRD (43.65%) as compared to patients in general population (26.48%). Infectious complications were observed four times more often and hospital mortality reached 8.96% for patients with hemodialysis. The authors report 6.6% mortality in the present study (2 patients from group I receiving chronic hemodialysis), mean hospital stay — 19.5 bed/day.

J.R. Lieberman et al in their work report overall rate of various complications after primary hip replacement as 8%, and revision rate related to aseptic loosening and infection as 19% [9].

Russian national literature has publications on primary hip arthroplasty in patients with chronic hemodialysis and authors report 7.4% revision rate related to dislocations and aseptic loosening of acetabular components [23]. The authors of the present study observed 5 (16.7%) orthopedic complications resulting in revisions.

In cases of secondary hyperparathyroidism parathyroidectomy prior to arthroplasty decreases the risk of components



migration, periprosthetic fractures and improved bone mineral density. L. Rolighed et al report significant improvement of BMD values of the forearm, spine and proximal femur in 2.5 year after parathyroidectomy [24]. H.W. Chan reports that in his study 13 patients with hemodialysis who underwent total parathyroidectomy due to secondary hyperparathyroidism and none of 13 patients demonstrated bone fractures within mean follow up of 37.7 months [25]. In the present study the authors calculated relative risk of complications with 95% confidence interval in cases of increased PTH and decreased D3 in blood serum. Thus, in patients with chronic hemodialysis the relative risk of postoperative complications was 5.2%.

In the present study the outcomes of primary arthroplasty in patients with chronic hemodialysis (group I) on Harris score and Barthel's index were significantly worse as compared to patients after renal transplantation and patients without CRD but with osteoporosis. However, the overall percentage of improvement for such parameters in dynamics and compared to preoperative stage was higher in patients of group I. Primary hip replacement in patients after renal transplantation has no specifics and in mid-term perspective shows no differences as compared to outcomes in patients without CRD but with senile osteoporosis.

Further study of the outcomes of primary and revision hip replacement in patients with end-stage CRD is needed to elaborate new algorithms of perioperative management for such patients to decrease complications rate, minimize lethal outcomes and decrease hospital stay.

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#### Authors' contribution

*A.N. Tsed* — design of research, collection and processing of the data, literature review and writing the paper, staged and final editing of the paper.

*A.K. Dulaev* — analysis of study results, approval of final version of the paper.

*N.E. Mushtin* — statistical processing of the data, approval of the final version of the paper.

*K.G. Ilyushchenko* — literature review.

*A.V. Shmelev* — literature review.

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#### INFORMATION ABOUT AUTHORS:

*Alexander N. Tsed* — Cand. Sci. (Med.), assistant professor, the head of Department of Traumatology and Orthopedics, Research Institute of Surgery and Emergency Medicine, Pavlov First St. Petersburg State Medical University, St. Petersburg, Russian Federation

*Alexander K. Dulaev* — Dr. Sci. (Med.), professor, the head of Department of Traumatology and Orthopedics, Research Institute of Surgery and Emergency Medicine, Pavlov First St. Petersburg State Medical University, St. Petersburg, Russian Federation

*Nikita E. Mushtin* — lecturer, Department of Traumatology and Orthopedics; orthopedic surgeon, Research Institute of Surgery and Emergency Medicine, Pavlov First St. Petersburg State Medical University, St. Petersburg, Russian Federation

*Konstantin G. Iliushchenko* — orthopedic surgeon, Department of Traumatology and Orthopedics, Research Institute of Surgery and Emergency Medicine, Pavlov First St. Petersburg State Medical University, St. Petersburg, Russian Federation

*Anton V. Shmelev* — orthopedic surgeon, Department of Traumatology and Orthopedics, Research Institute of Surgery and Emergency Medicine, Pavlov First St. Petersburg State Medical University, St. Petersburg, Russian Federation