



Comparative analysis of clinical and instrumental study of the results of using standard and modified stromal-vascular fractions in the treatment of patients with chondromalacia patellae

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Abstract

Introduction Chondromalacia patellae is a leading cause of anterior knee pain and is considered an early form of degenerative patellofemoral cartilage disease. The limited regenerative potential of the hyaline cartilage and the variable effectiveness of conservative treatments motivate the search for biological technologies capable of providing structure-modifying effects. A promising approach is the use of autologous stromal vascular fraction (SVF) of adipose tissue that has anti-inflammatory and regenerative potential.

The **purpose** of the work is to conduct a comparative assessment of clinical and instrumental studies of the results of standard and modified SVF therapy technologies in the treatment of patients with chondromalacia patella.

Materials and Methods A non-randomized, retrospective, multicenter cohort study was performed. It included 41 patients with Outerbridge grades I–III chondromalacia patellae. Patients were divided into two groups according to treatment protocol provided: standard SVF ($n = 20$) and modified SVF ($n = 21$). Assessments were performed before treatment and after one, six, and 12 months. VAS, KOOS-PS, and quantitative parameters of cartilage defect based on MRI data (linear dimensions, area, volume) were analyzed. Differences were considered statistically significant at $p < 0.05$.

Results In both groups, a significant reduction in pain and improvement in function were noted after 12 months ($p < 0.001$). In the standard SVF group, the defect area decreased by 27.4 % and volume by 44.6 %; in the modified SVF group, by 40.2 % and 53.8 %, respectively ($p < 0.001$). Intergroup comparison revealed a more pronounced decrease in defect width with the modified technique ($p = 0.007$). One month after treatment, the modified SVF group showed a more pronounced reduction in pain and improvement in function ($p < 0.01$), while the differences leveled out at six and 12 months.

Discussion The modified SVF therapy technique resulted in earlier pain reduction and improved function compared to the standard technique. These differences leveled over the long term, confirming the high efficacy of SVF therapy regardless of the protocol variant. Comparable morphological results based on MRI data indicate that the structural effect was maintained with the modified technique. Limitations of the study include the non-randomized design and a moderate sample size.

Conclusion SVF therapy demonstrates significant clinical and structural benefits in chondromalacia patellae. The modified technology provides a more rapid onset of clinical effect with comparable long-term morphological changes based on MRI data, suggesting it as a promising option for optimizing cell therapy.

Keywords: stromal-vascular fraction, chondromalacia, adipose tissue, mesenchymal stromal cells

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INTRODUCTION

Chondromalacia patellae is traditionally considered an early form of degenerative articular cartilage disease of the patellofemoral joint and one of the leading causes of pain in the anterior knee joint [1, 2]. Modern concepts have evolved from an isolated mechanical concept to an understanding of the multifactorial nature of the disease, including biomechanical disturbances, changes in the intra-articular environment, and molecular mechanisms of matrix degradation [3–5]. Impaired patellar tracking, imbalances in muscle control, and changes in lower limb kinematics lead to increased contact stresses in the patellofemoral joint and the progression of cartilaginous damage [6, 7]. At the molecular level, chronic overload initiates a cascade of inflammatory-degenerative reactions accompanied by the activation of proinflammatory cytokines (IL-1, TNF- α), disruption of TGF- β /BMP signaling pathways and the formation of a phenotype of hypertrophied and senescent chondrocytes [8–9]. Low-intensity chronic inflammation is considered a key mediator of the progression of degenerative changes in the cartilage [10, 11]. Given the limited regenerative potential of hyaline cartilage [12], traditional conservative approaches, including exercise therapy and load modification, demonstrate variable effectiveness and do not have a proven structure-modifying effect [13, 14].

Surgical methods of cartilage restoration (microfracture, autologous chondrocyte implantation, osteochondral grafting) can provide clinical improvement; however, they are characterized by invasiveness, limited indications, and variability in long-term results [15–19]. The limitations of both conservative and surgical treatment methods have led to an active search for biological approaches aimed not only at relieving symptoms but also at modifying the intra-articular microenvironment and stimulating reparative processes. In recent years, the use of cell technologies, in particular mesenchymal stromal cells (MSCs) and stromal vascular fraction (SVF) of adipose tissue, has attracted considerable interest. Adipose tissue is considered an available and rich source of regenerative cells [20, 21]. SVF contains mesenchymal stromal cells, pericytes, endothelial and immunomodulatory elements, which provide a pronounced paracrine and immunoregulatory effect [22, 23]. Experimental data indicate the ability of these cells to reduce inflammatory activity and stimulate cartilage tissue remodeling processes [24].

Clinical studies demonstrate pain reduction and improved function following intra-articular administration of autologous adipose-derived cell products [25–27]. Reviews and analyses of clinical trials confirm the potential of SVF and adipose-derived mesenchymal cells in knee osteoarthritis; however, they point to significant heterogeneity in study designs, cell product production methods, and administration regimens, highlighting the need for protocol standardization [28–30].

Despite growing data on the use of SVF for degenerative cartilage lesions, comparative studies of its effectiveness in chondromalacia patellae remain limited. The impact of cell product preparation on the clinical effect and severity of post-injection synovial reactions has also been insufficiently studied. Therefore, a comparative evaluation of the results of standard and modified SVF therapy is relevant.

The **purpose** of the work is to conduct a comparative assessment of clinical and instrumental studies of the results of standard and modified SVF therapy technologies in the treatment of patients with chondromalacia patella.

MATERIALS AND METHODS

A non-randomized, retrospective, multicenter cohort study was conducted. It included 41 patients with chondromalacia patellae who underwent treatment in 2021–2024 at Medsi Group of Companies (Moscow) and the Ilizarov National Medical Research Center of Traumatology and Orthopedics (Kurgan). The study

was conducted in accordance with the ethical principles set forth in the World Medical Association's Declaration of Helsinki (2013 edition and subsequent amendments) and with the requirements of Good Clinical Practice (GCP) and the Rules of Clinical Practice in the Russian Federation, approved by Order of the Ministry of Health of Russia dated April 1, 2016, No. 200n. All study participants signed informed consent to participate and publish anonymized findings obtained during the study.

The sample was selected based on predefined inclusion and exclusion criteria. The study included patients aged 25 to 80 years with clinically significant anterior knee pain lasting more than three months and its severity greater than 40 mm on the visual analog scale (VAS), along with chondromalacia patellae grades I–III according to the Outerbridge classification, confirmed by magnetic resonance imaging. A mandatory inclusion condition was the absence of a clinically significant effect from previous conservative therapy lasting at least three months, including kinesitherapy, nonsteroidal anti-inflammatory drugs, chondroprotectors, and/or intra-articular hyaluronic acid injections.

The study did not include patients with grade IV chondromalacia, clinically significant axial deformities of the lower limb (varus, valgus, patella alta), active systemic inflammatory diseases (rheumatoid arthritis, seronegative spondyloarthropathies, systemic connective tissue diseases), a history of infectious lesions of the knee joint, severe somatic pathology (decompensated diabetes mellitus, chronic heart failure of functional class III–IV, oncological diseases), as well as with clinically significant abnormalities of laboratory parameters. Also excluded were patients who received intra-articular injections of biological preparations (PRP, SVF, BMAC) or hyaluronic acid less than six months before the study, individuals with hemostatic disorders, history of anticoagulant therapy, a body mass index of more than 35 kg/m², women during pregnancy and lactation. Occasional use of NSAIDs was allowed before enrollment in the study in the absence of systematic anti-inflammatory therapy. This minimized the impact of systemic diseases and concomitant medications on clinical outcomes.

All patients were divided into two groups based on the orthobiological treatment method used. Group I ($n = 20$) included patients who underwent a single intra-articular injection of SVF obtained mechanically using the standard ACT technology recommended by the manufacturer SOLOPHARM. Group II ($n = 21$) included patients treated using a modified protocol for mechanical SVF production [31]. Hyaluronic acid preparations were not used for 12 months after the procedure in any group.

The patients' average age was 45.4 ± 11.7 years, ranging from 27 to 73 years. The distribution of gender, age, body mass index (BMI), and chondromalacia severity did not differ significantly between the groups, allowing the study cohorts to be considered comparable and allowing for valid intergroup comparative analysis. Detailed patient characteristics are presented in Table 1.

Table 1

Patients' data

Parameter		SVF standard ($n = 20$)		SVF modified ($n = 21$)	
		n	%	n	%
Age, years	(M $\pm$ SD)	$47,2 \pm 11,3$		$43,8 \pm 11,8$	
	18–44	10	50,0	11	52,4
	45–59	7	35,0	8	38,1
	60–74	3	15,0	2	9,5
Gender	Males	14	70,0	12	57,1
	Females	6	30,0	9	42,9
BMI, kg/m ²	Norm (18.5–24.9)	7	35,0	5	23,8
	High (25.0–29.9)	9	45,0	12	57,1
	Obesity grade I (30.0–34.9)	4	20,0	4	19,0
Chondromalacia severity (Outerbridge)	Grade I	1	5,0	3	14,3
	Grade II	10	50,0	11	52,4
	Grade III	9	45,0	7	33,3

Clinical effect assessments were conducted before treatment and after one, six, and 12 months of follow-up. Pain was assessed using a visual analogue scale (VAS). Knee joint function was analyzed using the KOOS-PS score. Patients completed all questionnaires independently under physician supervision.

The instrumental evaluation included magnetic resonance imaging of the knee joint, performed before treatment and 12 months after the intervention using systems with a magnetic field strength of 1.5 T and 3.0 T. In every patient, the initial and follow-up examinations were performed with the same system using an identical scanning protocol, which ensured comparability of the obtained data. The thickness of the articular cartilage in the areas of interest, defect location (medial facet, lateral facet, interfacet groove), linear dimensions of the lesion (width, height, depth) as well as the area (mm²) and volume (mm³) of the defect were analyzed. MRI signs of synovial reaction were additionally taken into account. For the intergroup analysis, the magnitude of the change in the indicator (Δ) was calculated, defined as the difference between the values after treatment and the baseline data.

Statistical data processing was performed using the R software environment (version 3.2.4). Statistical analysis was performed using standard methods of variation statistics. The normality of the distribution of quantitative indicators was preliminarily assessed using the appropriate criteria. If normal distribution was confirmed, the intragroup dynamics of quantitative parameters were analyzed using the paired Student's t-test for dependent samples. To assess the intragroup dynamics of indicators obtained from clinical scales (VAS, KOOS), the Friedman criterion was used. Intergroup comparison of independent samples was performed using the Mann-Whitney U-test. Differences were considered statistically significant at $p < 0.05$. The results are presented as the mean and standard deviation ($M \pm SD$) or the median and interquartile range ($Me [Q1-Q3]$).

RESULTS

In the standard SVF therapy group, a statistically significant reduction in chondral defect size ($p < 0.001$) was recorded after 12 months of follow-up. The lesion area decreased by an average of 27.4 %, and its volume by 44.6 % compared to baseline. The changes reflect moderate structural reorganization of the damaged area and the development of reparative processes in the cartilage tissue. These results demonstrate the structurally beneficial effect of standard SVF therapy, manifested in a significant reduction in defect size and stabilization of the degenerative process (Table 2).

Table 2

MRI dynamics of cartilage defect parameters according to MRI data

Parameter	SVF standard ($n = 20$)					SVF modified ($n = 21$)				
	Before therapy	After therapy	Δ (after-before)	t	Before therapy	After therapy	Δ (after-before)	Δ (after-before)	t	p
Defect width, mm	6,78 $\pm$ 2,61	5,84 $\pm$ 2,52	-0,95 $\pm$ 0,52	8,14	< 0,001	6,85 $\pm$ 3,31	5,19 $\pm$ 2,48	-1,65 $\pm$ 1,10	6,86	< 0,001
Defect height, mm	7,03 $\pm$ 2,17	5,81 $\pm$ 2,11	-1,22 $\pm$ 0,76	7,22	< 0,001	6,97 $\pm$ 4,18	5,54 $\pm$ 3,30	-1,43 $\pm$ 0,95	6,87	< 0,001
Defect depth, mm	1,96 $\pm$ 0,52	1,46 $\pm$ 0,40	-0,50 $\pm$ 0,29	7,56	< 0,001	2,66 $\pm$ 0,94	2,05 $\pm$ 0,88	-0,61 $\pm$ 0,46	6,06	< 0,001
Defect area, mm ²	50,32 $\pm$ 30,52	36,53 $\pm$ 25,39	-13,79 $\pm$ 8,62	7,15	< 0,001	50,11 $\pm$ 37,73	29,97 $\pm$ 20,59	-20,14 $\pm$ 17,84	5,17	< 0,001
Defect volume, mm ³	105,28 $\pm$ 91,90	58,36 $\pm$ 56,02	-46,92 $\pm$ 41,82	5,02	< 0,001	123,65 $\pm$ 96,03	57,16 $\pm$ 52,15	-66,48 $\pm$ 51,49	5,92	< 0,001

Analysis of the linear and volumetric parameters of the patellar chondral defect in the modified SVF therapy group demonstrated a statistically significant reduction in all studied parameters 12 months after the procedure ($p < 0.001$) (Table 2). The defect area decreased by 40.2 % on average and its volume by 53.8 % from the baseline values. These results indicate significant structural reorganization of the damaged area and the development of beneficial morphological dynamics in the patellofemoral joint.

In the standard SVF therapy group, pain relief was progressive and sustained. The most pronounced change according to VAS was noted by the sixth month of observation, with the achieved level being maintained by the 12th month. The obtained data indicate the formation of a stable analgesic effect, increasing over time and reaching its maximum expression in the late period. Statistical analysis confirmed the reliability of changes over time (Friedman criterion: $\chi^2(3) = 58.13$; $p < 0.001$) (Table 3). The dynamics of functional indicators according to the KOOS-PS scale corresponded to the reduction in pain: the most pronounced improvement was noted by the sixth month, with the achieved level being maintained by the 12th month of observation. Statistical analysis confirmed the reliability of changes over time (Friedman criterion: $\chi^2(3) = 59.71$; $p < 0.001$) (Table 3). The findings indicate a persistent functional improvement after SVF therapy, which is consistent with the positive MRI dynamics of morphological changes.

In the modified SVF therapy group, pain relief was noted as early as one month after the intervention. The VAS score showed early and significant improvement, with further reduction by the sixth month and maintenance of the achieved level by the 12th month of follow-up. Statistical analysis confirmed the significance of changes over time (Friedman criterion: $\chi^2(3) = 57.75$; $p < 0.001$) (Table 3). The obtained data indicate a rapid analgesic effect, followed by stabilization and long-term maintenance of the clinical result. The dynamics of functional indicators according to the KOOS-PS scale were also early: improvement was recorded as early as one month and by the sixth month reached a level comparable to the results of the standard SVF therapy group, with the achieved values maintained by the 12th month of follow-up. Statistical analysis confirmed the significance of changes over time (Friedman criterion: $\chi^2(3) = 61.32$; $p < 0.001$) (Table 3). The obtained data indicate the rapid formation and stable maintenance of functional improvement, which corresponds to the positive MRI dynamics of morphological changes.

Table 3

Dynamics of questionnaire findings

Term	Шкала ВАШ						Шкала KOOS-PS					
	SVF standard ($n = 20$)			SVF modified ($n = 21$)			SVF standard ($n = 20$)			SVF modified ($n = 21$)		
	median	Q1–Q3	min–max	median	Q1–Q3	min–max	median	Q1–Q3	min–max	median	Q1–Q3	min–max
Baseline	6,0	4,5–7,5	3–9	6,0	5,0–7,0	2–9	11,0	7,0–15,3	3–26	11,0	4,0–15,0	3–26
1 month	5,0	4,0–6,5	2–8	3,0	2,0–5,0	1–6	9,5	5,0–13,3	3–24	5,0	2,0–11,0	1–16
6 months	3,0	1,0–4,5	1–6	2,0	1,0–3,0	1–5	3,5	2,0–9,0	1–15	2,0	1,0–7,0	0–12
12 months	1,0	1,0–1,0	1–2	1,0	1,0–2,0	1–2	1,0	0–2,0	0–10	1,0	1,0–2,0	0–10

Intergroup comparison

In an intergroup comparison of the dynamics of the linear and volumetric parameters of the defect, a significant advantage of the modified technique over the standard technique was revealed in terms of decreasing the defect width ($p < 0.05$). No statistically significant differences were found for other parameters ($p > 0.05$) (Table 4).

Table 4

Comparative dynamics of chondral defect MRI parameters

Parameter	SVF standard Δ	SVF modified Δ	p
	Me (Q1–Q3)		
Defect width, mm	0.98 (0.46–1.29)	1.42 (1.18–1.66)	0.007
Defect height, mm	1.14 (0.54–1.91)	1.14 (0.92–1.54)	0.629
Defect depth, mm	0.44 (0.25–0.72)	0.36 (0.30–0.92)	0.705
Defect area, mm ²	12.54 (7.10–16.41)	15.99 (5.78–16.90)	0.540
Defect volume, mm ³	33.49 (24.43–61.15)	37.22 (19.33–114.69)	0.382

An intergroup analysis of pain dynamics using the VAS scale revealed differences in the time to clinical effect depending on the technique used. The modified SVF therapy group demonstrated a more pronounced reduction in pain one month after the procedure compared to standard SVF therapy ($p < 0.01$). At longer follow-up periods (six and 12 months), no statistically significant differences were found between the groups ($p > 0.05$) (Fig. 1).

Intergroup analysis of the KOOS-PS score demonstrated a similar pattern: the use of modified SVF therapy was associated with earlier functional improvement compared with standard SVF therapy. Statistically significant differences in the dynamics of KOOS-PS indicators were detected one month after treatment ($p < 0.01$). At six and 12 months, the differences between the groups did not reach the level of statistical significance ($p > 0.05$) (Fig. 2).

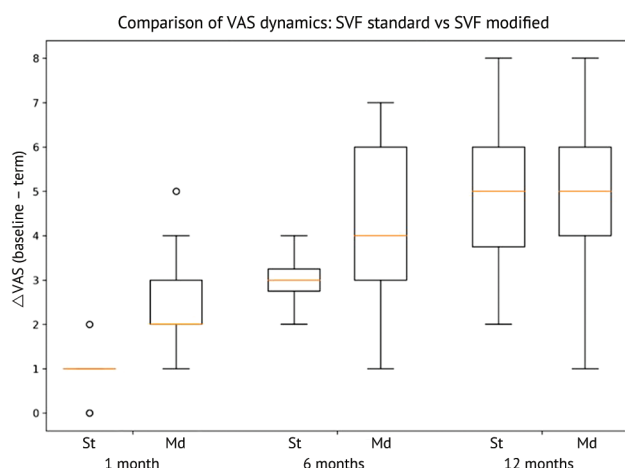


Fig. 1 Intergroup comparison of VAS score

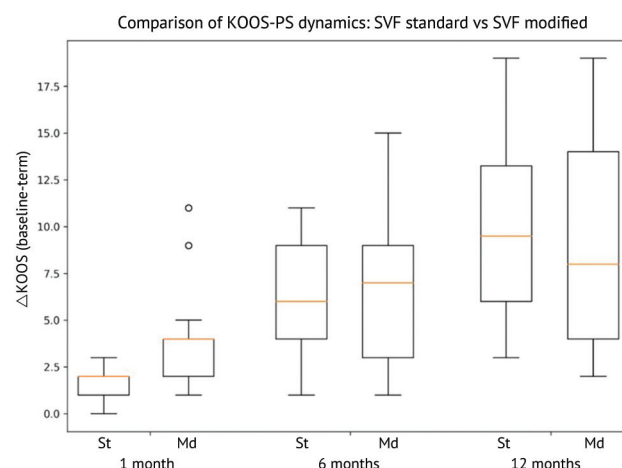


Fig. 2 Intergroup comparison of KOOS-PS

DISCUSSION

The analysis revealed that the use of modified SVF therapy provides a faster onset of clinical effect compared to the standard technique. Already during the first month of observation, we noted a significantly more pronounced relief of pain and an earlier improvement in functional indicators. This dynamics has important clinical significance, as it allows patients to quickly return to physical activity, including targeted programs to strengthen the muscles of the lower extremities, which helps to stabilize the achieved result. In addition, faster pain relief and a milder course of the early post-injection period increase the tolerability of the procedure and create a higher level of confidence in the therapy.

Despite the identified early benefit of the modified technique, pain scores on the VAS and KOOS-PS functional scales were comparable in both groups in the long-term period (6–12 months), confirming the overall high efficacy of SVF therapy regardless of the cell substrate treatment method. The absence of significant intergroup differences in the morphological parameters of the defect,

as measured by MRI, also indicates the preservation of regenerative potential with the modified technique. These data suggest that the protocol modification is primarily aimed at optimizing cell composition and procedure tolerability, without reducing cell viability or diminishing the structure-modifying effect of the therapy.

The results of the present study are consistent with the data of a number of clinical studies devoted to the use of stromal-vascular fraction and micro-fragmented adipose tissue in degenerative lesions of the knee joint. Thus, in the study of Yokota et al., the reduction in pain syndrome according to the VAS scale after six months in the SVF group was 44.0 % [32], whereas in our study, by this time, pain relieved more than 50 % with a further increase in the effect with a longer follow-up. A similar trend in dynamics was shown by Bisicchia et al., where the use of micro-fragmented SVF in combination with microfragmentation led to a decrease in VAS to (2.6 ± 1.8) points after 12 months [33]. In our study, at 12 month, the median VAS score decreased from 6 to 1 point in both SVF groups and reflected a pronounced analgesic effect of cell therapy. Similar results were obtained by Hudetz et al.: pain relief by movement was approximately 56–57 %, and at rest up to 85 % by the 12th month [34], which is comparable with the 80–85 % pain reduction in our study. In the work of Onoi et al., after a single administration of ADRCs, a 75–80 % pain reduction by the sixth month and an improvement in KOOS scores were also noted [35]. The findings of Michalek et al. confirm the sustainability of the effect of SVF therapy: pain reduction reached 65–70 % by the 12th month and was maintained up to 36 months of observation [36]. Finally, Russo et al. demonstrated a median pain reduction of 40–50 % and an improvement in KOOS of 30–35 % after 12 months [37], which also confirms the pronounced clinical and functional effectiveness of adipose cell therapy.

Taken together, these data indicate the reproducibility of the analgesic and functional effects of SVF therapy, with pain reduction rates obtained in our study being in a range comparable to or greater than the results published.

Limitations of the study include the non-randomized nature of patient allocation and the moderate sample size. However, the standardized treatment protocol and comparability of the groups minimize the influence of potential systematic factors.

CONCLUSION

The study demonstrated the high clinical and structural efficacy of SVF therapy in the treatment of chondromalacia patellae. Both groups showed a significant relief in pain, significant functional improvement, and a statistically significant reduction in the linear and volumetric parameters of the chondral defect, as measured by quantitative MRI analysis, confirming the structurally beneficial effect of cell therapy.

The modified SVF technology provided a more rapid onset of clinical effect with comparable structural changes according to MRI data in the long-term period, which indicates the preservation of the regenerative potential of the cell substrate with the optimization of its preparation protocol.

The obtained data allow us to consider SVF therapy as an effective biological method for correcting degenerative changes in the patellofemoral joint, and the modified technology as an option that ensures accelerated formation of a clinical response while maintaining structural effectiveness.

Conflict of interests None.

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Informed consent All study participants signed informed consent to participate and publish anonymized data obtained during the study.

Information on the use of generative artificial intelligence Artificial intelligence was used for checking spelling and grammar editing.

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