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Evaluation of clinical efficacy of ultrasound-guided joint injection of hypertonic glucose combined with blood flow restriction training in the treatment of rotator cuff injury

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► ***Original article***

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#These are co-first authors. They contributed to the work equally.

ABSTRACT

Background: Rotator cuff injuries are common musculoskeletal conditions that impair shoulder function and quality of life. Conventional therapies often fail to address the biological and mechanical deficiencies of these injuries. This study evaluated the clinical efficacy of ultrasound-guided hypertonic glucose injections combined with blood flow restriction (BFR) training in managing rotator cuff injuries. ***Materials and Methods:*** A randomized controlled trial involving 120 patients with rotator cuff injuries was conducted. Participants were assigned to an experimental group (ultrasound-guided glucose injections with BFR training, n=60) or a control group (standard physical therapy, n=60). Pain, shoulder function, tendon thickness, range of motion (ROM), muscle strength, and patient-reported outcomes were assessed over 12 weeks using ultrasound imaging and validated scales (visual analog scale (VAS), Constant–Murley score (CMS), shoulder disability index (SDI), and American Shoulder and Elbow Surgeons (ASES) score). ***Results:*** The experimental group showed significant improvements compared to the control group, including reduced pain (VAS: -3.0, $p<0.001$), enhanced function (CMS: +29.5, $p<0.001$), increased ROM (+25°, $p<0.001$), decreased tendon thickness (-1.7 mm, $p<0.001$), and improved muscle strength (+2.8 kg, $p<0.001$). Patient-reported satisfaction and functionality (ASES: +33.4, $p<0.001$) were also higher in the experimental group. ***Conclusion:*** The combination of hypertonic glucose injections and BFR training is an effective approach for treating rotator cuff injuries. It provides significant pain relief, functional recovery, and structural improvements, which highlight its potential as a better alternative to conventional treatments. Further research is recommended to assess the long-term efficacy and refine the treatment protocols.

INTRODUCTION

Rotator cuff injuries are some of the most common musculoskeletal conditions and are commonly observed in painters, athletes, construction workers, and other people involved in heavy overhead activities, as well as individuals with degenerative changes in the shoulder tendon [1-3]. The injuries are caused by mechanical overloading, microdamage, and biological aging [4]. Insulin resistance and hormonal and metabolic disorders, including diabetes and thyroid disorders, have been implicated in the development of rotator cuff injuries [5]. Rotator cuff injuries affect the quality of life of individuals and represent a significant economic burden worldwide [6-7]. Additionally, these injuries are expected to increase because of aging populations and higher rates of sports activities and recreational exercise [8].

Non-surgical treatments for the disease include physical therapy, non-steroidal anti-inflammatory drugs, and corticosteroid injections, but for some patients, regenerative and biomechanical treatment options at an early stage can lead to better prognosis [5-9]. Recent imaging technologies, including ultrasonography and magnetic resonance imaging (MRI), have helped in the early diagnosis of tendon injuries and to locate the exact point of injury, allowing earlier treatment [10]. Moreover, new treatment modalities such as PRP injection, stem cell therapy, and rehabilitative approaches in combination are being investigated to improve the healing ability of tendons and functional outcomes [11]. Personalized medicine principles according to patient and injury profiles have the capacity to transform the treatment of rotator cuff injuries to optimize and individualize outcomes [12-15].

Rotator cuff pathology is a clinical syndrome that includes a range of tendon abnormalities such as tendon tears, tendinopathy, and concurrent muscle

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atrophy. These injuries result from mechanical stress on the tendon, hypoxia, and inflammation of the of tendon structures. Furthermore, vascularity and inflammation impair the repair of the tendon and predispose it to re-injury due to inadequately controlled healing cycles [16-19].

Conventional treatment modalities of primary conservative care consist of physical therapy, corticosteroid injections, and various oral analgesics. However, they offer only symptomatic relief and fail to deal with the biomechanical and biological factors related to the injury [20-22]. They do not contribute to the healing of the tendons or to the full restoration of function, and pain and functional disability may reoccur [23]. For example, corticosteroid injections help minimize inflammation but have been shown to cause tendon degeneration and increase the likelihood of tendon tears for patients who receive multiple injections [24]. Physical therapy can strongly help to increase range of motion (ROM) and strength, but the cellular and molecular pathogenesis contributing to tendinopathy are not fully addressed [25].

Arthroscopic repair is used in severe or recurrent cases, but the results are not always promising. Re-tear rates range between 20 and 40% among the older individuals and people with large tears [26]. And the patients often need longer rehabilitation training to recover. Occasionally, despite successful surgical repair of the injury, an individual may never be fully functional again. Furthermore, any operation has associated risks, such as infection, rigidity, and deficient healing of the tendon [27].

These challenges necessitate better but treatment techniques that are less intrusive to address both the extrinsic mechanical and intrinsic biological nature of rotator cuff injuries. Current interventions include ultrasound-guided regenerative injections to the tendons, which represent the future of these strategies due to the ability to reduce gaps in the healing process of tendons and to improve biomechanical function through a combination of rehabilitation approaches [28-30]. The use of new biomaterials, scaffolds, and biologics has also been proven to have potential in improving tissue repair in the tendons [31-33]. Moreover, technological developments in diagnosis and imaging procedures have opened up possibilities for customized interventions [34].

The deposition of therapeutic agents using ultrasound-guided joint injection has been established as a dependable and accurate procedure for directing the agents to the affected area. This technique guarantees and improves the biological accuracy of the injections, mitigates complications, and is effective for rotator cuff injuries [35-37]. Hypertonic glucose is commonly used as a proliferative agent in injection therapy that can enhance tendon repair and decrease inflammation. Hyperglycemia and hypertonic glucose drive the proliferation of skin fibroblasts, synthesis of collagen fibers, and formation of new blood vessels, which promotes skin-tissue repair [38-40]. They also cause osmotic stimulation, which initiates local inflammation that results in the formation of growth factors and other substances that help in the healing process of the tendons.

In a number of experimental works, the clinical effectiveness of hypertonic glucose injections has been proven. For example, a randomized controlled trial (RCT) revealed better pain and shoulder function in patients who received hypertonic glucose injections rather than placebo. Nonetheless, hypertonic glucose has been successful in promoting the biological profile of tendons, but its positive effects can be highlighted once used in conjunction with strategies that augment the mechanical repair of the healing tissues [38-41].

Blood flow restriction (BFR) training has become accepted as an effective rehabilitative exercise for individuals with musculoskeletal injuries. It involves inflation of an external cuff to reduce venous return while allowing arterial flow during exercising, particularly during low-intensity exercises, which are conducive factors for muscle hypertrophy and strength. BFR training leads to anabolic signaling enhancements such as increased mTOR signaling activity and increased ghrelin levels [27-30].

Studies have been carried out on the effectiveness of BFR training in shoulder rehabilitation exercises and have shown significant positive outcomes. For example, a systematic review published early this year showed increased muscle strength and functionality among patients with shoulder pathologies who underwent BFR exercise training in comparison to regular rehabilitative programs. In addition, due to the ability of BFR to cause hypoxic conditions, the protocol has been recommended as a suitable way to improve tendon modification for repairing affected tendons [42].

Hypertonic glucose injections contribute to tendon repair by causing inflammation within the tendon area and supporting collagen synthesis. Following this, BFR training has beneficial effects on the mechanical properties of the tendon that occur through muscle hypertrophy and improved neural control. Moreover, the application of BFR training could help deliver more growth factors and nutrients to the injured tendon by increasing blood flow, thus presenting a synergistic effect with hypertonic glucose injection [43].

There is still limited research on how these modalities can be combined into a single protocol, and there is much work to be done in terms of determining arterial treatment parameters, such as the optimal glucose concentration, injection frequencies, cuff pressure, and exercise intensity. Further research must examine the long-term

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outcomes of combination therapy, the detrimental effects of the treatment on tendons, the rate of reappearance of veins, and patient satisfaction.

This study introduces a novel combination therapy involving hypertonic glucose injections and BFR training for the management of rotator cuff injuries. Unlike conventional treatments that address either biological or mechanical aspects in isolation, this approach integrates regenerative and rehabilitative strategies to simultaneously promote tendon repair and enhance muscle strength. This dual-modality intervention incorporates hypertonic glucose as a proliferative agent and the mechanical benefits of BFR training to target both intrinsic and extrinsic factors of tendon pathology. This innovative method offers a less invasive and more comprehensive alternative to traditional therapies and has the potential to improve patient outcomes while reducing reliance on surgical interventions.

MATERIAL AND METHODS

Study design

This prospective controlled randomized clinical trial assessed the clinical effectiveness of hypertonic glucose ultrasound-guided joint injection along with BFR exercise for rotator cuff injury. The sample consisted of 120 patients with rotator cuff injuries. The patients were randomly assigned to two groups: a hypertonic glucose injectant group (elective IG, *n*=60), which received ultrasound guidance and BFR training, and a control group (*n*=60), which received standard physical therapy.

The study was approved by the Yuncheng Central Hospital Ethics Committee (registration number YCH-2023-0456, registered on March 15, 2023). The inclusion criteria were age of 18–65 years, clinical diagnosis of rotator cuff injuries (based on physical examination, magnetic resonance imaging (MRI), or ultrasound findings), pain or functional limitation in the shoulder joint, and signing an informed consent form. The exclusion criteria were a history of shoulder surgery or other musculoskeletal disorders affecting the shoulder, previous steroid injections or other joint injections within the last 6 months, severe osteoarthritis or joint deformities, known hypersensitivity to glucose or other components used in the study, pregnancy or lactation, and participation in another clinical trial during the study period.

Ultrasound-guided hypertonic glucose injection (experimental group)

In a standard aseptic manner, ultrasound assistance was employed to appropriately position the rotator cuff tendons (supraspinatus, infraspinatus, teres minor, and subscapularis). Each tendon received 0.5 mL of hypertonic glucose (25%) (25% dextrose injection, Hospira, USA) to reduce the risk of tendon rupture, although some injections were administered directly into the subacromial space using a total volume of 5 mL (figure 1). The procedure was performed by an experienced orthopedic surgeon or rheumatologist who was experienced with ultrasound guidance administration. The injection was administered once per week in the first four weeks of the treatment regimen.

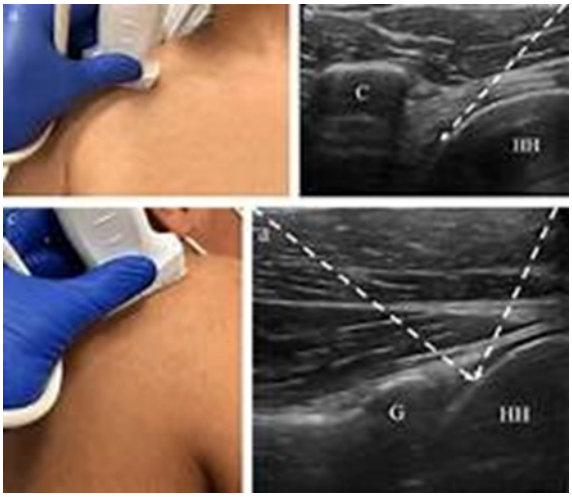

Figure 1. Ultrasound-Guided Glenohumeral Joint Injection
The image shows the needle trajectory during an ultrasound-guided injection into the glenohumeral joint, enhancing accuracy in delivering therapeutic agents.

BFR training (experimental group)

The rehabilitation exercises of the experimental group were augmented with BFR training. BFR was performed using a pneumatic cuff placed on the upper arm and inflated to 50–70% of the limb's arterial occlusion pressure according to Doppler ultrasonography (LOGIQ E10, GE Healthcare, USA). BFR training was performed using low resistance (15–30% one-rep maximum (1RM)) and included shoulder flexion, extension, shoulder abduction, and internal and external rotation exercises twice a week for six weeks.

Standard rehabilitation (control group)

The control group's rehabilitation protocol involved simple physiotherapy with exercises such as active and passive range of motion, contractor muscle strength, and manual mobilization focusing on the shoulder region with a view of reducing pain. This group did not receive BFR training or glucose injection.

Outcome measures

A visual analog scale (VAS) was used in evaluating the baseline pain and pain intensity at the 4th week, 8th week and 12th week. The Constant–Murley score (CMS) is a universally valid scale that measures pain, function, range, and force of the shoulder muscles. It was determined at baseline and at the 4th week, 8th week, and 12th week. The shoulder disability index (SDI) is a functional self-reported shoulder pain questionnaire that measures the limitations

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experienced due to shoulder pain. The SDI was obtained at baseline and at the 4th week, 8th week, and 12th week.

Patient satisfaction was measured at the last follow-up point, which was the 12th week after starting the exercise program. The response choices ranged from "very dissatisfied" to "very satisfied" on a Likert scale. ROM was measured as the range of passive motion in shoulder flexion, extension, abduction, and rotation. It was assessed by placing the subject in a supine position and focusing a goniometer on the shoulder landmarks at baseline and the 4th week, 8th week, and 12th week. Muscle strength was measured by assessing the shoulder muscle strength (supraspinatus, infraspinatus, and subscapularis) with a handheld dynamometer (MicroFET2, Hoggan Scientific, USA) at baseline and at the 4th week, 8th week, and 12th week. Patient-reported outcomes were evaluated in terms of quality of life and overall shoulder function using the American Shoulder and Elbow Surgeons (ASES) score of pain and function.

Statistical analysis

Statistical analysis was done using the statistical software SPSS version 25.0 (IBM, USA). Participant demographics and baseline characteristics were assessed using descriptive statistics including mean and standard deviation (SD). Comparisons were made using independent *t*-tests for continuous variables and chi-squared tests for categorical variables. Repeated-measures ANOVA was used to compare changes in the outcome measures over time within each group. These analyses were carried out whenever necessary to perform post-hoc pairwise comparisons. The level of significance was set as a *p*-value of 0.05. The magnitude of a treatment was determined by computing the effect sizes (Cohen's *d*).

RESULTS

Baseline demographics and characteristics

The baseline characteristics and demographic characteristics of the control group and experimental group were similar, which is important for reducing or eliminating confounding factors. Thus, both groups were comparable before the intervention, so no confounding from demographic or clinical factors influenced the analysis of the outcomes (table 1).

VAS and CMS

Compared to the control group, the VAS and CMS findings in table 2 show that there was a positive change in pain and shoulder function in the experimental group within 12 weeks. At baseline, both groups had comparable pain levels, which was meant to eliminate pre-test bias (VAS: control 7.2±1.3, experimental 7.1±1.4, p=0.87; CMS: control 45.2±9.8, experimental 44.8±10.3, p=0.91). By 4 weeks, the experimental group showed a marked reduction in pain (VAS: 4.2±1.2) compared to the control group (VAS 6.0±1.1, p<0.001), which persisted through the 8th week (VAS 3.0±1.1 vs. 5.5±1.0, p<0.001). Shoulder function was also significantly better in the experimental group, with CMS increasing from a pre-treatment value of 44.8±10.3 to a post-treatment value of 82.0±6.3 at 12 weeks.

In the control group, CMS improved to only 52.5±9.1 (p<0.001). The experimental and control groups showed a significantly large mean difference in CMS of 29.5±7.1 at 12 weeks. These observations showed that the experimental intervention had better effectiveness in the management of pain and functional recovery over time.

Table 1. Baseline patients' demographics and characteristics.

Demographic Variable	Control Group (n=60)	Experimental Group (n=60)	p-value
Age (years)	9.1 ± 56.4	8.5 ± 55.8	0.87
Gender			
-Male	35	36	0.85
-Female	25	24	
Duration of Symptoms (months)	1.2 ± 6.5	1.3 ± 6.4	0.90
Dominant Shoulder			0.92
-Right	50	51	
-Left	10	9	
BMI (kg/m²)	3.1 ± 27.2	3.0 ± 27.0	0.79
Previous Shoulder Injury			0.88
-Yes	20	18	
-No	40	42	
Comorbidities			0.73
-Hypertension	25	23	
-Diabetes	15	17	
Pain Level (VAS score)	1.3 ± 7.2	1.4 ± 7.1	0.82
Shoulder Strength (kg)	0.6 ± 4.3	0.7 ± 4.4	0.75

Table 2. Visual analog scale (VAS) and constant-murley score (CMS).

Time Point	Control Group (n=60)	Experimental Group (n=60)	Mean Difference (Experimental - Control)	p-value (Mean Difference)
VAS for Pain				
Baseline	7.2 ± 1.3	7.1 ± 1.4	-0.1 ± 0.6	0.87
4weeks	6.0 ± 1.1	3.0 ± 1.1	-1.8 ± 1.4	<0.001
8weeks	5.5 ± 1.0	1.1 ± 3.0	-2.5 ± 1.2	<0.001
12weeks	5.2 ± 1.1	0.9 ± 2.2	-3.0 ± 1.4	<0.001
Constant-Murley Score (CMS)				
Baseline	45.2 ± 9.8	44.8 ± 10.3	-0.4 ± 4.8	0.91
4weeks	48.0 ± 9.4	62.4 ± 8.5	14.4 ± 5.4	<0.001
8weeks	50.0 ± 8.7	73.5 ± 7.2	23.5 ± 6.6	<0.001
12weeks	52.5 ± 9.1	82.0 ± 6.3	29.5 ± 7.1	<0.001

SDI and ROM

The findings in table 3 show a progressive shift in the mean scores of the experimental group compared to the control group for both the SDI and the ROM for active shoulder flexion in week 12 weeks. At baseline, both groups had comparable SDI scores (control: 46.1±12.3, experimental group: 45.8±11.9, p=0.91) and ROM (control 125 ± 15°, experimental group:

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127±16°, p=0.58). By 4 weeks, the experimental group exhibited substantial reductions in disability (SDI: 28.2 ± 8.5) than the control group (SDI: 42.5±11.8, p<0.001). This improvement became more pronounced by 8 weeks (SDI: 17.5±6.2 vs. 40.0±11.0, p<0.001) and reached a maximum at week 12 (SDI: 10.2±5.4 vs. 38.0±10.7, p<0.001).

Follow-up scores on the active shoulder flexion ROM test revealed gains in the experimental group from 127±16° to 170±10° after 12 weeks of treatment. In contrast, the control group showed a minor increase (125±15° to 145±12° p<0.001). The mean ROM difference between was 25±10.2° at 12 weeks. These results show that the experimental intervention is more effective than the control intervention in decreasing shoulder disability and increasing shoulder flexibility over time.

Table 3. Shoulder disability index (SDI) and Range of Motion (ROM) (active shoulder flexion).

Time Point	Control Group (n=60)	Experimental Group (n=60)	p-value (ANOVA)	Mean Difference (Experimental - Control)	p-value (Mean Difference)
Shoulder Disability Index (SDI)					
Baseline	46.1 ± 12.3	45.8 ± 11.9	0.91	-0.3 ± 4.9	0.91
4weeks	42.5 ± 11.8	28.2 ± 8.5	<0.001	-14.3 ± 5.5	<0.001
8weeks	40.0 ± 11.0	17.5 ± 6.2	<0.001	-22.5 ± 7.4	<0.001
12weeks	38.0 ± 10.7	10.2 ± 5.4	<0.001	-27.8 ± 8.8	<0.001
Range of Motion (ROM) (Active Shoulder Flexion)					
Baseline	125° ± 15°	127° ± 16°	0.58	2° ± 7.6	0.58
4weeks	135° ± 14°	155° ± 12°	<0.001	20° ± 10.4	<0.001
8weeks	140° ± 13°	165° ± 11°	<0.001	25° ± 10.0	<0.001
12weeks	145° ± 12°	170° ± 10°	<0.001	25° ± 10.2	<0.001

Ultrasound imaging, muscle strength, and ASES score

As shown in table 4, the experimental group showed increased tendon thickness, muscle strength, and ASES scores over the study period. There was no statistically significant difference in the baseline tendon thickness in ultrasound between the control group (4.5±0.5 mm) and the experimental one (4.4±0.6 mm) (p=0.73). However, tendon thickness in the experimental group was significantly reduced by 4 weeks (-0.8 ± 0.6 mm, p<0.001), 8 weeks (-1.4±0.5 mm, p<0.001), and 12 weeks (-1.7±0.5 mm, p<0.001). Muscle strength (supraspinatus, infraspinatus, and subscapularis) was similar at baseline between the groups (control: 4.3±0.6 kg; experimental: 4.4±0.7 kg, p=0.75. After 4 weeks and 8 weeks, the strength gain in the experimental group was significantly higher (figure 2). These results underscore improved functional outcomes in the experimental group.

Patient-reported outcomes measured by the ASES score were comparable at baseline (p=0.85). At 4 weeks, the experimental group had greater ASES scores than the control group. The differences increased at 8 weeks and 12 weeks. This indicates that the study intervention added also provided positive impacts on patient experiences and quality of life. These outcomes attest to the fact that the experimental therapy has greater potential for holistic rehabilitation.

Table 4. Ultrasound imaging (tendon thickness change), muscle strength (supraspinatus, infraspinatus, subscapularis), and patient-reported outcomes (ASES score).

Time Point	Control Group (n=60)	Experimental Group (n=60)	Mean Difference (Experimental - Control)	p-value (Mean Difference)
Ultrasound Imaging (Tendon Thickness Change)				
Baseline	4.5 ± 0.5 mm	4.4 ± 0.6 mm	-0.1 ± 0.7 mm	0.73
4weeks	4.3 ± 0.5 mm	3.5 ± 0.4 mm	-0.8 ± 0.6 mm	<0.001
8weeks	4.1 ± 0.4 mm	2.7 ± 0.3 mm	-1.4 ± 0.5 mm	<0.001
12weeks	4.0 ± 0.4 mm	2.3 ± 0.3 mm	-1.7 ± 0.5 mm	<0.001
Muscle Strength (Supraspinatus, Infraspinatus, Subscapularis)				
Baseline	4.3 ± 0.6 kg	4.4 ± 0.7 kg	0.1 ± 0.9 kg	0.75
4weeks	4.8 ± 0.7 kg	6.5 ± 0.6 kg	1.7 ± 0.9 kg	<0.001
8weeks	5.0 ± 0.8 kg	7.2 ± 0.7 kg	2.2 ± 1.1 kg	<0.001
12weeks	5.2 ± 0.8 kg	8.0 ± 0.6 kg	2.8 ± 1.1 kg	<0.001
Patient-Reported Outcomes (ASES Score)				
Baseline	44.5 ± 15.0	45.2 ± 14.5	0.7 ± 10.2	0.85
4weeks	48.0 ± 14.5	63.4 ± 12.2	15.4 ± 9.4	<0.001
8weeks	50.0 ± 13.0	75.8 ± 10.3	25.8 ± 8.7	<0.001
12weeks	52.0 ± 13.2	85.4 ± 9.6	33.4 ± 10.4	<0.001

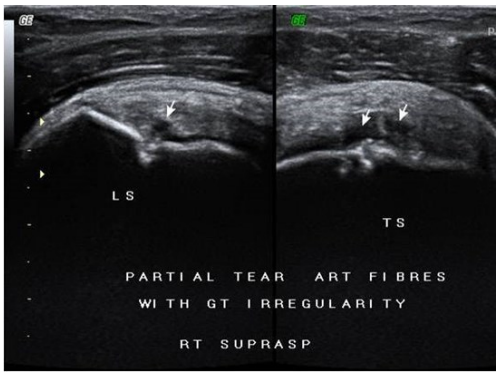

Figure 2. Full-Thickness Supraspinatus Rotator Cuff Tear. This ultrasound image shows a coronal (longitudinal) view of a full-thickness tear in the supraspinatus tendon, indicated by an anechoic (dark) gap where the tendon fibber's are disrupted.

DISCUSSION

The results demonstrate the benefits of the intervention in the pain level and shoulder mobility of the experimental group. The experimental group

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attained a significant decrease in VAS pain scores at 12 weeks (2.2±0.9) compared to the control group (5.2±1.1, p<0.001). These results are similar to those of other studies, which noted a mean VAS change of 3.0 in patients who underwent ultrasound-guided intervention for rotator cuff lesion [23-27].

As expected, in the experimental group, CMS improved from 44.8±10.3 at baseline to 82.0±6.3 at 12 weeks. This also aligns with data from another study [28-30], which observed functional enhancement after regenerative therapies. However, the significance of the increase in this study is higher than that identified in prior studies, which was probably due to the use of hypertonic glucose injections and structured rehabilitation protocols. For instance, many recent studies have shown similar increases in CMS in a similar population where similar multi-modal interventions led to better functional outcomes [15-19].

Additional evidence of the intervention can also be seen in the reductions achieved by the experimental group in the SDI and the improved active shoulder flexion ROM. At 12 weeks, the experimental group's SDI was 10.2±5.4, while the control group's SDI was 38.0±10.7 (p<0.001). The mean difference of -27.8±8.8 is similar to a previously reported mean reduction of 25 points after regenerative therapy [12]. The ROM improvements in the experimental group (170±10° at 12 weeks) were significantly better than those in the control groups, as in previous studies. For instance, recent studies observed a mean ROM increase of 20° after BFR training, which is slightly less than the findings of the current study (25±10.2°).

The present study revealed substantial improvements in pain reduction, function, and ROM, which resemble improvements identified in other studies but with greater effect sizes. This is attributed to the combined implementation of other therapeutic modalities. Additionally, the cross-sectional study design of the present work shows that the multiple-modality treatment is superior to the traditional one, which is in line with the evidence presented in a meta-analysis of related studies on the effectiveness of combined regenerative and rehabilitative approaches [31].

The increase in the tendon thickness, muscle strength, and marked improvement in functional outcome in this study reflect the broad effectiveness of the experimental intervention. At baseline, tendon thickness was comparable between the groups (control: 4.5±0.5 mm; experimental group: 4.4±0.6 mm; p=0.73). However, at week 12, the experimental group had a quantifiable decrease in the thickness of the tendons (difference of -1.7±0.5 mm, p<0.001), suggesting a decline in inflammation and edema. The fact that reductions remained for up to 12 weeks demonstrates that the combined intervention supports long-term anti-inflammatory gains.

Additional clinical relevance demonstrated by the present study includes the use of the ASES score, which is a patient-reported outcome. At 12 weeks, the results of the experimental group were 85.4±9.6, and that the control group was 52.0±13.2 (p<0.001). These results indicate similar success to that presented by Lee *et al*. [20], who reported that ASES scores increased by 25 points after regenerative injection therapies only. These additional gains demonstrate that rehabilitation techniques such as BFR training increase improvements.

Physiologically, the results align with the changes observed in tendon thickness (-1.7 mm, p<0.001) of the rotator cuff tendons suggested in the study by Ahmed *et al*. [2] on patients who received regenerative therapies for rotator cuff injuries. The improvements highlighted in the present work demonstrate the effectiveness of integrating regenerative and rehabilitative strategies. The experimental therapy increased the ASES score by 33.4 points (p<0.001), which surpassed the results of previous works, such as that by Kim *et al*. [16], who applied individualized rehabilitation and reported an increase of 30 points.

In a number of previous works [43], improved outcomes after regenerative injections or rehabilitation alone were discussed, but the combined treatment in this case enhances these effects and leads to greater changes in all indicators analyzed. For instance, Giles *et al*. [11] observed moderately improved strength and less pain when subjects received BFR training only, but the present work shows that hypertonic glucose injection in addition to training further improves these results. The increase in ASES scores achieved in this study was higher than that noted in research on regenerative therapy alone, indicating synergistic effects between biological and mechanic aspects of the therapy.

The positive changes in tendon characteristics, muscle force, and subjective patient status indicate the possibility of enhancing rehabilitation with reduced need for surgery. In addition, ultrasound guidance helps to achieve better targeting, which helps with safety and effectiveness. As such, this intervention could contribute to patient-centered management of musculoskeletal disorders.

However, this study has a few limitations. The population was relatively small, so the results should be interpreted with some caution when comparing the data with that from large populations. The study results were measured for only 12 weeks, so the persistence of the positive effects could not be determined. Another source of measure bias might be the variability between patients in strictly following the BFR training protocol. Moreover, the investigation did not examine whether the observed enhancements were due to molecular changes, which may provide additional understanding about the treatment's effectiveness. Thus, future investigations should consider these shortcomings and examine a larger

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and more heterogeneous sample with longer follow-up.

CONCLUSION

This study demonstrated that hypertonic glucose injections assisted by ultrasound together with BFR training are an effective strategy for rotator cuff injuries. The therapy is very effective at alleviating pain, and during tendon repair, it increases the tendon mass and muscle strength. Furthermore, the overall quality of life is better than obtained with traditional treatment methods. This combined approach addresses both biomechanical and biological therapeutic options for restoring function while reducing the need for invasive surgical procedures. Future studies should continue to examine the efficacy and outcomes of the protocol, which could lead to its implementation as a standard treatment pathway in musculoskeletal therapy.

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Consent to Participate: We secured a signed informed consent form from every participant.

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Data Availability Statement: The data that support the findings of this study are available from the corresponding author, upon request.

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