

How to Avoid knee Arthroplasty in Patients with Grade Iv Osteoarthritis – Combination of Adipose-Derived Stem Cells and Radiofrequency Ablation. A Case Series of 30 Consecutive Patients with 12-Months Follow-up



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Abstract

Introduction: OA of the knee is a progressive disease that, to the best of our knowledge, cannot be stopped. There are conservative or operative treatment options for knee OA including intraarticular injections of cortisone, hyaluronic acid or platelet-rich-plasma (PRP). Joint replacement is the most common surgical procedure in patients with grade IV OA of the knee. As with every surgical procedure, KA has a risk profile of possible complications. In the present study, we report on thirty consecutive patients with grade IV knee OA who underwent treatment with stem-cell rich fat graft combined with radiofrequency (RF) ablation.

Material and Methods: We enrolled thirty consecutive individuals (mean age 64.5; range 57-92) with grade IV OA of the knee. There were 11 female and 19 male patients. All patients were treated between January and June 2022. Patients were consented for liposuction and knee liparthroplasty and for selective RF ablation (Coolief, Avanos Medical, USA) of the sensory branches of the genicular nerves. At follow-up, VAS, range of motion (ROM) and the Knee Injury and Osteoarthritis Outcome Score (KOOS) were assessed. Furthermore, we assessed patients' subjective satisfaction. Level of statistical significance was set at $p < 0.05$.

Results: At follow-up, no patient converted to KA. All patients attested they would have the procedure done again if necessary. VAS was significantly improved ($p < 0.05$) in all the patients. No patient had worse or equal VAS at follow-up. The Median ROM before the intervention was 0-2-130. Median ROM was 2-0-145 at follow-up. No patient showed worse ROM at follow-up. In all KOOS categories, significant improvement was shown at follow-up ($p < 0.05$). No patients showed worse or equal KOOS values at follow-up.

Conclusion: To the best of our knowledge, this is the first study reporting on ASC in combination with RF ablation in a population of patients with severe OA of the knee who already were scheduled for KA. According to our results, the herein described treatment regime appears to be safe and effective at twelve months follow-up.

Introduction

Worldwide, around 654.1 million (CI 565.6-745.6) individuals (forty years or older) suffered from osteoarthritis of the knee in the year 2020 [1,2]. People suffering from knee OA report pain, swelling, stiffness and limited range of motion [3,4]. Accordingly, OA of the knee is also a major burden for socio-economic structures of a system as it leads to loss of productivity of the population. The reasons for knee OA include normal cartilage ageing, knee trauma, joint infection, or metabolic disorders [5]. OA of the knee is a progressive disease that, to the best of our knowledge, cannot be stopped. There are conservative or operative treatment options for knee OA including intraarticular

injections of cortisone, hyaluronic acid or platelet-rich-plasma (PRP) [6,7]. Operative options include arthroscopic debridement, microfractures, mosaicplasty, chondrocyte transplantation or partial or total knee arthroplasty (KA) [8-10]. Joint replacement is the most common surgical procedure in patients with grade IV OA of the knee. As with every surgical procedure, KA has a risk profile of possible complications. These include perioperative complications such as bleeding, nerve lesions or thromboembolic complications as well as postoperative complications such as infection, limited range of motion or persisting pain [11-13]. Recently, more regenerative strategies have been reported to be

effective including the administration of adipose-derived stem cells (ACS) or bone-marrow stem cells (BMSC) for cartilage repair [14,15]. Radiofrequency (RF) ablation of the genicular nerves around the knee is a viable options for minimally invasive pain management and has been highlighted in various studies [16-18]. In the present study, we report on thirty consecutive patients with grade IV knee OA that were scheduled for KA before consulting our practice.

Material and Methods

We enrolled thirty consecutive individuals (mean age 64.5; range 57-92) with grade IV OA of the knee who were told that joint preservation would not be possible and who were scheduled for KA accordingly by other facilities. There were 11 female and 19 male patients. All patients were treated between January and June 2022. Patients were included if they had grade IV OA in at least two compartments of the knee (medial, lateral, patella-femoral).

All patients had unilateral treatment.

Treatment protocol

Patients were consented for liposuction and knee liparthroplasty [19] and for selective RF ablation (Coolief, Avanos Medical, USA) of the sensory branches of the genicular nerves.

Radiofrequency Ablation

Patients were placed and prepared in supine position. Then, 10mL Lidocaine 2% with epinephrine 1:10.000 were injected at each of the four genicular nerve locations (Figure 1). After waiting for some minutes, ultrasound (Clarius HD, Canada) was used to identify the branches of the four genicular nerves. Then, the RF electrodes were placed on the four sensory branch locations (Figure 2). Then, the nerve branches were ablated by cooled RF ablation (maximum 63° Celsius, 100 Ohm impedance and 7 Watt for) for two minutes and thirty seconds in each location.

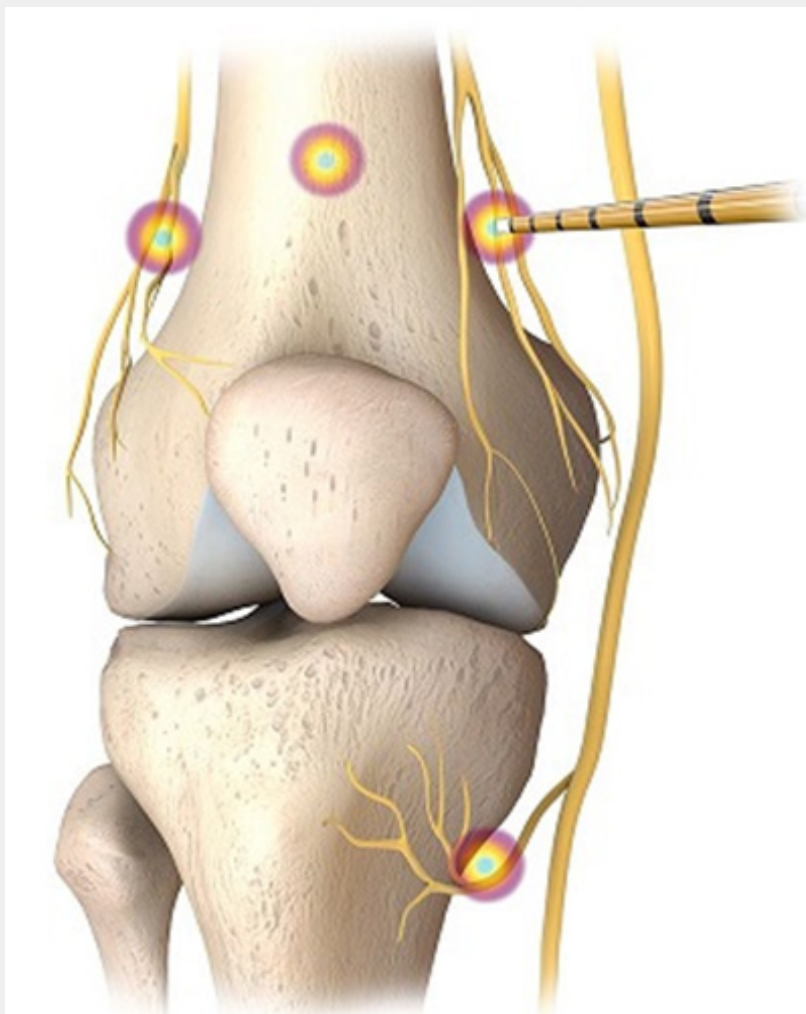


Figure 1: The four sensory branches of the genicular nerves.



Figure 2: Manual abdominal liposuction.

Adipose-derived stem cells

After RF ablation, the left abdominal region was prepared and draped for liposuction. Local anesthesia (1% lidocaine with epinephrine 1:10.000) was used to numb the area. A tumescent solution (250 mL of saline solution, 1 mL of 1:200,000 adrenalin, and 600 mg of lidocaine, 8.4% sodium-bicarbonate) was inserted over a little incision with a 100mL syringe. After some minutes of waiting, a manual liposuction was performed with a 20mL syringe and a 3mm liposuction cannula (Tulip Medical, USA) (Figure 3). We routinely used four 20mL syringes with fat-aspirate for further processing.

The fat fraction in each of the syringes was isolated and separated from the fluid and oil fraction by using the so-called decanting method without centrifuging the fat aspirate. This technique was described recently in past studies [20,21]. Then, we used the so-called shuffling method to mechanically shift the fat graft between two syringes. For this, a three-way-valve was

used. By using this method, the membranes of the fat cells are ruptured manually, and the then more refined fat graft gets easier injectable (Figure 4). By an assistant 15mL venous whole blood was drawn from a cubital vein into a double chamber syringe (Arthrex, Naples, US). This double syringe and the whole-blood sample were subsequently centrifuged in a standard centrifuge (Rotofix 32 A, Hettich, Germany) with 1500 rounds for 5 minutes. By centrifugation, 5mL of PRP fraction was isolated and was then inserted into the syringe with the fat graft. The supercharged fat graft was then inserted into the knee joint by a single-use 20-gauge needle and by using the ultrasound-scanner to avoid insertion into Hoffa's fat pad. Wounds were covered with plasters and patients were advised to fully bear weight as tolerated by pain. All patients were followed-up after six weeks in our office.

Study follow-up

All thirty individuals were followed-up after twelve months at least (12.0-14.2 months). At follow-up, VAS, range of motion

(ROM) and the Knee Injury and Osteoarthritis Outcome Score (KOOS) were assessed. Furthermore, we assessed patients' subjective satisfaction. For statistical analysis SPSS was used (SPSS, USA). Level of statistical significance was set at $p < 0.05$.

Results

We did not record any complications or any adverse effects after manual liposuction, fat injection or radiofrequency ablation. Three patients had mild hematoma at the liposuction site. One patient had quadriceps weakness that resolved the next day.

Twenty-one patients had minimal or mild effusion of the knee. At follow-up, no patient has converted to KA. All patients attested they would have the procedure done again if necessary.

Visual Analogue Scale

Mean VAS before the intervention was 7.8 (range 6-10). At twelve-month follow-up, VAS was significantly improved ($p < 0.05$, Figure 5) in all the patients. No patient had worse or equal VAS at follow-up.



Figure 3: Two of the four radiofrequency electrodes in situ.

Range of Motion

The Median ROM before the intervention was 0-2-130. Median ROM was 2-0-145 at follow-up. No patient showed worse ROM at follow-up.

KOOS

In all KOOS categories, significant improvement was shown at follow-up ($p < 0.05$; Figure 6-10). No patients showed worse or equal KOOS values at follow-up.

Discussion

The use of intraarticularly injectable substances to treat knee OA has been vastly described in the past [6,7]. Intraarticular administration of stem cell-rich fat grafts is relatively new and not a common practice, yet. Froschauer et al. published a study describing the results after liparthroplasty of the first carpo-metacarpal joint and the same group reported improved outcome scores after five years [20,21]. Jo et al. reported encouraging results after intraarticular injection of adipose-derived

mesenchymal stem cells for the treatment of OA of the knee in a series of eighteen patients [22]. This is also in accordance with

the publication of Lee et al. who found improved outcome after six months follow-up [23].



Figure 4: Preparation of the adipose-derived fat graft with the shuffling method.

In a recent study by Kim et al., the authors showed cartilage regeneration visualized in magnetic resonance imaging (MRI) scans and significant pain relief in patients with knee OA after arthroscopic implantation of ASC [24]. Also, Lapuente et al. found improved clinical outcome after ASC injection and correlated this with ultrasound imaging and biochemical parameters by showing a marked decrease of pro-inflammatory molecules and a significant increase of anabolic and anti-inflammatory parameters [25]. Despite different non-surgical treatment options are available for patients with symptomatic knee OA, KA often still is the first-line treatment and recommended by most orthopedic surgeons. As already described in the Introduction section, complications that might be connected to the operation or to the post-operative period are inevitable. It also needs to be pointed out that KA hardware has limited duration and revision surgery has to be considered in younger patients. These revision surgeries

are associated with higher morbidity and mortality compared to the index operation [26].

Resulting from extended life-expectancy and a subsequently resulting over-aged population, the incidence of knee OA is expected further to rise [1,2]. Also, the extended life-expectancy might lead to a population with higher rates of co-morbidities. This combination may lead to a dilemma in which relatively old and ill patients will undergo high-risk operations such as KA. Considering the recently ended SARS-CoV 2 pandemic with long waiting lists of cancelled operations, the here described technique might be of value to treat patients without the need for an operation. The protocol is used for in-office treatment without the need for highly sophisticated hospital infrastructure such as intensive care or blood bank. From a socio-economic point of view the here described regime combining ASC with RF ablation is cheaper than KA and might also be useful for patients in poorer countries or in

countries with underdeveloped medical infrastructure. As shown in the here presented study, no adverse effects were found in our population that mainly included elderly patients. We also point out that symptom improvement and pain relief was found in every single patient. As a result, patient satisfaction was 100% at follow-up, which is very seldom in medicine.

Although high patient satisfaction and improved outcome parameters one has to be cautious when interpreting the results.

We only have data of a small study population with twelve-month follow-up. We cannot extrapolate to higher numbers or longer follow-up. Further, it is not clear what caused outcome improvement: ASC administration or RF ablation or both. In this context, we also need to highlight the study by Salzmann et al. who found improved symptoms in patients with knee OA even after administration of saline [27]. Therefore, further studies with longer observational periods seem necessary.

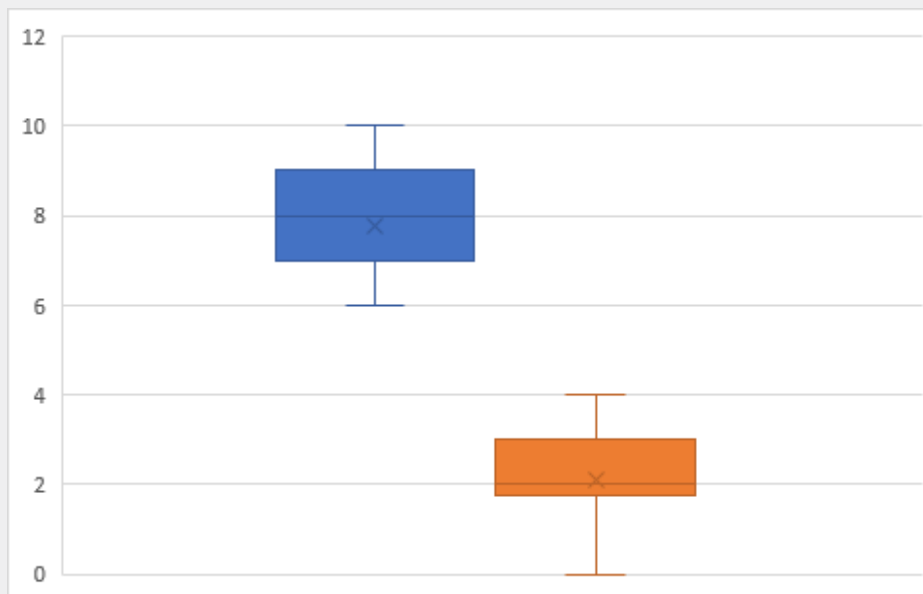


Figure 5: mean VAS before (blue) and after (orange) the intervention.

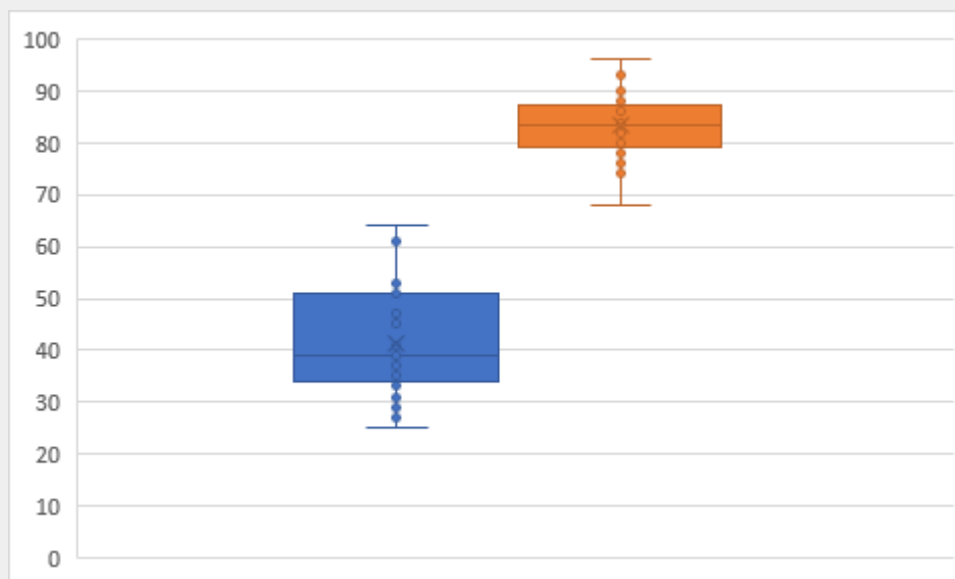


Figure 6: Mean KOOS Pain before (blue) and after (orange) the intervention.



Figure 7: Mean KOOS Symptoms before (blue) and after (orange) the intervention.

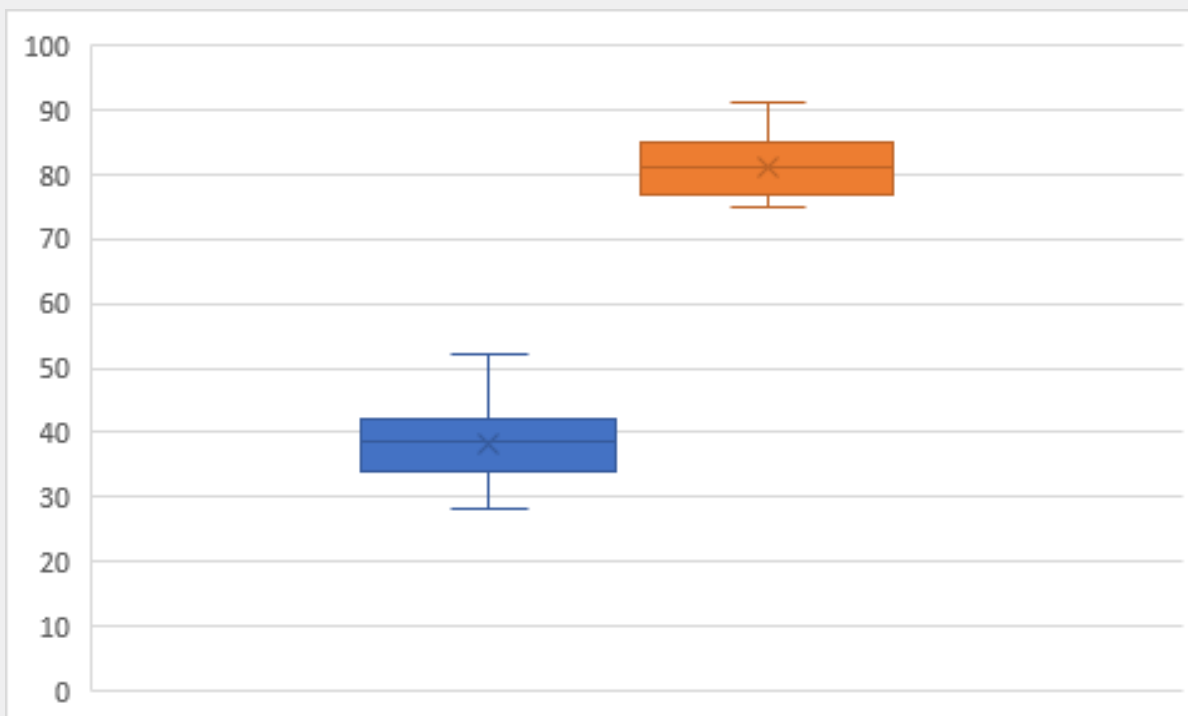


Figure 8: mean KOOS Activities of Daily Living before (blue) and after (orange) the intervention.

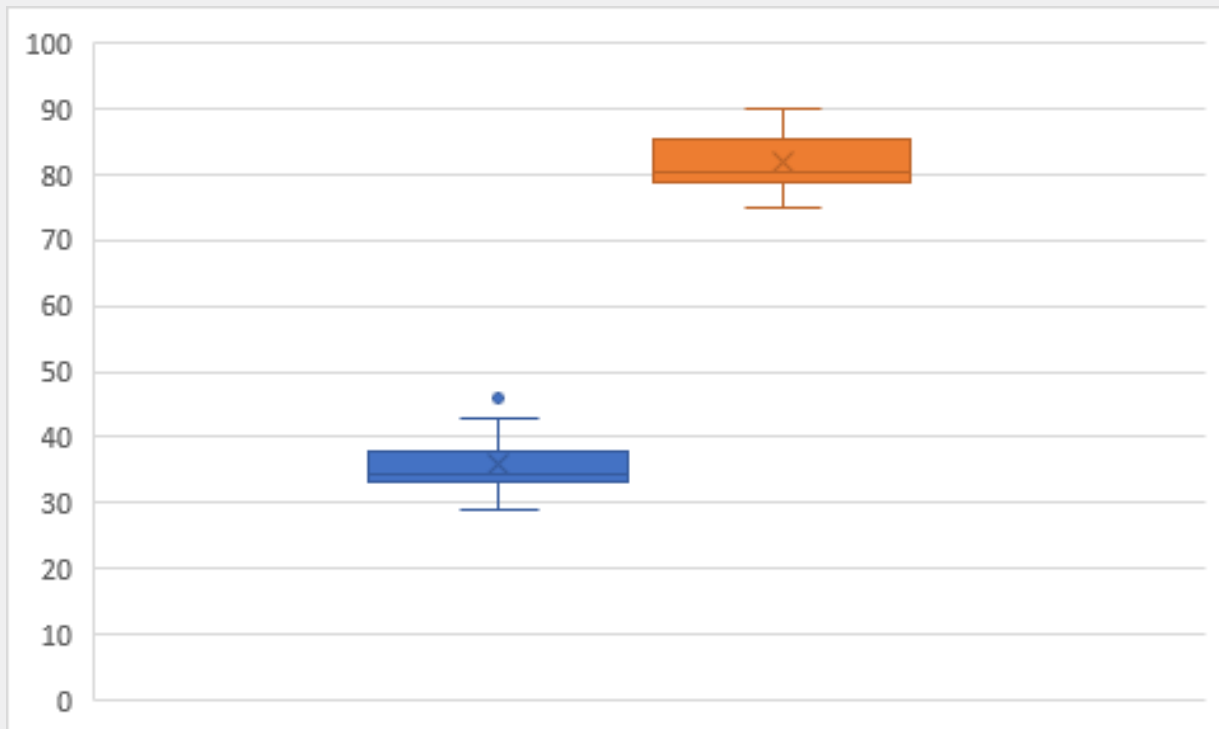


Figure 9: Mean KOOS Sports and Recreation before (blue) and after (orange) the intervention.

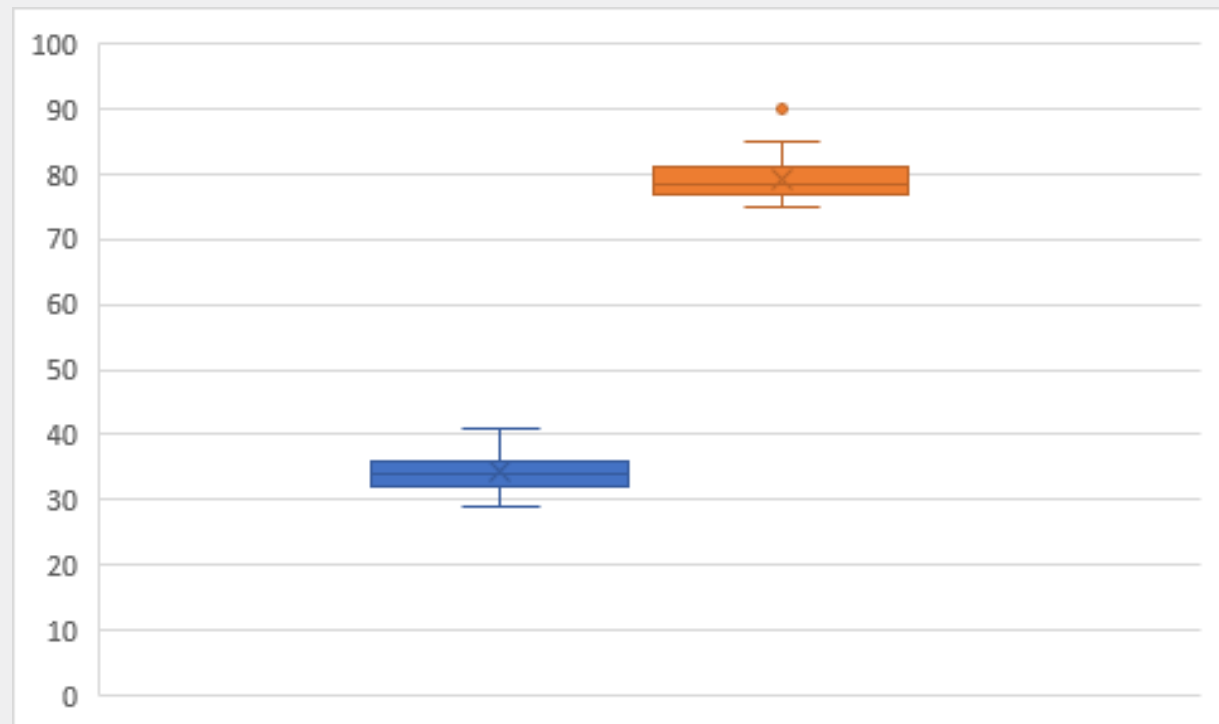


Figure 10: Mean KOOS Quality of Life before (blue) and after (orange) the intervention.

Conclusion

To the best of our knowledge, this is the first study reporting on ASC in combination with RF ablation in a population of patients with severe OA of the knee who already were scheduled for KA. According to our results, the herein described treatment regime appears to be safe and effective at twelve months follow-up.

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