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EUROVISCO Good Medical Practice Recommendations for the Use of Viscosupplementation with Hyaluronic Acid in the Management of Knee Osteoarthritis

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Abstract

Objective: Viscosupplementation (VS) by intra-articular injections of hyaluronic acid (HA) is a commonly used treatment of knee osteoarthritis. However, there are no clear recommendations for its use in clinical situations not usually addressed in therapeutic guidelines. *Design*: Members of the European Viscosupplementation Consensus Group (EUROVISCO), made up of rheumatologists, orthopedic surgeons, and rehabilitation physicians from seven European countries, were asked to make a therapeutic decision on 30 clinical scenarios based on their clinical experience and data from the literature, using the Delphi method. For each scenario, the strength of agreement and the level of consensus were calculated by the chairman of the group. *Results*: The expert panel reached consensus on 18 of the 30 clinical scenarios proposed. According to the experts, the factors that most influence the decision to use VS with HA to treat knee osteoarthritis are the nature and severity of symptoms, the presence of comorbidity, the absence of therapeutic alternatives, and the patient's refusal to undergo knee arthroplasty. Obesity and an advanced radiological degree of osteoarthritis have been identified as the two main factors for poor response to VS with HA and should be considered before any decision is made to viscosupplement. *Conclusion*: This set of recommendations, based on common clinical scenarios, is intended to help practitioners make decisions about HA VS in patients with osteoarthritis of the knee.

Keywords

clinical scenario, knee, osteoarthritis, hyaluronic acid, viscosupplementation, EUROVISCO, recommendations

Introduction

Osteoarthritis (OA) is the leading cause of disability among the older population with worldwide[1,2] The incidence of knee OA (KOA) is constantly increasing due to the longevity of population and the increasing obesity, especially in Western countries.[3] Treatment for OA is multimodal, and its goal is to relieve pain and improve knee function. The basic treatment consists of three main non-pharmacological modalities: education in OA, weight reduction if appropriate, and physical activity.[4]

Regarding their safety profile topical non-steroidal anti-inflammatory drugs (NSAIDs) can be considered as first line of pharmacological treatment for relieving knee pain in OA.[5] If there is no response and the patient has no contraindications, oral NSAIDs, intra-articular (IA) corticosteroids or hyaluronic acid (HA) can be prescribed.[4-7] IA steroids are indicated in the presence of inflammatory signs (i.e., pain at rest, joint effusion)[8] and viscosupplementation (VA) with HA in moderate OA and when there is no inflammatory flare-up.[5]

However, HA treatment in KOA remains controversial, with some meta-analysis and guidelines supporting its use and others not.[4] In general, recommendations have been formulated based on a review of randomized clinical trials

including patients who are not representative of all the clinical phenotypes encountered in daily medical practice.[9]

The European Viscosupplementation Consensus Group (EUROVISCO) is a working group of European experts on OA that aims to provide consensus recommendations on the use of VS in the treatment of this condition. In this article, the EUROVISCO expert group examined different clinical scenarios from their daily clinical practice. Based on the analysis of these cases, they recommended whether HA VS should be used or not and what are the factors influencing this decision. These real-life situations are missing from the global international recommendations, which only state if a treatment can be used or not without giving precision on the indications and the factors that influence the rate of success.

Methods

The EUROVISCO working group was composed of 12 members from seven European countries (Belgium, France, Germany, Italy, Spain, Sweden, and Turkey). This was a multidisciplinary panel of practitioners specializing in musculoskeletal system disorders. Seven of them were rheumatologists (JM, XC, AM, DB, PR, HB, and TC), three were orthopedic surgeons (JJ, RR, and MB), and finally two were physical therapy and rehabilitation specialists (YH and DD). All were experienced in clinical research, cumulatively authoring more than 600 PubMed-referenced publications concerning OA. All have a clinical practice and have been performing VS and/or research on VS for more than 15 years.

Thirty clinical scenarios were proposed by the experts based on their experience and data from the literature and debated during working sessions. For each scenario, the members of the working group had to evaluate if they would recommend HA VS or not, and justify their response by identifying the criteria that influenced it. The vote was conducted anonymously using interactive software (Quizzbox©, Clermont-Ferrand, France), via voting handsets for those in-person or by smartphone for those participating online. Results of the vote were therefore available in real-time for the group. The degree of consensus was calculated by the chairman of the group (TC) from the percentage of experts choosing one of the two options. It was classified as "unanimous" if 100% of experts chose the same option; it was classified as "high" if 11 to nine experts chose the same option, it was considered as "moderate" if eight of experts chose the same option, and finally, "low" if seven or six experts choose the same option. Finally, it was classified as "no consensus" if fewer than six experts chose the same option. After each question, the answers were aggregated, shared with the group, and discussed, and, if necessary, additional Delphi rounds were organized in real-time during the consensus meeting. Recommendations for the different clinical conditions have been scripted based on the responses with a "unanimous, high, or moderate" consensus.

Results

Details of the clinical scenarios and degrees of consensus are given in Table 1.

Among the 30 scenarios, 21 received full or partial consensus and are listed below:

1. Male, 48 years old with medial meniscectomy 2 years previously, playing badminton and jogging 3 times a week with mild to moderate pain while walking (4/10) but no pain at rest. The x-ray was normal at the time of meniscectomy but now shows grade 1 medial tibiofemoral OA (TFOA).

Degree of Consensus*: Unanimous in Favor of HA VS*

Comment: The experts underlined the importance of a careful analysis of risk factors of OA progression. In this particular case, meniscectomy and joint space narrowing worsening since the meniscus surgery were the most important factors considered by the experts for the treatment

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Table 1. EUROVISCO: Clinical Scenario for Viscosupplementation.

1a	Male, 48 years, medial meniscectomy 2 years before, badminton and jogging 3x/week, pain 4/10, x-ray: medial TFOA grade 1 Oarsi, Rx pre-op normal	Yes	Unanimous
1b	Male, 48 years, medial meniscectomy 2 years before, badminton and jogging 3x/week, asymptomatic, x-ray: medial TFOA grade 1 OARSI, RX pre-op normal	No	Unanimous
2a	Male, 29 years, lateral meniscectomy 5 years before, professional footballer, asymptomatic, x-ray: lateral TFOA grade 2 OARSI, worsening of JSN compared 1 year ago	Yes	Low
2b	Male, 29 years, lateral meniscectomy 5 years before, professional footballer, asymptomatic, x-ray: lateral TFOA grade 2 OARSI, no worsening of JSN compared 1 year ago	No	Low
2c	Male, 29 years, lateral meniscectomy 5 years before, professional footballer, mild pain and effusion after match, x-ray: lateral TFOA grade 2 OARSI, no worsening of JSN compared 1 year ago	Yes	Unanimous
3a	Female, 43 years, cycling and swimming 1x/week, x-ray: medial TFOA grade 3, pain 3/10, paracetamol and NSAIDs effective and well tolerated, no wants per os treatments	Yes	High
3b	Female, 43 years, cycling and swimming 1x/week, x-ray: medial TFOA grade 3, pain 3/10, paracetamol and NSAIDs effective but poorly tolerated, no wants per os treatments	Yes	Unanimous
3b	Female, 43 years, cycling and swimming 1x/week, x-ray: medial TFOA grade 3, pain 3/10, paracetamol and NSAIDs effective and well tolerated, started treatment with glucosamine sulfate 1,500 mg/day	Yes	No consensus
4a	Female, 71 years, x-ray: lateral TF and PFOA grade 4, since 6 months pain 8/10 without effusion, walk 200 m with crutches, paracetamol ineffective, NSAIDs contraindicated, refuse prosthesis	Yes	Unanimous
4b	Female, 71 years, x-ray: lateral TF and PFOA grade 4, since 6 months pain 8/10 without effusion, walk 200 m with crutches, paracetamol ineffective, NSAIDs contraindicated, not opposed prosthesis soon	No	Unanimous
4c	Female, 71 years, x-ray: lateral TF and PFOA grade 4, since 6 months pain 8/10 without effusion, walk 200 m with crutches, paracetamol ineffective, NSAIDs contraindicated, not opposed prosthesis postpone	Yes	Unanimous
5a	Female, 81 years, x-ray: lateral TF and FP OA grade 3, KOA moderately symptomatic for 5 years, walk 3 to 4 km/day, pain 6/10, paracetamol effective (2 g/day)	Yes	Unanimous
5b	Female, 81 years, x-ray: lateral TF & FP OA grade 3, KOA slightly symptomatic for 5 years, walk 3-4 km/day, pain 2/10, paracetamol effective (0.5g/day)	No	Moderate
5c	Female, 81 years, x-ray: lateral TF and FP OA grade 3, KOA moderately symptomatic for 5 years, walk 3-4 km/day, pain 4/10, paracetamol weakly effective (2 g/day)	Yes	High
6a	Male, 64 years, no comorbidity, BMI = 25, x-ray: KL 1, pain only running after 5 km (5/10), US: mild chronic effusion	Yes	High
6b	Male, 64 years, no comorbidity, BMI = 29, genu varum, x-ray: KL 1, pain only running after 5 km (5/10), US: mild chronic effusion	Yes	No consensus
6c	Male, 64 years, no comorbidity, BMI = 29, genu varum, x-ray: KL 3, pain only running after 5 km (5/10), US: mild chronic effusion	Yes	High
7a	Female, 37 years, pain when going up and down stairs, NSAIDs effective and tolerated, x-ray: trochlear dysplasia, MRI: patellar chondropathy and mild synovial effusion	No	Low
7b	Female, 18 years, pain when going up and down stairs, NSAIDs effective and tolerated, x-ray: trochlear dysplasia, MRI: patellar chondropathy and mild synovial effusion	No	High
8a	Female, 64 years, obesity (BMI = 34), arterial hypertension, type 2 diabetes, moderate pain walking (6/10), NSAID contraindication, x-ray: moderate medial TFOA (KL grade 3)	Yes	Unanimous
8b	Female, 64 years, morbid obesity (BMI = 46), arterial hypertension, type 2 diabetes, moderate pain walking (6/10), NSAID contraindication, x-ray: moderate medial TFOA (KL grade 3)	Yes	High
9a	Female, 91 years, arterial hypertension, renal failure, heart failure, diabetes, severe pain walking (8/10), NSAID, opioids, and surgery contraindication, x-ray: severe medial TF and FP OA (KL grade 4)	Yes	Unanimous
9b	Female, 91 years, no significant comorbidity, coumadin treatment after stroke recovered without sequelae, severe pain walking (8/10), x-ray: advanced medial TF and FP OA (KL grade 4)	Yes	Unanimous
9c	Female, 80 years, no significant comorbidity, BMI = 27, coumadin treatment after stroke recovered without sequelae, severe pain walking (8/10), x-ray: advanced medial TF and FP OA (KL grade 4)	No	High
10a	Male, 78 years, arterial hypertension, dyslipidemia, aspirin after stroke recovered without sequelae, x-ray: mild medial TFOA (KL grade 2), severe pain walking (8/10) treated with TA IA injection 2 months ago, pain since TA 2/20	Yes	Low
10a	Male, 78 years, arterial hypertension, dyslipidemia, aspirin after stroke recovered without sequelae, x-ray: mild medial TFOA (KL grade 2), severe pain walking (8/10) treated with TA IA injection 2 months ago, pain since TA 5/20	Yes	Unanimous
11a	Female, 58 years, no comorbidity, no treatment, bilateral knee pain (3-5/10) treated BD IA injection 6 months ago, pain since BD intermittent < 3/10, x-ray: mild PFOA (KL grade 2), begs for VS	Yes	Moderate
11b	Female, 58 years, no comorbidity, no treatment, bilateral knee pain (3-5/10) treated BD IA injection 6 months ago, pain since BD intermittent < 3/10, x-ray: normal, MRI: lateral meniscopathy with little lateral FT BML, begs for VS	Yes	No consensus

DC = degree of consensus; NSAID = non-steroidal anti-inflammatory drug; TA = triamcinolone hexacetonide; BD = betamethasone dipropionate; VS = viscosupplementation; EUROVISCO = European Viscosupplementation Consensus Group.

decision. The analysis of these factors led to a unanimous decision to treat this patient with HA VS, both to relieve symptoms and to slow the progression of OA, although, in this particular case, no study had demonstrated a structural effect of VS with HA.

2. Male, 48 years old with medial meniscectomy 2 years ago, playing badminton and jogging, three times a week, asymptomatic knee and x-ray showing grade 1 medial TFOA (mild JSN and osteophytes) while pre-op x-ray was normal.

Degree of Consensus: *Unanimous against HA VS*

Comment: The experts recommended in that case frequent monitoring of the radiological evolution of knee osteoarthritis. They also stressed that, in the absence of pain, HA VS was not appropriate.

3. A 29-year-old professional soccer player with lateral meniscectomy 5 years ago and mild pain and clinically evidenced effusion, 2 days after each game. The x-rays showed grade 2 lateral TFOA (OARSI score, moderate JSN, and osteophyte). No worsening of JSN compared with 1 year ago.

Degree of Consensus: *Unanimous in Favor of HA VS*

Comment: The presence of a risk factor for OA progression (meniscectomy, professional athlete), the presence of moderate pain and radiological signs of knee osteoarthritis were the key elements that helped the experts decide to treat this patient with KOA.

4. A 43-year-old woman, cycling and swimming once a week with pain rated 3/10 on VAS relieved by paracetamol and NSAIDs. The x-ray showed a grade 3 medial TFOA (OARSI score, moderate JSN, and large osteophyte). She no longer wants oral treatments.

Degree of Consensus: *High in Favor of HA VS*

Comment: If a patient does not want oral treatment and prefers an IA injection, the doctor must consider the wish.

5. A 43-year-old woman with pain rated 3/10 on the VAS and relieved by paracetamol and NSAIDs. However, these drugs are poorly tolerated by the patient. She goes cycling and swimming once a week. Her x-ray showed grade 3 medial TFOA (OARSI score, moderate JSN, and large osteophytes). She no longer wants to continue oral treatments.

Degree of Consensus: *Unanimous in Favor of HA VS*

Comment: The entire working group considered that the poor tolerance of oral treatment justified its discontinuation and replacement by VS, one of the main advantages of which is its excellent tolerance.

6. A 71-year-old woman with lateral TFOA and patellofemoral osteoarthritis (PFOA) (x-ray K&L grade 4, moderately symptomatic for 5 years [pain 4/10 on VAS with analgesic]). For 6 months, the pain has gradually increased to 8/10 on VAS. She cannot walk more than 200 m with two crutches. Paracetamol is ineffective and NSAIDs are contraindicated. She refuses the prosthesis.

Degree of Consensus: *Unanimous against HA VS*

Comment: In this case, a total knee replacement is recommended. Nevertheless, experts underline that the patient's choice is of paramount importance and must be respected.

7. A 71-year-old woman with radiological KL grade 4 TF and PFOA. The knee has been moderately symptomatic for 5 years (VAS pain 4/10 with analgesic). For the last 6 months, the pain has gradually increased from 4 to 8/10 without joint effusion. She cannot walk more than 200 m with two crutches. Paracetamol is ineffective and NSAIDs are contraindicated. She agrees to a prosthetic replacement as soon as possible.

Degree of Consensus: *Unanimous against HA VS*

Comment: TKR must be considered as soon as possible.

8. A 71-year-old woman with radiological lateral TF and grade 4 PFOA on the KL scale. KOA has been moderately symptomatic for 5 years (pain 4/10 on VAS with analgesic). For 6 months, the pain gradually increased to 8/10 on the VAS without joint effusion. She cannot walk more than 200 m with two crutches. Paracetamol is ineffective and NSAIDs are contraindicated. She concurs with a joint replacement but wishes to postpone it.

Degree of Consensus: *Unanimous in Favor of HA VS*

Comment: Although the success rate is lower in the case of advanced knee osteoarthritis, VS can be tried to relieve pain for a few months, until the patient decides to undergo surgery.

9. An 81-year-old woman still active with grade 3 lateral TF & FP OA, moderately symptomatic for 5 years. She can easily walk more than 3-4 km, every day. VAS pain on walking is 6/10. Paracetamol (2 g/day) is effective.

Degree of Consensus: *Unanimous in Favor of HA VS*

Comment: The patient met all required criteria for an appropriate VS decision: symptomatic KOA, active patient, walking pain > to PASS (Patient Acceptable Symptom State) threshold and taking painkillers. Limited use of pain killers is an objective of HA VS.

10. An 81-year-old active woman with x-rays showing lateral TF and PFOA grade 3 on the KL scale. KOA has been moderately symptomatic for 5 years. She can easily walk more than 3-4 km every day. Walking pain is 2/10 on VAS and paracetamol is very effective (0.5 g/day)

Degree of Consensus: *Moderate against HA VS*

Comment: The experts' decision was based on the level of walking pain, which is very low and controlled with a mild dose of paracetamol.

11. An 81-year-old active female with radiographs showing lateral TF and grade 3 PFOA. KOA has been moderately symptomatic for 5 years. She can easily walk more than 3-4 km every day. Pain on walking is measured at 4/10 on the VAS by the patient. Paracetamol is weakly effective (2 g/day, three times a week).

Degree of Consensus: *High in Favor of HA VS*

Comment: the patient fulfills the required criteria for HA VS, which are moderate KOA, active patient, and acceptable walking pain reaching the PASS threshold.[10]

12. A 64-year-old man with no comorbidity (BMI = 25) and radiological KL 1 TFOA (tibial osteophyte, no JSN). No pain in daily activities. Pain was scored 5/10 on VAS by the patient only after running 5 km. Ultrasound shows mild effusion.

Degree of Consensus: *High in Favor of HA VS*

Comment: Experts recommended VS concurring that an osteophyte is sufficient to confirm the diagnosis of KOA in a 64-year-old subject. Pain on exertion and especially joint effusion, even minimal, are evidence of active OA that requires treatment.

13. A 64-year-old man without comorbidity but BMI of 29 and knee malalignment (genu varum). The x-ray shows a KL 3 TFOA (tibial osteophyte, moderate JSN). No pain during daily activities is reported but pain appears after running 5 km (5/10 on VAS). Mild effusion is visible on ultrasound.

Degree of Consensus: *High in Favor of HA VS*

Comment: In the present case, OA is radiologically proven and there are two major risk factors for OA progression (overweight and knee malalignment).

14. An 18-year-old female with anterior pain (6/10 on VAS) while ascending and descending stairs and squatting. NSAIDs are well-tolerated and effective. The x-ray is normal except for major trochlear dysplasia. MRI shows patellar chondropathy and mild synovial effusion.

Degree of Consensus: *High against HA VS*

Comment: The majority of experts favored the continuation of NSAIDs and rehabilitation considering that the evidence for the effectiveness of HA in that case is insufficient.

15. A 64-year-old obese woman (BMI = 34) with hypertension and type 2 diabetes. There is moderate pain on walking (VAS = 6/10) and NSAIDs are contraindicated. The x-ray shows moderate medial TFOA (KL grade 3).

Degree of Consensus: *Unanimous in Favor of HA VS*

Comment: Given its excellent risk/benefit ratio, VS is a very well-suited treatment for patients with comorbidities and/or risks of drug intolerance.

16. A 64-year-old woman with morbid obesity (BMI = 46), hypertension and type 2 diabetes. Moderate pain when walking (VAS = 6/10) is reported. NSAIDs are contraindicated. The x-ray shows a moderate median TFOA (grade KL 3)

Degree of Consensus: *High in Favor of HA VS*

Comment: The majority of the experts considered VS a first-line treatment in patients with comorbidities even if the chances of success were low due to significant obesity.

17. A 91-year-old woman with hypertension, renal failure, heart failure and diabetes. Significant pain when

walking (VAS = 8/10) is reported. The use of NSAIDs, opioids, and surgery are contraindicated. The x-ray shows a severe median TF and a PFOA (grade KL 4).

Degree of Consensus: *Unanimous in Favor of HA VS*

Comment: In elderly patients with multiple comorbidities and contraindications to surgery, the use of VS is all the more justified as there are few alternative solutions.

18. A 91-year-old woman without comorbidity. She is being treated with coumarin after a stroke that recovered without sequelae. She has severe bilateral knee pain on walking (VAS = 8/10) and advanced medial TF and PFOA (KL grade 4) on x-ray.

Degree of Consensus: *Unanimous in Favor of HA VS*

Comment: In very elderly patients, the working group unanimously considered that it is unreasonable to propose a total knee arthroplasty before having tried all the other therapeutic procedures, including VS. The benefit/risk ratio makes it an appropriate solution for the elderly and frail subjects.

19. An 80-year-old woman with no comorbidity and a BMI of 27. She was treated with coumarin after a stroke that recovered without sequelae. Severe bilateral knee pain when walking (VAS = 8/10) has been reported. The x-ray shows advanced medial TF and OA FP (grade KL 4).

Degree of Consensus: *High against HA VS*

Comment: The recommended experts did not recommend SV, as surgery should be considered the most appropriate treatment.

20. A 78-year-old man with hypertension and dyslipidemia, on aspirin after a stroke who recovered without sequelae. The x-ray shows a slight medial TFOA (grade KL 2). Severe bilateral knee pain on walking (VAS = 8/10) is reported. He was treated with an IA injection of triamcinolone hexacetonide 2 months ago. The pain remains at 5/10 on the VAS despite the corticosteroid injection.

Degree of Consensus: *Unanimous in Favor of HA VS*

Comment: In patients with comorbidities and moderate KOA who responded partially to IA corticosteroid injection, VS is considered the most appropriate treatment by all members of the working group.

21. A 58-year-old woman without comorbidity suffering from bilateral knee pain on walking (3-5/10) and treated with an IA injection of betamethasone dipropionate 6 months ago. A weak intermittent pain after a long walk (<3/10) is reported by the patient since the corticosteroid injection. Mild PFOA (KL grade 2) was evident on x-rays. She would like a VS because her husband was happy with it.

Degree of Consensus: *Moderate in Favor of HA VS*

Comment: Despite the benign clinical and radiological characteristics of this OA, the experts considered that the patient's choice to be treated with HA should be considered. They recommend informing the patient of other possible pharmacological and non-pharmacological therapeutic modalities and letting her choose the treatment.

Discussion

VS as a therapeutic alternative for the management of KOA remains controversial.[11] The French Society of Rheumatology stated that IA injections of HA can be offered, without expecting a chondroprotective effect, in cases of symptomatic KOA without or with minimal effusion.[5] The ESCEO (European Society of Clinical and Economical Aspects for Osteoporosis, Osteoarthritis, and Musculoskeletal Diseases) working group affords a recommendation on the use of HA VS in patients who have contraindications to NSAIDs, or if the patient is still symptomatic despite the use of NSAIDs.[12] The American College of Rheumatology conditionally recommended against IA HA injections in patients with KOA while for the Osteoarthritis Research Society International (OARSI) use of HA VS was conditionally recommended in individuals with KOA with or without gastrointestinal or cardiovascular comorbidities or even widespread pain or depression. The word "conditionally" was associated with a low effect, heterogeneous data, or poor quality of the study. However, these therapeutic guidelines failed to consider individual characteristics that may influence the response to HA VS.[12–14] This global approach is regrettable, as it excludes a proportion of patients who could benefit from HA VS. A more patient-centered approach to HA VS, considering individual patient characteristics, would enable a better selection of patients potentially responsive to this treatment. To give an example, it is well established that HA VS is less efficient in obese patients with advanced radiological grades.[15–17] In general, clinical trials with HA in KOA include patients with intermediate radiological grades and moderate/high pain grades but exclude, advanced stages,

young patients under 40, elderly patients over 80 as well as subjects with multiple comorbidities, mainly for safety reasons.[18]

As the treatment recommendations are based on these studies, they are hardly applicable in real life and do not give recommendations for special cases, such as obese patients with or without comorbidities or with multiple concurrent treatments. These guidelines also failed to consider patients with low radiological grades or with very advanced radiological grades. They also excluded subjects with low pain or asymptomatic and those who practice sports or have undergone surgical meniscectomy.[19–21]

To fill this gap, a series of cases not included in clinical trials but often encountered in everyday medical practice were submitted to a panel of HA VS experts. Thirty clinical scenarios were submitted to these experts who had to recommend in favor or against the use of HA VS.

The first question addressed was the use of HA according to the radiological severity of OA knee. The experts recommended HA VS for patients with radiological KL grade 1 TFOA but only if they are symptomatic. In patients with severe TFOA (KL grade 4), HA VS was recommended only in patients with significant pain and loss of function and who declined or wanted to delay knee replacement surgery.

Few studies assessed HA VS in patients with lateral TFOA. In such cases, the EUROVISCO experts recommended HA VS in patient with symptomatic KOA and moderate radiological severity (grades 2/3) especially in those with lateral meniscectomy. In the case of high-grade lateral TFOA, the experts recommended the use of VS only when conventional treatments are inadvisable and when the patient refuses to undergo knee arthroplasty. In the case of PFOA, experts recommend using HA VS when patients have residual pain after IA steroids. However, in the case of major trochlear dysplasia, the panel of experts was against the use of HA VS.

The use of HA VS in recreational and professional athletes is common in daily practice despite the lack of scientific evidence in these cases. Our expert panel recommends the use of HA VS, not so much to prevent progression but to alleviate symptoms in patients who present with knee pain, impaired knee function and/or joint effusion. Meniscectomy is recognized as one of the risk factors for the progression of OA.[22] However, the experts across the presented clinical scenarios recommended VS only in patients who had symptoms. Even though there is scientific evidence that recognizes obesity as a poor prognostic factor when treatment with HA is indicated, our panel of experts did recommend the use of VS in overweight or obese patients with comorbidity and in the presence of risk factors for disease progression.

Table 2 summarizes the main factors influencing, for or against, the use of HA VS in patients with knee OA.

Table 2. Factors Influencing, for or Against, the Use of Hyaluronic Acid Viscosupplementation in Patients with Knee Osteoarthritis.

	HAVS decision-making criteria	
In favor of HAVS		Against HAVS
x	Risk factor of OA progression	
x	Tibiofemoral JSN progression	
x	Low or moderate radiological TFOA	
	Severe radiological TFOA	x
x	Low or moderate radiological PFOA	
	Severe radiological PFOA	x
x	Low to mild pain	
x	Severe pain	
x	Mild effusion	
	Large effusion	x
	Obesity	x
	Patient's wish to follow oral treatment	x
x	Patient's wish to stop oral treatment	
x	Bad tolerance of oral treatments	
x	Response to IA CS	
	The patient wishes to knee prosthesis	x
x	Contraindication to surgery	
x	Presence of comorbidities	
	Limited walking distance	x
x	Active patient	

HAVS = viscosupplementation; JSN = joint space narrowing; TF = tibiofemoral; OA = osteoarthritis; PF = patellofemoral; IA = intra-articular; CS = corticosteroid.

We recognize that our approach suffers from certain methodological limitations that could affect the strength of the recommendations. First, a limited number of experts participated in the Delphi exercise. Second, some medical disciplines were under-represented, such as orthopedic surgeons, and others were not consulted, such as sports medicine specialists. It is also clear that some scenarios are missing, such as osteoarthritis patients with knee flessum or with significant loss of muscle performance as in the case of sarcopenia. However, despite these limitations, these case-based recommendations can help doctors make decisions in the most frequent cases of their daily practice.

Conclusion

Through different clinical cases, our panel of experts has made a series of recommendations based on real clinical practice.

The factors that most influence the indication for VS in any circumstance are the presence of symptoms, comorbidity, the lack of therapeutic alternatives, and the patient's refusal to undergo knee arthroplasty.

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Ethical Considerations

Patient involvement: This review did not require an ethical board approval because patients were not involved in the design or conduct or reporting or dissemination plans of this research.

Patient Consent for Publication

Not required.

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