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Platelet Rich Plasma use in Tendon Injuries

Abstract

Chronic tendon injuries and tendon tears afflict everyone from grandparents to teenagers, and pro athletes to afternoon joggers. Everyday use can wear at tendons and cause small tears which lead to inflammation and pain [Plantar Fasciitis]. Larger tears can happen in a variety of different circumstances, but usually occur when an individual performs sharp turns, twists, and stops. Depending on the location of the injury, tears can severely hamper daily activities as they result in intense pain, swelling, and reduced range of motion. Often times, surgery is used to mend tears and removed inflamed tissue in order to let a patient heal. However, surgery can take weeks or months to heal and runs the risk of reducing a patient's movement later in life. Platelet Rich Plasma, an autologous blood product, is promoted as a possible alternative to surgery for healing tendon injuries. Though there have been several clinical trials, most have produced interesting but unverifiable data.

CORE Orthopedic Medical Center is a clinic which treats orthopedic injuries and runs clinical trials. Doctors commonly use Platelet Rich Plasma as a treatment in their clinics, outside of any research study. Over the course of three years, CORE Orthopedic Medical Center has tracked patient results after Platelet Rich Plasma injections. Data from these studies was analyzed and constructed based on notes from phone call interviews with patients. As such, data is difficult to quantify and is entirely subject to bias. A patient may have considered a treatment effective, while a physician could argue that the

injury healed of its own accord. Additionally, almost 50% of patient data was lost to the inability to contact patients for follow up conversations. However, there is still valuable information that can be found from an evaluation of the patient's medical history following the PRP treatment. While Platelet Rich Plasma may enhance the healing process of an injury, data shows that it is only an effective alternative to surgery for certain tendon injuries. Of the five general areas of injection, only elbow injections showed improvement. Injections of PRP for the treatment of the tendons in the foot, knee, shoulder, and the achilles tendon are not showing signs of efficacy. However, in order to truly evaluate the efficacy of Platelet Rich Plasma treatment in tendon injuries, or in any clinical use, further case studies are necessary.

Introduction

Throughout the rigors of an individual's daily life, it is only reasonable to expect that they will injure themselves at some point. It happens to everyone. The real challenge is how to treat injuries in the way that is most beneficial to the patient. The goal of medical care has not changed through the years, yet the methods have. When it comes to severe tendon injuries, surgery is often seen as one of the only solutions. However, surgery is like a tattoo: it is not guaranteed to make the situation better and, once performed, it cannot be undone. Surgery, while not usually the primary response to an injury, is resorted to once other treatments have failed.

Unfortunately, in the world of tendon injuries, there are limited treatments which vary in efficacy from patient to patient. For example, one patient troubled with tennis elbow may find his or her symptoms completely relieved with physical therapy and a few weeks off; someone else might not. Regardless of whether the patient is a professional athlete or a middle aged accountant, his or her goal

will be to reach previous levels of mobility as soon as possible. After months of failed treatment, surgery may become appealing, solely because it presents an opportunity for the patient to return to normal life.

Also like a tattoo, surgery can seem like a reasonable option when someone is in his or her twenties, but can have serious repercussions with age. One example of this is a common knee injury. Occasionally, when someone performs a difficult turn or falls on their knees, the piece of padding between the upper and lower bones of the leg can be pinched and torn, like getting a finger caught in a door jam. As one can imagine, having a piece of this padding, called cartilage, torn and flapping around inside the knee can be very painful. Surgery is usually the go to treatment for this kind of injury, as the cartilage won't heal itself [Pujol, Nicolas, MD, Etienne Salle De Chou, MD, Philippe Boisrenoult, MD, and Philippe Beaufils, MD]. Depending on the size of the lesion and its location, different kinds of procedures can be performed. However, there are certain tears that can not be sewn back together; they are usually removed completely. The damaged cartilage is shaved off in a procedure called subtotal meniscectomy [Cole, Brian J., M. Mustafa Gomberawalla, MD, and Jon K. Sekiya, MD]. There is still cartilage left once the surgeon is finished, but not enough to withstand the wear and tear of life for another sixty years. This surgery just set a young patient up for early arthritis.

Treatments for tendon injuries are not always capable of addressing the needs of the patient. The methods used to treat orthopedic injuries range widely, from surgical procedures to rest and relaxation. However, there are many cases where a patient sustains an injury that is difficult to treat. These include certain meniscal tears and even forms of tendonitis [Dines, Josh, MD, and Rock Positano, MD]. Tendonitis is the inflammation and irritation of the fibrous connective tissue which joins muscle and bone. A patient with tendonitis will experience a dull ache that increases to a sharp pain when the affected tendon is used or touched [Pietrangelo, Ann, and Brenda B. Spriggs, MD]. This is a

condition which commonly affects athletes and can prevent them from continuing participation in their sport. Achilles tendonitis is accountable for almost 20% of injured runners and effectively takes them out of competition [DeHeer, Patrick, DPM, and Stephen M. Offutt, DPM, MS].

The current methods of treatment for tendonitis include RICE, an acronym which stands for rest, ice, compression, and elevation. If that is insufficient and does not relieve pain, a patient can expect the injured site to be stabilized, worked in physical therapy, injected with corticosteroids, or operated upon. If more moderate treatments, such as RICE or physical therapy, provide no relief, the patient may decide on surgical procedures or injections. Are there better alternatives? Yes.

When evaluating for treatments to soft tissue injuries, a patient is looking for several basic attributes: mainly little risk with the possibility of a timely reward. Patients should not have to trade efficacy for six weeks of their life, as there is a great deal of post operative recovery time involved before a patient can do even simple activities [Knowledge Center: Patient]. Platelet rich plasma, a treatment which is rapidly gaining popularity, has the potential to become the primary treatment for a variety of soft tissue injuries. This treatment is fast acting, non-invasive, and best of all, completely composed of the body's own healing cells.

Background

Platelet rich plasma, or PRP, is to normal blood the way an espresso shot is to coffee. People who want an espresso shot are looking to get very specific, concentrated benefits from their morning drink. Likewise, researchers and doctors are looking for really concentrated benefits from blood, so they isolate PRP. Platelet rich plasma is exactly what it sounds like, plasma with a greater concentration of platelets than normally identified within the human body. Platelets are the small colorless ovals that

float around in the bloodstream and are famous for their ability to clot wounds. The platelets are suspended in plasma similar to the way pulp floats around in thick orange juice. Plasma itself is a slightly pale yellow color and makes up more than half of blood, the other portion being cells. Most every elementary school kid learned that platelets clot, but what most people don't know is how important they are in helping a wound heal. Platelets contain growth factors, the building blocks of cell regeneration.

The process to create platelet rich plasma is relatively simple, because it is just a portion of the patient's blood. [Sports Medicine] It all revolves around a very simple principle: heavy things float to the bottom. For example, if rocks, water, and oil are all put into a bottle, they separate into layers. The rocks are much heavier and denser than both the water and the oil, so they go directly to the bottom. The oil is lighter and less dense than the water, so it floats to the top. Whole blood is very similar, but with red blood cells, platelets, and plasma instead. When the blood is centrifuged, the red blood cells are heaviest, so they make up the bottom layer. Next come a thin layer of platelets and then the plasma floats to the top. The plasma and platelets are sucked out with a pipet, and stored in another tube. Then the blood is spun again to get all of the platelets.

Once the PRP is injected into the injury, it also acts like a beacon. Not only do platelets carry growth factors and help wounds clot, they also make sure that every other cell in the body knows there is an injury. This means all the passing immune and stem cells cluster to help repair. [Properties and Clinical Applications] A certain type of stem cell called mesenchymal stem cells always group around platelets. Mesenchymal stem cells are like specialists because they have the right equipment to help heal injuries. These stem cells can turn into bone, muscle, and cartilage cells, which is what is usually damaged in an injury. [Stem Cells] Fibroblasts also help build connective tissue, but they are more like

concrete; they can only be one building block, but they're going to do that really well. [News Medical Fibroblast] Seeing as the body also needs to be protected from infection when healing, macrophages are drawn to platelets just in case microbes got into the body through whatever caused the injury.

[News Medical Macrophage]

Since its first use in 1950, platelet rich plasma has been helping patients get back into their everyday lives. Due to the fact that PRP can be administered without the permanent negative consequences of surgery or other treatments, it has been widely experimented with. It has been utilized to treat everyone from grandmothers to pro athletes with varying degrees of success. With the media enumerating the revolutionary success of platelet rich plasma, fact must be separated from fiction. Does PRP actual work, and more importantly, is it a viable alternative to surgery for tendon injuries?

Materials and Methods

Patients at CORE Orthopedic Medical Center were injected with Platelet Rich Plasma as treatment for a variety of tendon injuries. The majority of patients received injections in the elbow for conditions such as epicondylitis, but treatment was administered for everything from plantar fasciitis to achilles tears. The patients were evaluated after approximately a year and a half after their treatment by way of a phone conversation. Approximately eighteen participants out of thirty two treated individuals were successfully contacted and interviewed as to the effect of their treatment. Each patient was questioned as to whether he or she still experienced symptoms from the tendon injury that was treated, as well as if he or she would undergo PRP therapy again. Though eighteen patients is a relatively small and seemingly insignificant number of people, there is still much that can be learned from their experiences and opinions.

This study was conducted at CORE Orthopedic Medical Center in Encinitas, California over the course of three years. CORE Orthopedic Medical Center is a clinic which treats orthopedic injuries ranging from osteoarthritis to sports injuries. CORE is also a research site which recruits patients for studies proposed by outside corporations. For example, when a company develops a new surgical procedure and is in stage two clinical trials, the company will reach out to sites. These sites are chosen based upon the surgeons who practice there, the facilities available, and the previous history of the site. Once a clinic makes an agreement with the company to run the trial, the doctors at said clinic begin the recruitment of patients. All procedures are conducted at the site and any adverse events are monitored by the research coordinator. However, as PRP has passed clinical trials and is no longer an experimental treatment, CORE Orthopedic Medical Center administers it regularly to patients, although outcomes are still monitored.

This study is the accumulation of patient responses to Platelet Rich Plasma methods, between one and two years post injection. The use of PRP treatment in this scenario was not a part of a formal research study conducted at CORE Orthopedic Medical Center. All patients involved chose this form of treatment alongside their doctor with the hope that it would potentially relieve their symptoms. As such, the treatment was administered in the typical fashion, as an injection of the autologous blood product directly into the injury.

The data was analyzed and constructed based on notes from phone call interviews with patients. As such, data is difficult to quantify and is entirely subject to bias. A patient may have considered a treatment effective, while a physician could argue that the injury healed of its own accord. Additionally, almost 50% of patient data was lost to the inability to contact patients for follow up conversations. However, there is still valuable information that can be found from an evaluation of the patient's medical

history following the PRP treatment. Did the patient seek out additional treatment? Was this treatment surgical? How does that connect with the type of injury? Many ligament tears generally require surgical procedures to remedy, however tennis elbow surgeries are much more rare. If the patient suffered from tennis elbow and eventually went in for surgery, the PRP would be determined to be less effective than if the patient with an achilles tendon tear had surgery.

Although there is error associated with this method of data collection, it was the most effective form of research given the time and financial constraints. In order to be a recognised study, patients would need to be blinded as to their form of treatment, placebo versus PRP, and followed over several years with more frequent contact and higher retention rates.

Results

This study produced data and numbers which can be used to summarize the effects of Platelet Rich Plasma on certain tendon injuries. A total of 18 people were surveyed, which was only 50% of the total number of people who received treatment. There were 9 injuries and areas treated, including injuries in the right elbow, left foot, left knee, left elbow, right achilles, right foot, right shoulder, and several cases of right lateral epicondylitis and left plantar fasciitis. That totaled to four foot injuries, ten elbow injuries, two knee injuries, one shoulder injury, and one achilles injury. In terms of complete efficacy, only two patients with lateral epicondylitis reported PRP injections to be entirely successful. Half of all study participants reported that the treatment caused no change in their symptoms. 50% of patients also said that they experienced a positive result from their injections. Only one patient with lateral epicondylitis reported a negative effect. 33% of patients went in for surgery after treatment, mostly patients complaining of elbow pain. One third of elbow patients went in for surgery, while both

the shoulder and achilles patients went in for surgery, along with one of two patients suffering from a tendon injury in the foot.

Discussion

While Platelet Rich Plasma may enhance the healing process of an injury, data shows that it is only an effective alternative to surgery for certain tendon injuries. Of the five general areas of injection, only elbow injections showed improvement. However, 50% of treated injuries showed improvement after injection with the PRP, which is significant enough a number to assume that the treatment has healing potential. Although the initial interest in PRP did arise from its potential as a complete alternative to surgery, all previous trials have shown limited success [Harmon, Kim, MD]. At first glance, 50% may seem like a reasonable number that speaks to relative success of the injection. However, this means that a patient is, in essence, flipping a coin as to how effective his or her treatment will be. This study, as limited as it was, has gone to show that PRP cannot claim to be a viable alternative to surgery, which is 90% effective [Tennis Elbow (Lateral Epicondylitis)]. Despite the results from treatment on tendon injuries overall, PRP is shown to have higher success rates and greater benefits when injected in certain sites.

Platelet Rich Plasma injections have the most success when used to treat epicondylitis. Chronic Lateral epicondylitis, commonly known as tennis elbow, comes from overuse and can cause the patient a great deal of pain. Though commonly associated with sports such as tennis, epicondylitis can be caused by a wide range of movements and repetitions, such as those done by painters or carpenters. Pain is usually localized on the outside of the elbow, where the muscles of the forearm attach to tendons which allow the elbow to bend and flex.

As the limited data shows, PRP injections for epicondylitis seem to be the most effective out of all groups treated. Ten patients were treated for this overuse injury, and only 30% needed surgery after their injections. 20% of patients reported complete healing from the PRP treatment, while 40% sought additional non-surgical procedures. These follow up treatments, such as corticosteroid injections, were not designed to heal the injury, only relieve symptoms. Although it may seem that these secondary treatments show that the PRP injection was not effective, the truth may actually be surprising. These patients did require more treatment to manage their pain, but they did not resort to surgery in order to deal with the actual injury. Therefore, these cases carry the possibility of healing from the Platelet Rich Plasma injection itself. This could be proven by imaging of the injuries whereas phone interviews cannot offer conclusive evidence.

Injections of PRP for the treatment of the other sites surveyed are not showing signs of efficacy. Other treatment sites are the tendons in the foot, knee, shoulder, and the achilles tendon. There was only one patient who received treatment for a shoulder injury, however this patient was administered three individual doses and reported no improvement. The patient had a tear, and eventually went in for surgery, after PRP treatment was determined to be completely ineffective. Plantar fasciitis and injuries in the ankles made up most of the tendon issues patients who received treatment in their feet. Plantar fasciitis is characterized by intense heel pain and stiffness in the foot which originates from small tears in the tendon which connects the heel and the ball of the foot [Plantar Fasciitis]. Although no patient reported a negative result from treatment, 75% claimed that they experienced no change whatsoever. Overall, approximately 28% of patients said that they did not experience any effects whatsoever from PRP. Additionally, 78% of patients who had injuries in locations other than the elbow, went in for other treatment, including surgery.

There are several possible reasons for a difference in results between epicondylitis and other tendon injuries. In particular, the torn tendon in the shoulder presents a strong case for the hypothesis that Platelet Rich Plasma is not capable of healing a tear. When a muscle or tendon is stressed continuously, it cannot heal. That is why surgery is necessary, because sutures are used to hold together two pieces. Despite the numerous reasons why PRP does induce healing, it is not capable of holding two pieces of tendon together in order for growth to occur. However, in overuse injuries such as tennis elbow, the tendon is still intact and therefore PRP is more effective.

The practical use for PRP in tendon injuries is in conjunction with surgery. The International Cellular Medicine Society displays a study by researchers within the group, which shows that PRP is quite effective in speeding the healing time of postoperative acute muscle tears [Harmon, Kim, MD]. In addition, the aforementioned case study on horizontal meniscus tears shows that surgery with PRP has faster healing times than surgery alone. This is especially true in many acute injuries which stop healing after 12 months. If the injury has not mended itself by then, blood flow often no longer permeates damaged tissues [Harmon, Kim, MD]. Similar to how the PRP aides meniscal healing, because certain areas are avascular, use of this treatment in conjunction with surgery on old injuries should produce similar results.

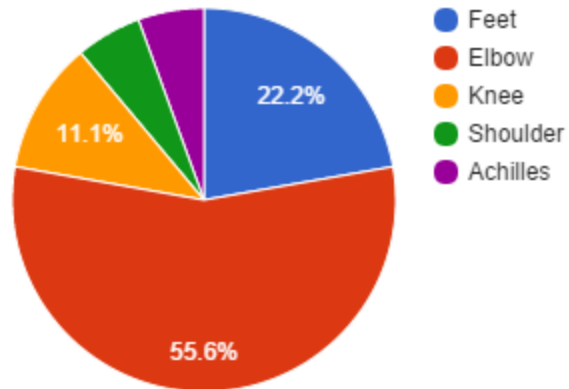
However, in order to truly evaluate the efficacy of Platelet Rich Plasma treatment in tendon injuries, or in any clinical use, further case studies are necessary. Very few randomized and blinded clinical trials have been performed as of yet, which means that the treatment has not been properly evaluated [Paoloni J, and B Hamilton]. In order to prove the ability of PRP to treat tendon injuries alone or alongside surgery, studies need to be conducted which have higher retention rates, a greater study population, and incorporate placebo injections. Higher retention rates mean that more study patients

report the effects of treatment for a longer period of time. As was obvious from this data set, a small group is incapable of providing unbiased data. 75% failure for a treatment is an important number, but if it means that three of four people had unsuccessful injections, that number becomes irrelevant.

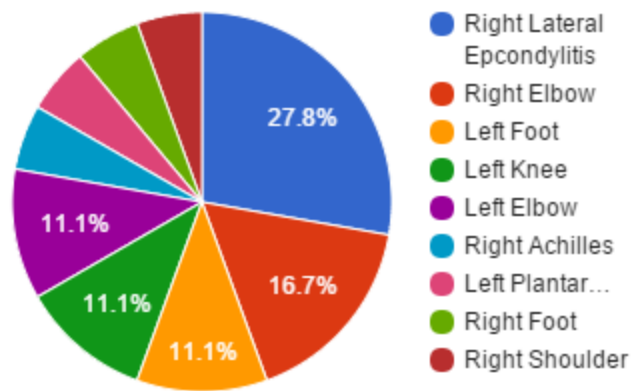
Additionally, studies need to incorporate a placebo injection, or no injection at all, in order to determine whether the injury would have healed without the PRP. There is promise in this treatment, but more comprehensive studies need to be conducted before any conclusions may be drawn.

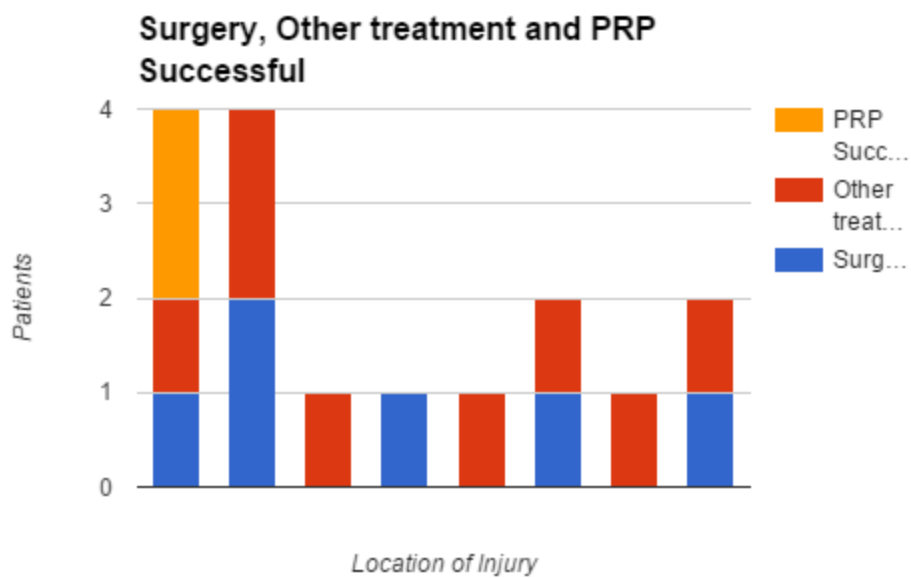
Appendix

Areas of Injuries and Injections



Areas of Injuries and Injections





	Number	Surgery	Other treatment	PRP Successful	Positive result	Negative result	No Change	Pain at Injection
Right Lateral Epicondylitis	5	1	1	2	2	1	2	2
Right Elbow	3	2	2		3		1	1
Left Foot	2		1				2	1
Left Knee	2	1			2			2
Left Elbow	2		1		1		1	
Right Achilles	1	1	1				1	1

Left Plantar								
Fasciitis	1				1			
Right Foot	1		1				1	2
Right								
Shoulder	1	1	1				1	
Total	18	6	8	2	9	1	9	9
Feet	4		2		1		3	3
Elbow	10	3	4		6	1	4	3
Knee	2	1			2			2
Shoulder	1	1	1				1	1
Achilles	1	1	1				1	
Total	18	6	8		9	1	9	9

Evidence of Efficacy

The purpose of this review is to evaluate the efficacy of platelet rich plasma. In order to be effective, PRP has to do one thing and one thing only: it has to heal injuries. Whether or not PRP actually accomplishes this is difficult to discern from just one case study. Just like the way in which Newton discerned that gravity existed by watching its effects repeated exactly on multiple objects, PRP

must show similar results in a variety of different cases with different factors. Newton established that gravity existed and had constant properties because the apples always fell down, never up. Though medical treatment is affected by more factors than Newton's apple, PRP must still show its ability to improve healing in multiple cases and provided comparable outcomes to surgery.

Repair of Horizontal Tears of the Meniscus

Platelet rich plasma use in surgeries for young patients produced higher success rates than patients who underwent surgery without platelet rich plasma.

The meniscus provides vital support and stabilization to the knee. The meniscus is composed of two "C" shaped pieces of cartilage located between the tibia and femur to cushion the joints. Together, both the lateral meniscus on the outer side of the knee and the medial meniscus on the inner side absorb approximately 30% of any impact to the knee and provide stabilization.[OA Meniscus] The majority of the meniscus is avascular, with the majority of the vascular areas in the outer rim.[MedicineNet Torn Meniscus] This means there is little to no blood flow to certain areas and the cartilage does not bleed when injured.

However, when the meniscus sustains a tear or other damage, the entirety of knee function is affected. The femur usually slides smoothly over the surface of the meniscus and pain is caused when the femur catches on a tear.[MedicineNet Torn Meniscus] What was a smooth surface now catches in the event of movement. The inflammatory response is usually apparent as fluid accumulation occurs within mere hours of the injury. This fluid may prevent normal flexion of the knee joint, which results in a limitation on movement. Occasionally, the patient experiences minor symptoms that do not directly point to a tear. However, in extreme cases, the tear may fold over on itself and prevent the knee from bending

or straightening beyond 15°-30°. In addition, the patient may hear popping or clicking sounds from the knee when it bends or straightens.[MedicineNet Torn Meniscus] In many cases, a torn meniscus restricts the activities of the patient and causes pain in daily activities.

There are multiple instances in which the meniscus can be torn. Injury commonly occurs when the femur pinches the meniscus when a forceful pivot or stop is performed, which is called a traumatic meniscus tear. Traumatic tears can be radial, vertical, horizontal, oblique, or complex. However, the meniscus sustains wear and loses approximately 20% of previous blood flow as a patient ages.[MedicineNet Torn Meniscus] These tears are quite common, found in 60% of the population over the age of 65.[Medscape] In this situation, when the previously compromised meniscus tears it is called a degenerative tear. For the purpose of this study, the focus will be on horizontal traumatic tears of the meniscus.

Horizontal lesions are often more difficult to repair surgically than vertical tears [Pujol, Nicolas, MD, Etienne Salle De Chou, MD, Philippe Boisrenoult, MD, and Philippe Beaufils, MD]. Horizontal lesions often span both the vascular and avascular areas, especially when the patient is young. Due to the low probability that these lesions will be successfully repaired, subtotal meniscectomy, in which the damaged portions of the meniscus are removed, is a common procedure. However, this procedure leaves the meniscus at a greater risk of deteriorating and subsequent flattening of the articular cartilage surface, the cartilage that covers the tibia and femur to form a joint.[Pujol, Nicolas, MD, Etienne Salle De Chou, MD, Philippe Boisrenoult, MD, and Philippe Beaufils, MD]. The meniscus can be preserved by attempting to repair these tears can be repaired with sutures, however there is still the issue of insufficient blood flow to the lesion. For this reason, the injection of platelet rich plasma into the surgical site has the potential to encourage successful healing of the tear.

Study Procedure

In order to verify the efficacy of PRP in the repair of horizontal tears of the meniscus, researchers injected PRP into the surgical site after meniscal repair through open approach arthrotomy. The effect on the healing of the lesion was then evaluated over one year with MRI scans and knee examinations. This study was performed by Nicolas Pujol, Etienne Salle De Chou, Philippe Boisrenoult, and Philippe Beaufils.

The study group consisted of thirty four individuals between the ages of thirteen and forty with horizontal meniscal tears, in which 65% had meniscal cysts. The average lesion size was between 28 and 30 mm and patients were only accepted with grades II and III lesions. In order to participate in this study, patients must have sought alternative medical treatment for their injury, which had not been effective for six months. To insure that pain and ability to move could be properly monitored, the patient was denied for any other knee injuries such as ACL or PCL injuries, advanced osteoarthritis, and concomitant chondral injuries, which is damage to the articular cartilage. This study group was then split into two groups of seventeen, one which would receive the PRP injection, Group 1, and one group which would not, Group 2.

Both groups were operated on in the same manner and received identical physical therapy regimens. Initially, both groups underwent diagnostic arthroscopy in order to evaluate the situation. Only grade III lesions could be identified through diagnostic arthroscopy, and any fragments of cartilage or fibrous tissue was removed during this procedure. The actual repair was performed through posteromedial mini-arthrotomy, also known as the open approach. This procedure required the surgeon to open and enlarge an arthroscopy portal on the inside middle (on a right knee, this would be the left

side) of the knee.[Sports Medicine] From there, the surgeon scraped the meniscus and stitched it vertically. In Group 1, the surgeon then injected the lesion directly with 5 ml of PRP before closure. Group 2 was not injected and the mini-arthrotomy portal was closed.

Study Results

The patients were monitored and evaluated after their operations through several different methods. Primarily this study evaluated patient recovery through the 2000 International Knee Documentation Committee, or IKDC, examination score at twenty four months following the operation. After one year, an MRI was taken to evaluate the hypersignal of the knee, however the scans were difficult to interpret as hypersignal is persistent. The table below shows the results of the study. Active flexion describes the degree to which the patients are able to bend their knees while failure is described as the patient having to seek further surgeries as this procedure did not reduce his or her pain and increase mobility.

	Group 1	Group 2
Active Flexion	135°	130°
Number of patients who got an IKDC of A	10	9
Number of patients who got an IKDC of B	6	5

Number of patients who got an IKDC of C	1	2
Median IKDC	90.7	87.9
Failure Rate	5.8%	11.8%

Overall, the researcher who conducted this study considered it to be a success for PRP, as the subjects in Group 1 healed more rapidly with fewer adverse effects than Group 2 [Pujol, Nicolas, MD, Etienne Salle De Chou, MD, Philippe Boisrenoult, MD, and Philippe Beaufils, MD]. In addition, the results from Group 2's repair of a horizontal lesion was consistent and comparable to results from the repair of vertical lesions, which are considered to maintain a higher success rate.

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