Editorial Commentary: Platelet-Rich Plasma: The Devil Is in the Details, and the Details Need to Be Better Reported

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Abstract: The use of biologics may be the next big revolution in sports medicine since the use of the arthroscope. However, we are currently in the infancy of both the understanding of biologics in sports medicine and in the methods we are employing to evaluate their efficacy. As surgeons undertake further studies to elucidate the efficacy of platelet-rich plasma in the treatment of a variety of sports medicine pathologies, adherence to minimum guidelines such as the minimum information for studies evaluating biologics in orthopedics will help to clarify the true benefits of platelet-rich plasma and allow colleagues to reproduce these therapies in their respective practices.

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In the Level IV study, "Outcomes of Anterior Cruciate Ligament Reconstruction Using Biologic Augmentation in Patients 21 Years of Age and Younger,"[1] Berdis, Veale, and Fleissner report on 143 patients who underwent a primary hamstring anterior cruciate ligament (ACL) reconstruction coupled with a platelet-rich plasma (PRP)/collagen membrane augmentation. At an average duration of follow-up of 52 months, their KT-1000 side-to-side difference averaged 1.2 mm. Revision ACL reconstructions were performed in 5% of patients, whereas 15% of patients tore their contralateral ACL. Because this was a Level IV study, and also due to the fact that the contents of the PRP were not quantified, caution must be used in interpreting this data.

The senior author (R.F.L.) has been a big proponent of pushing the use of evidence-based medicine to promote biologic augmentation for the healing of sports medicine–related injuries.[2] He also has advocated that the use of biologics should be the next big revolution in sports medicine since the use of the arthroscope. With that in mind, this study reports that ACL reconstruction with a hamstring autograft coupled with PRP (incorporated within a porous collagen membrane) decreased the rate of ipsilateral ACL re-tears in these young patients, and it also was interpreted that these young patients were able to return to activities sooner than current peer-reviewed literature reports. Thus, the question about this study is whether it is embarking on the quest for the Holy Grail or if the study may not be reproducible by others. Only time will tell in terms of how this question can be answered. In addition, there are some important points to review regarding this study to put the author's findings in perspective.

It is well recognized that the use of biologics to augment healing is in its infancy. In general, we started using biologic products to try to augment healing far before we understood what the components of the products were and what specific growth factors influence different pathologies. In addition, there are a limited number of Level I studies that can definitively determine whether the use of biologics is contributing to improved outcomes, if the reported outcomes are solely a type 1 error, or if there is a huge placebo effect involved in a study's reported outcomes. Certainly, all of us want to see these products work, and many of us already use them with the full knowledge that, although they may do no harm, they may do no good

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either. As we delve further into the use of biologics, it is important that we do this in a scientific manner to ensure that we have truly identified if and how these products make a difference in healing or recovery times for our patients.

In particular, use of the minimum information for studies evaluating biologics in orthopedics guidelines has been promoted as a way to ensure transparency of preparation methods and product components, and to ensure that other physicians may replicate the biologic treatments that demonstrate favorable patient outcomes.[3] Also, a recent systematic review has noted that the vast majority of studies using PRP are not able to be replicated by others because of the lack of information that is presented in their peer-reviewed papers.[4] Thus, it behooves us to ensure that more basic science and clinical studies are performed and that we truly have Level I studies to ensure that the true benefits of biologics are able to be discerned.

There are some important things to recognize about biologics. First, outside the use of leukocyte-poor PRP for osteoarthritis,[5] there are not a lot of clinical studies that have shown that biologics work in the knee. In particular, the use of PRP in an animal model of medial collateral ligament found that at best it did not affect healing for an acute grade III medial collateral ligament tear, and high levels of platelets in the PRP were actually detrimental to healing.[6] In addition, the largest Level I study to date to report on the use of PRP for the treatment of patellar tendinopathy found that neither leukocyte-rich nor leukocyte-poor PRP demonstrated a therapeutic advantage compared with saline. Both PRP preparations did, however, correlate with increased negative side effects.[7]

Obviously, the results of these 2 studies were very disappointing for the advancement of biologics in treating sports injuries. However, they do point to the fact that further studies are needed because we are effectively injecting some type of primordial soup into the knee or surrounding knee structures, and there are both anabolic and catabolic factors that can affect healing for different pathologies. The use of a more patient-specific PRP, with specific cytokines or growth factors knocked out for treating different knee conditions, may better direct the biological healing potential of PRP for different pathologies such as meniscal healing, articular cartilage resurfacing, and patellar tendinopathy.[8]

Although the present study could certainly be demonstrated by others to be valid in future studies, there are some points that need to be addressed in biologics research to ensure that we are providing the best care for our patients. Among other essential criteria described by the minimum information for studies evaluating biologics in orthopedics guidelines, the methods of PRP preparation and the product components (platelets, leukocytes, and red cells) with their respective concentrations were not reported in the present study by Berdis et al. Thus, others cannot duplicate this study as it is presented. In addition, the authors injected activated PRP into the tunnels, which has been reported in the literature to provide no clear prevention of widening. Bone tunnel administration of PRP has therefore not been recommended.[9,10] Another finding reported in this study was that patients could return back to their activities considerably sooner. Because the devil is in the detail in terms of what was contained in the PRP soup, caution must certainly be exercised when considering this timeline of return to sport until further information is validated by others before performing similar studies. In line with this concern, the contralateral ACL tear rate of 15% could indicate that the shorter rehabilitation timeline precluded patients from obtaining appropriate proprioception, strength, and endurance to return back to activities, which may have led to their contralateral ACL failure. For comparison, a 2016 meta-analysis examined second ACL injury rates of young athletes who underwent ACL reconstruction without PRP supplementation. Within a follow-up time ranging from 2 to 15 years, the meta-analysis found a contralateral ACL injury rate of 12% and an ipsilateral re-tear rate of 10% when young athletes returned to sport.[11] Although the present study demonstrates improved ipsilateral re-tear rates at an average follow up time of 52 months, the early beneficial outcomes of the operative knee are functionally negated by an increased contralateral ACL tear rate.

In conclusion, there will be multiple upcoming studies reporting on the use of biologics to treat multiple sports medicine pathologies. It is our responsibility to ensure that while we are attempting to advance science as we investigate biologics use in the knee, we are also providing appropriate documentation to make certain we are truly seeing a benefit from their use. We all look forward to the time when we can further optimize our patients' ability to heal their injuries and reconstruction grafts to allow an accelerated timeline of return to activities. Whether biologics is the answer to this still remains to be determined.

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