

Systematic Review

The Effect of Platelet Concentrates on Graft Maturation and Graft-Bone Interface Healing in Anterior Cruciate Ligament Reconstruction in Human Patients: A Systematic Review of Controlled Trials

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Purpose: To systematically review the current evidence for the effects of platelet concentrates on (1) graft maturation and (2) graft-bone interface healing in anterior cruciate ligament (ACL) reconstruction in human, controlled trials and for ensuing differences in clinical outcomes. **Methods:** A systematic search of PubMed, CINAHL (Cumulative Index to Nursing and Allied Health Literature), Embase, Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews was performed for controlled trials of human ACL reconstruction with and without platelet concentrates. Data validity was assessed, and data were collected on graft maturation, graft-bone interface healing, and clinical outcome. **Results:** Eight studies met the inclusion criteria. Seven studies reported on graft maturation with significantly better outcomes in the platelet groups in 4, and there were large differences in means in an additional 2 studies. Five studies reported on tunnel healing, and 4 found no difference between groups. Three studies assessed clinical outcome but found no differences, regardless of whether they had shown a beneficial effect (1 of 3) or no effect (2 of 3) of platelets on graft and tunnel healing. **Conclusions:** The current best evidence suggests that the addition of platelet concentrates to ACL reconstruction may have a beneficial effect on graft maturation and could improve it by 20% to 30% on average, but with substantial variability. The most likely mode of action is that treatment with platelets accelerates graft repopulation and remodeling, and this interpretation is supported by the existing data and is biologically plausible. However, the current evidence also shows only a very limited influence of platelet concentrates on graft-bone interface healing and no significant difference in clinical outcomes. **Level of Evidence:** Level III, systematic review of Level I, II, and III studies.

Platelet concentrates are a popular tool in clinical orthopaedics and orthopaedic research.^{1,2} As a rich source of growth factors, platelets are used in fracture healing, in spine fusion, as local injections in

tendinopathies, and as adjuncts in tendon repair procedures.³⁻¹⁰ One promising field of platelet concentrate use is sports medicine.^{1,2} Platelets, often in combination with scaffolds, are used in the management of

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anterior cruciate ligament (ACL) ruptures and rotator cuff tears.^{11,12} A number of new tissue engineering-based regenerative treatments, such as bioenhanced ACL repair, are being investigated,^{11,12} but in this study we want to focus on the effectiveness of clinically available platelet-based treatments for the ACL.

The current gold standard for treating ACL tears is ACL reconstruction, using autogeneic or allogeneic tendon grafts.^{13,14} Although a number of techniques for tendon preparation and fixation are available, all methods share a common postoperative scenario consisting of 2 main biologic processes: graft-to-bone healing in the femoral and tibial tunnels^{15,16} and ligation of the intra-articular portion of the tendon graft.^{17,18} The success of ACL reconstruction depends heavily on these processes, and to improve their outcomes and ensure optimal clinical results, platelet concentrates are being used. The rationale behind the use of platelets is the assumption of improved tunnel healing and faster and/or better graft remodeling as a result of the growth factors released from activated platelets.^{1,19,20} It was the aim of this study to systematically review the current literature for evidence that would substantiate this assumption.

The primary objective of this study was to systematically accrue evidence for the effects of platelet concentrates on (1) graft maturation and (2) graft-bone interface healing in ACL reconstruction in human, controlled trials. Our primary hypothesis was that the addition of platelet concentrates improves both graft maturation and graft-bone interface healing.

Furthermore, data were collected for clinical outcomes, if provided in the same studies, to assess associations between differences in clinical outcome and differences in maturation and interface healing based on platelet use. We hypothesized that the improvement in graft maturation and graft-bone interface healing would be reflected in improved clinical function in the immediate postoperative phase.

METHODS

This systematic review was performed following the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) statement.²¹ The PRISMA statement (www.prisma-statement.org), put forward by the CONSORT (Consolidated Standards of Reporting Trials) Group (www.consort-statement.org), is an evidence-based guideline for conducting and reporting systematic reviews and was formerly known as the

QUOROM (Quality Of Reporting Of Meta-analysis) statement.²²

Eligibility Criteria

Studies were included if they reported on graft maturation and/or graft-bone interface healing in human patients undergoing ACL reconstruction augmented with platelet concentrates. All types of ACL reconstruction were eligible. Platelets could be applied as a liquid or gel, with or without a carrier scaffold to the graft or tunnel(s), or both, at the time of surgery. Studies with repeated applications, postoperative injections, or combination of platelets with other chemicals or bioactive reagents (growth factors, cytokines, and so on) were not eligible. Animal studies were not eligible. No limit was set for minimum follow-up duration because it is sensible to assume the effects of platelet concentrates to be strongest in the short-term and to plateau in the long-term. Reporting of clinical data was searched for but not an inclusion criterion.

Data Sources

The online databases PubMed, CINAHL (Cumulative Index to Nursing and Allied Health Literature), Embase, Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews were searched for relevant publications. All dates and languages were included. The last search was performed on May 1, 2011.

Search Strategy

The search algorithm was “((((ACL) OR (anterior cruciate ligament)) AND (reconstruction)) OR (ACL reconstruction)) AND platelets” and was replicated using the keywords as MeSH terms as well. The search algorithm was intentionally kept fairly general to maximize return. All searches were unlimited, that is, considering publications in all languages and regardless of publication date. In addition to the online searches, the bibliographies of the included studies were reviewed to identify additional publications.

Study Selection

Studies were excluded if title and abstract clearly refuted eligibility. Full texts were obtained for all studies matching the inclusion criteria and all with unclear eligibility. The obtained full texts were reviewed to reconfirm eligibility. All study selections

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