Comparison of In Vitro and In Vivo Complement Activation by Metal and Bioabsorbable Screws Used in Anterior Cruciate Ligament Reconstruction

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Purpose: The purpose of the study was to evaluate the biocompatibility of polylactide (PLLA) screws in comparison with standard metal screws for fixation of the patellar tendon graft in human anterior cruciate ligament (ACL) reconstruction. **Methods:** A total of 41 patients (22 women and 19 men) were prospectively randomized for the use of metal interference screws (20 patients) or biologically resorbable PLLA screws from Linvatec, Largo, FL (21 patients). Average age at the time of surgery was 26 years (15 to 51 y). Synovial fluid and plasma were collected preoperatively and after 6 weeks in both groups. Plasma was analyzed for C5a and synovial fluid, as well as for terminal SC5b-9 complement complex (TCC) and interleukin (IL)-8. At 1 year after surgery, serum was incubated with metal, PLLA, and no screws; this was followed by analysis of C5a after 1 and 6 hours of incubation. Inflammatory mediators were measured through enzyme-linked immunosorbent assay (ELISA). **Results:** In the BioScrew group, 4 patient samples showed high C5a concentration in synovial fluid after 6 weeks, but no statistically significant difference was observed between the 2 groups ($P = .11$). One patient in the BioScrew group had a high TCC value after 6 weeks, but no statistically significant difference was seen between the 2 groups ($P = .20$). In the in vitro study, no increased C5a generation was observed in sera incubated with a BioScrew or a metal screw compared with controls. **Conclusions:** No statistically significant difference was observed between the BioScrew and metal screw groups concerning C5a, TCC, and IL-8 formation. However, some patients in the BioScrew group showed elevated values. **Level of Evidence:** Level II, prospective randomized trial. **Key Words:** ACL reconstruction—Bioabsorbable interference screw—Polylactic acid—Complement activation—Patellar tendon graft

Metal screws have been used for several years for graft fixation of anterior cruciate ligament (ACL) reconstruction with bone-patellar tendon-bone (BPTB) grafts. Because the screws will be left in the bone and difficulties may be encountered when one revises a reconstruction with metal interference screws, a bioabsorbable screw has been developed. The use of this material for interference screws has potential benefit if the problems of inflammation are minimal and the fixation properties are sufficient. Many of these patients are young and prefer to have an implant that will disappear over time. A biochemical pullout study[1] comparing bioabsorbable with metal screw fixation showed no significant differences. However, Kocabey et al.[2] found unacceptable displacement of the semitendinosus graft after fixation with a bioabsorbable screw.

Other potential advantages for use of bioabsorbable screw fixation include a diminished need for hardware

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The BioScrews used in this study were provided free of charge by Linvatec, Largo, Florida.

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removal and simplification of revision surgery. Postoperative magnetic resonance imaging (MRI) diagnostics also are made easier without artefacts from metal.[3] Warden et al.[4] found that all but 1 of the BioScrews (19 of 20) was evident in all serial scans after 24 months. These showed minimal decrease in size over time. The 1 screw that had completely disappeared 8 months after reconstruction had cracked during insertion. Friden[5] reported a case of severe synovial reaction to biodegradable rods used for fixation of osteochondritis dissecans of the knee, and Smith et al.[6] described fractures of the screws on insertion. Tegnander et al.[7] showed that the C5a concentration in plasma incubated in the presence of polylactic acid was found to be higher than in plasma incubated in the absence of polylactide (PLLA). Activation of the alternative pathway of the complement system may occur when blood or other bodily fluids are exposed to foreign substances. Therefore, complement analyses are being used to evaluate the biocompatibility of biomaterials. C3a, C4a, and C5a are polypeptides that are enzymatically cleaved from their parent complement components during complement activation.[8,9] C5a is the most biologically potent of these peptides; it is capable of inducing a series of cellular and humoral proinflammatory responses and is a very potent neutrophil chemoattractant. The soluble terminal SC5b-9 complement complex (TCC) is the final activation product generated when complement is activated. Both the C5a assay[8] and the TCC assay[10] used in the present study are based on monoclonal antibodies to neoepitopes expressed in the activation product but concealed in the native components, enabling direct, selective, and sensitive detection of complement activation that is superior to previously described assays based on nonneoepitope techniques.

The purpose of this study was to compare the biocompatibility of bioabsorbable screws with that of metal screws through the use of synovial fluid complement activation (C5a and TCC), cytokine release (interleukin [IL]-1β, IL-8, and IL-10), and C-reactive protein (CRP) as readouts. Furthermore, investigators sought to determine whether in vitro incubation of the 2 types of screws in serum was associated with differences in complement-activating potential.

METHODS

This was a level II, randomized, controlled trial. The inclusion period extended from June 6, 2000, to November 21, 2001. A total of 41 patients (22 women and 19 men) were prospectively randomized for the use of metal interference screws from Linvatec, Largo, FL (20 patients) or biologic resorbable PLLA screws, also from Linvatec (21 patients). Patients were randomized according to the envelope method. Those with isolated ACL-deficient knees or ACL rupture with minor meniscal lesions and cartilage lesions (Outerbridge grade I and II) were included, as were patients who needed partial meniscectomy; those who needed meniscal repairs were excluded.

All patients underwent reconstruction with a bone-patellar tendon-bone graft (BPTB) procedure performed endoscopically. Blood sampling and synovial fluid aspiration were carried out before surgery was begun. Plasma samples were analyzed for CRP and C5a. Preoperative synovial fluid and synovial fluid collected after 6 weeks were analyzed through measurements of C5a, TCC, IL-1β, IL-8, and IL-10. Serum samples were collected 1 year after the time of surgery for the biocompatibility studies. One patient in the BioScrew group was lost to follow-up.

Two surgeons performed surgery at the Department of Orthopaedic Surgery, Trondheim University Hospital. Follow-up was conducted by a single investigator. Informed consent was obtained from all patients. The study was approved by The Regional Ethics Committee.

Surgical Technique in ACL Reconstruction With BPTB Graft

This procedure was carried out with the use of a tourniquet with the patient under epidural or general anesthesia. After diagnostic arthroscopy was completed with assessment and, if necessary, treatment of the menisci, randomization between metal and BioScrews was carried out by means of the closed envelope system. Standard endoscopic ACL reconstruction with BPTB graft was performed with metal or bioabsorbable interference screw fixation.

Rehabilitation

The rehabilitation program was aggressive and was handled in the same manner in both groups[11]; the same 2 physiotherapists supervised both groups. Immediately after the operation had been completed, patients began knee movement, and full passive extension of the knee was carried out several times a day. No brace was used. Full weight bearing was allowed as soon as it could be tolerated. Closed-chain exercises with full extension and flexion of the knee were allowed as early as possible. After 6 months,