Patholaxity (Ligamentous) Issues

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Introduction

Successful treatment of knee ligament injuries emanates from the recognition of specific ligament tear patterns differentiated among multiligament knee injuries, along with the awareness of potentially subtle findings regarding symptoms of significant knee pathology [1]. Identifying concomitant injury patterns associated with specific injuries can aid in an accurate diagnosis and, furthermore, define the treatment that is necessary to adequately return patients to their previous forms of activity through kinematic reestablishment. Restoration of stability in knee kinematics is important, because in the incidence of an inaccurate diagnosis, failure to reconstruct torn structures that play a role in stability will induce more restraint upon the other remaining structures. The posterolateral corner (PLC) consists of structures that act as primary and secondary stabilizers in stability of the knee, and lack of addressing an absent PLC in anterior cruciate ligament (ACL) reconstructions has been shown to be the leading cause of ACL graft failure [2]. Greater awareness of severe injuries such as these has increased along with documented multiligamentous injuries, especially with injuries involving the ACL and PLC [3].

Procedures failing to diagnose and subsequently to restore the native anatomical and kinematic characteristics, stemming from incorrect graft placement or incomplete ligamentous restoration of deficient knees, can have dire consequences upon outcomes, further affecting knee pathology. This chapter focuses on ligamentous injuries sustained by the knee and the resultant outcomes of osteoarthritis (OA) following the variable treatment options used for isolated and concomitant injuries.

Anterior Cruciate Ligament (ACL)

Junkin et al. estimated 400,000 ACL injuries occur annually in the United States [4]. Furthermore, following ACL reconstruction (ACLR), the progression of OA can be as prevalent as 25% at 5 years, further breaching occurrence as high as 41% and 79%, at 7 and 13 years, respectively [5]. These rates of OA are important to consider when counselling a patient with an ACL injury, because it can lead to loss of range of motion and/or swelling upon activity, but more

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importantly could cause concomitant damage upon neighboring structures, which poses a significant issue for the population of young, active patients. Causation of OA can be associated to variable issues including graft malposition and the approach of single bundle (SB) rather than double-bundle (DB) reconstruction, which ultimately fails to restore anatomical and kinematic features relative to the intact knee [6]. Literature on concomitant ACL injuries remains disconnected among short- and long-term outcomes, but the assumption can be made that the incidence of OA increases as greater effects on biomechanics of the knee occur [2, 6–11]. Reconstruction is highly recommended in patients with instability because injured ACLs are unable to be restored without reconstruction, and to date the outcomes of repair are inconsistent; native anatomic restoration must be the primary goal in reducing the risk of OA.

Concomitant Posterior Lateral Corner (PLC) Injury

The PLC consists of three major static stabilizers including the fibular (lateral) collateral ligament (FCL), the popliteus tendon (PLT), and the popliteofibular ligament (PFL) [12]. The FCL and popliteus complex (PLT and PFL) provide secondary stabilization in external rotation, with the FCL providing primary restraint near extension and the popliteus complex providing greater restraint as flexion increases [12].

In recent years, the PLC has become more known in identification of injury and treatment options available. By imaging the anteromedial femoral condyle, medial compartment bone bruises are frequently found in patients with both acute isolated and combined PLC injuries [8]. The presence of a medial compartment bone bruise is therefore a strong indicator for the occurrence of a PLC injury [8]. Kannus et al. described the lateral ligament compartment and differential compensation for static instability accounted for between grade II and grade III sprains [13]. Dynamic stabilization of knee muscles and tendons compensated for static instability following grade II sprains; however, grade III sprains were found to have a severe amount of ligamentous laxity which would lead to posttraumatic osteoarthritis [13] (Fig. 8.1).

LaPrade et al. confirmed that grade III posterolateral injuries do not heal and that operative management is required to treat ligamentous laxity, which could lead to medial compartment arthritis if left untreated [10]. Furthermore, in cases of concomitant ACL injuries, failure to restore the PLC adequately has been shown to significantly increase force load upon grafts of ACLRs, compared to knees with an intact PLC [14] (Fig. 8.2).

Treatment

Following injury, ACL deficiency alters tibiofemoral cartilage contact points and can result in altered articular cartilage contact stresses [15]. ACL injury causes translation of the tibia in both anterior and medial directions [15]. Medial translation causes a lateral shift of the contact points in the medial and lateral compartments, ultimately altering stress distributions in the tibiofemoral cartilage that could lead to degenerative arthritis [15].

A study by Defrate et al. compared the use of anatomical graft placement with anteroproximal placement on the femur, using tibial tunnel-independent and transition techniques, respectively, and then measured the resultant knee kinematics [6]. By comparing these values to an intact ACL knee, orientation and length of the ACL graft during in vivo loading would then show the ability of each procedure to restore natural knee kinematics [6]. Overall, Defrate et al. found that anteroproximal femoral graft placement resulted in longer ACL grafts and had a relatively vertical orientation in both sagittal and coronal planes, while graft placement that greater resembled the native anatomy resulted in a more accurate restoration of length and orientation [6]. Relative to native ACL features, anteroproximally placed ACL grafts were oriented more vertically during knee flexion, 0–60° and 30–90°,

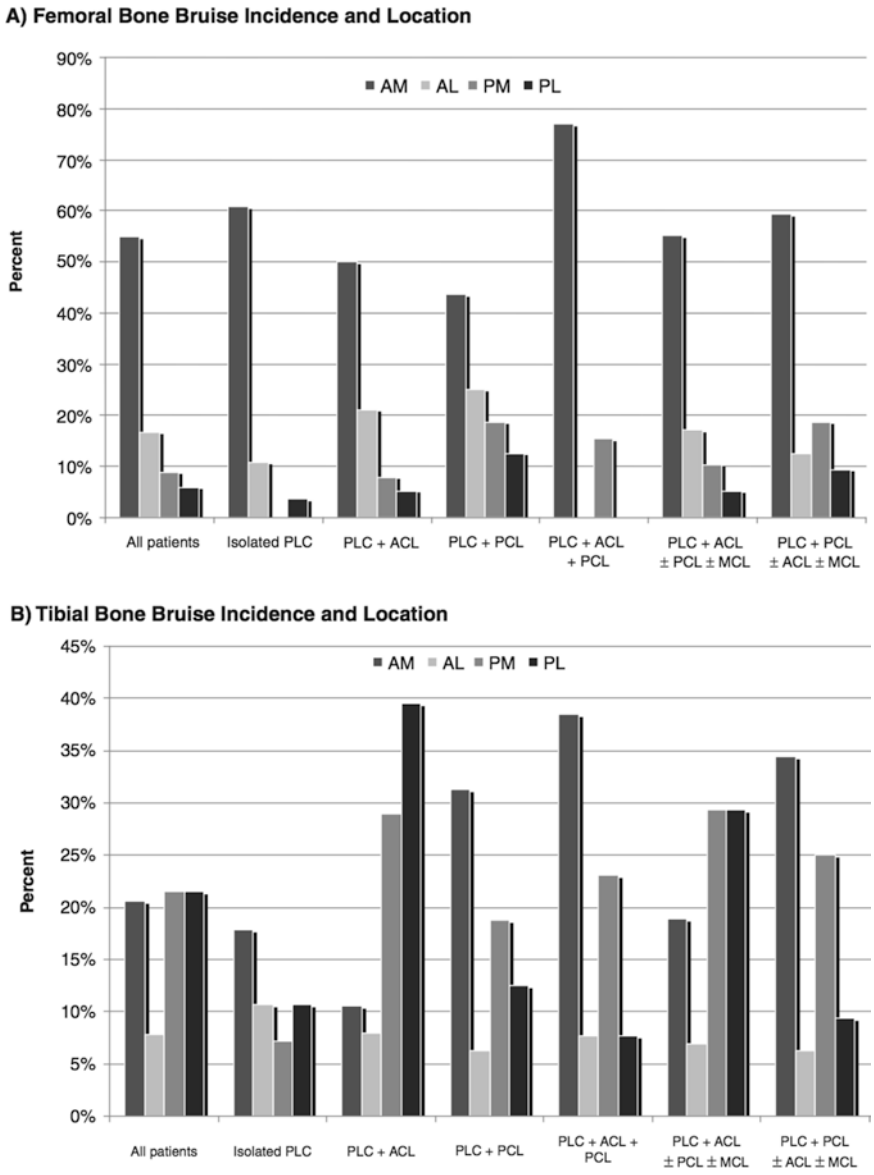

Fig. 8.1 (**a**) Femoral and (**b**) tibial incidence and location of bone bruises, reported as the percentage of knees with bone bruise, separated by subgroups of diagnosed injury. AM, anteromedial; AL, anterolateral; PM, posteromedial; PL, posterolateral. (Reprinted from Geeslin and LaPrade [8]. With permission of SAGE Publications, Inc.)

among sagittal and coronal planes, respectively, while anatomical graft placement showed no significantly different orientation in flexion [6]. Also, graft lengths were significantly greater following anteroproximal placement than anatomical placement, measuring 5.6 mm and 2.1 mm longer, respectively [6].

Surgical treatments are predominantly grounded by either the single-bundle (SB) or double-bundle (DB) reconstruction approach. Yagi et al. analyzed the differential in knee kinematics and in situ forces for SB versus DB reconstructions and determined that DB reconstructions not only resembled anterior tibial

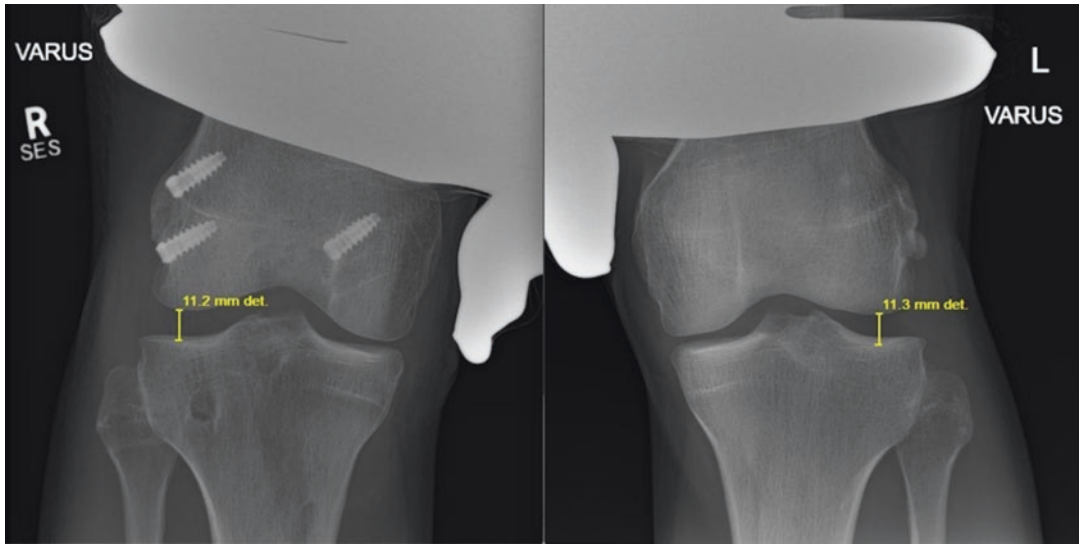

Fig. 8.2 Bilateral varus stress radiographs at 6 months post-op, following a multiligament injury and subsequent posterolateral corner reconstruction (PCLR). Radiographic measurements indicate lateral compartment gapping of 11.2 and 11.3 mm, displaying a negligible side-to-side difference

translation of the intact knee significantly more than SB, but in situ forces also more closely approximated that of the normal knee with combined rotatory load [16]. DB reconstruction theoretically better resembles native anatomy in restoring both the anteromedial (AM) and posterolateral (PL) bundles of the ACL. During knee flexion, the response differs between these bundles, as in situ force in the PL bundle is significantly affected by knee flexion angle, the AM bundle remains relatively constant [17]. Furthermore, SB reconstruction results in increased joint contact pressure through a decrease in cartilage contact area, while DB reconstruction more closely resembles contact area and pressure characteristics of the native ACL [16]. However, to date, clinical studies have not demonstrated any significant difference between SB and DB ACLR, and SB reconstructions are more commonly used for treatment. Going forward, there will be continued debate on the complex anatomy ("ribbon anatomy") and theoretically what is proven best in the biomechanical setting, perhaps from an all rectangular femoral tunnel or triple bundle, and what is feasible in patient surgery [18].

Multiligamentous Injuries (MLIs) of the Knee

Multiligament knee injuries are defined as a tear of at least two of the four major knee ligaments: the ACL, the posterior cruciate ligament (PCL), the posteromedial corner (PMC), and the PLC [19]. Multiligament knee injuries are commonly associated with a tear of both cruciate ligaments; however, studies have reported multiligament knee injuries with at least one cruciate ligament intact. Knee dislocations account for 0.02% to 0.2% of all orthopedic injuries occurring almost equally in both high- and low-energy settings (50.3% and 49.7%, respectively) [20]. High-energy vehicular collisions are responsible for 25.1% of multiligament injuries, while 44.2% have been reported to occur during low-energy sporting activities [20].

Widely used by surgeons today, patterns of multiligament tears are sorted using the Schenck classification system. Classifying multiligament injuries can aid in both the diagnosis and planning for treatment, which can lead to better outcomes of osteoarthritis. The choice of surgical

Table 8.1 Modification of the Schenck classification system, distributing multiligament injuries into separate classes

Class	Injury
KD-I	Injury to single cruciate + collaterals
KD-II	Injury to ACL and PCL with intact collaterals
KD-III-M	Injury to ACL, PCL, MCL
KD-III-L	Injury to ACL, PCL, LCL
KD-IV	Injury to ACL, PCL, MCL, LCL
KD-V	Dislocation + fracture

Adapted from Moatshe et al. [21]. With permission from British Medical Journal

ACL anterior cruciate ligament, *PCL* posterior cruciate ligament, *MCL* medial collateral ligament, *LCL* lateral collateral ligament

Table 8.2 Distribution of knee dislocation injuries according to the Schenck classification system. Study of 303 patients, the KD-III-M cohort was the most commonly diagnosed class of injury

Distribution of patients according to Schenck classification[a]		
KD class	No. of patients	Percentage of total
KD-II	16	5.3
KD-III-M	159	52.4
KD-III-L	85	28.1
KD-IV	39	12.9
NC	4	1.3
Total	303	100

Adapted from Moatshe et al. [20]. With permission from SAGE Publications, Inc.

[a]*KD* knee dislocation, *L* lateral, *M* medial, *NC* not classified

technique, correct diagnosis, time of surgery, and rehabilitation protocol can delay the progression of osteoarthritis for long-term health of the patient, as well as reduce the chance of failed reconstructions (Table 8.1).

The majority (80.5%) of patients in the study by Moatshe et al. were diagnosed with a tear of three of the major ligaments [21]. Of these, injuries classified as KD-III-M accounted for 52.4% of the study [20]. The KD-III-L classification was recorded to be the second highest diagnosis, while the occurrence of KD-IV and KD-II classifications were lower [20]. The frequency of each classification was similar to reports by Robertson et al., where KD-III-M occurred in 41% of patients, while KD-III-L injuries occurred in 28% of patients [17]. The occurrence of KD-IV and KD-II injuries was also lower in this study [17]. However, these results contrast with the 2013 data presented by Becker et al. where in a series of 106 patients, KD-III-L injuries were the majority, accounting for 43% of patients [22] (Table 8.2).

Prevalence of Concomitant Damage

Multiligamentous injuries have been shown to be commonly associated with concomitant meniscal and articular cartilage damage at the time of injury. Previous literature has found that 39% of patients had concomitant meniscal injuries, while 39% of patients had associated articular cartilage damage [23]. Similarly, in another study reporting the demographics of multiligament injuries, it was found that 37.3% of patients had concomitant meniscal injuries [20]. Meniscal injuries were reported as evenly distributed among medial and lateral tears (16.5% and 15.8%, respectively), with 5.0% of patients being diagnosed as having both menisci torn [20]. In addition, 28.3% of patients had associated articular cartilage damage, with 12.5% of damage occurring on the femoral condyles [20]. Of these, 20.1% of acute injuries and 47.7% of chronic injuries were associated with articular cartilage damage [20]. Studies vary in reported outcomes of meniscus injuries concomitant with ACL tears. Øiestad et al. reported OA rates in a 10-year follow-up study of isolated ACL injuries of 0–13% treated surgically and nonsurgically, respectively. This is significantly lower than rates of combined ACL and meniscal injuries treated surgically and nonsurgically (21–48%, respectively) [24]. A similar meta-analysis, with a minimum follow-up of 10 years, found an OA rate of 16% following ACLR, while the rate of OA in patients with concomitant meniscal resections was as high as 50% [7].

There is a high variability in the reported incidence of concomitant injuries [25, 26]. Richter et al. reported lower numbers of concomitant meniscal tears, with 15% having associated meniscal tears [26]. In a larger sample size, Krych et al. reported that 55% of patients

sustaining multiligamentous injuries had concomitant meniscal tears. Additionally, 48% had associated chondral injuries [25]. In the case of concomitant meniscal or articular cartilage damage, it is recommended that these structures be addressed concurrently with the reconstruction of the associated torn ligaments to avoid joint stiffness and graft failure [23]. Overall, the ability to understand the patterns of multiligament knee injuries and to recognize potential concomitant damage can greatly improve diagnosis and surgical preparation, ultimately, improving patient functional, subjective, and objective outcomes [23] (Fig. 8.3).

Treatment

Improved outcomes have been seen with the approach of anatomic reconstructions over repairs of the injured ligaments, because cruciate ligament repairs yield high rates of recurrent instability and reoperation for posterolateral injuries [1]. Based on biomechanical and clinical outcomes literature, tunnel convergence is an important factor along with addressing meniscal and articular cartilage damage prior to graft tension and fixation [11, 14, 21] (Fig. 8.4).

Clinical outcomes of patients undergoing multiligament reconstructions have shown a majority of satisfactory functional and subjective outcomes [19, 23, 26]. However, in short- and midterm clinical follow-ups, OA was prevalent in 23–87% of patients [19, 26]. Reported objective scores are relatively unsatisfactory, as 42% of patients developed OA in the surgically operated knee, compared to 4% in the non-treated, contralateral knee [23]. However, Fanelli et al. and Hirchman et al. reported lower numbers of degenerative changes at 23% and 30.9%, respectively, in surgically treated knees [27].

Although the progression of OA is relatively high in surgically treated knees relative to healthy knees, surgical treatment is highly recommended as lack of treatment results in significantly worse outcomes [23]. Literature shows 47.4% of patients treated surgically develop degenerative changes, far less than the 88% of patients that are treated nonsurgically [23]. Additional statistical analysis of the risk factors for OA development reported a positive correlation with greater age and BMI [23].

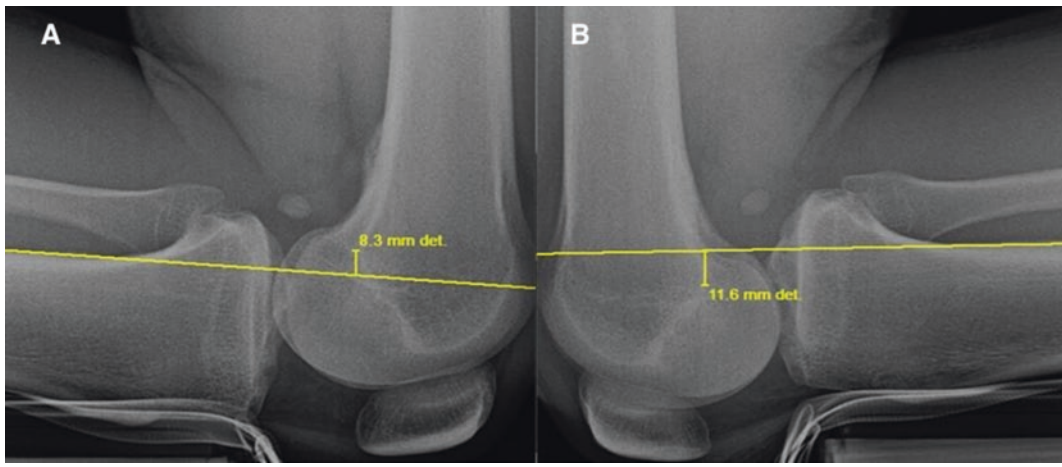

Fig. 8.3 Bilateral kneeling stress radiographs for evaluating posterior translation (PTT) relative to the most posterior aspect of the Blumensaat line. (**a**) 8.3 mm anterior to the Blumensaat line, (**b**) 11.6 mm posterior to the Blumensaat line; contralateral difference in PTT > 12 mm commonly indicates combined posterior cruciate ligament (PCL) and collateral ligament injury

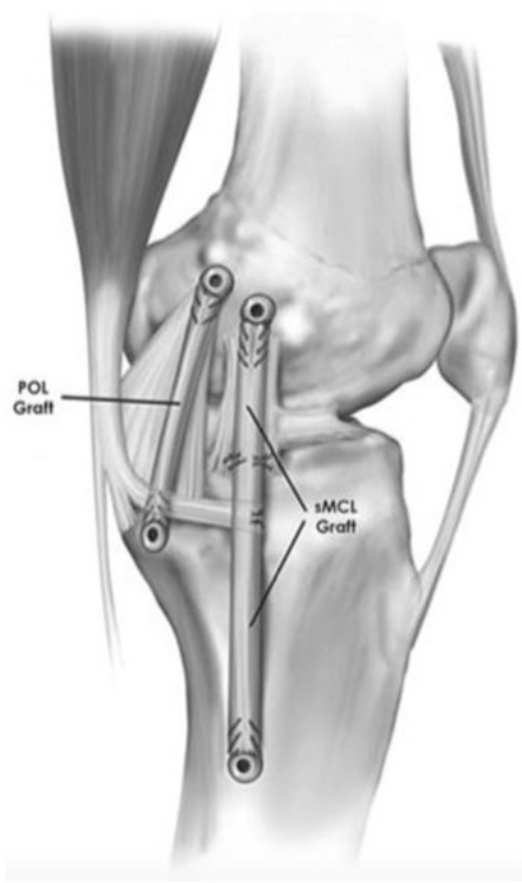

Fig. 8.4 Illustration (left knee) of the superficial medial collateral ligament (sMCL) and posterior oblique ligament (POL) anatomic reconstructions. (Reprinted from Coobs et al. [41]. With permission of SAGE Publications, Inc.)

Posterior Cruciate Ligament (PCL)

The PCL consists of two bundles: the larger anterolateral bundle (ALB) and the smaller posteromedial bundle (PMB). Locating their femoral and tibial attachment points can separately identify the two bundles. Historically, PCL tears were treated with either nonsurgical treatment or SB reconstruction. However, a recent biomechanical study by Kennedy et al. has shown that these bundles act synergistically with one another, and a more anatomical DB technique can better restore native knee kinematics compared to the SB approach [28].

PCL injuries occur after a posteriorly directed force acts on the anterior tibia [27]. This force is commonly experienced in high-energy vehicular collisions, which is responsible for 57% of all PCL injuries [27]. In addition, PCL tears have been reported to be prevalent in athletics and account for 2% of all sports-related injuries [27]. Instability of the knee joint due to PCL injury can alter knee kinematics by increasing patellofemoral joint pressure, internal femoral rotation, and posterior tibial translation, which ultimately leads to increased patellar cartilage loading and contact pressures [29]. Furthermore, altered knee joint kinematics can lead to degeneration of cartilage and increased risk of OA in the medial compartment of the knee, as well as lateral and inferior facets of the patella [29].

PCL tears account for 3–37% of all structural knee injuries while rarely occurring in isolation (18%) [30]. Earlier studies report PCL tears frequently occur with ACL (46%), MCL (31%), or PLC (62%) injuries [27]. In addition, 79% of grade III PCL tears are associated with multiligament knee injuries [22]. Fanelli et al. also reported higher rates of grade III PCL tears in males with 73–97% accounting for either isolated or combined injuries, respectively [27].

Prevalence of Concomitant Damage

Concomitant pathological changes occur with PCL-related injuries mostly affecting articular cartilage [31]. In a report of 25 total patients reviewed, 13 patients (52%) displayed signs of cartilage damage at the time of surgery, with 10 of these 13 patients presenting medial compartment chondrosis [31]. From this analysis, physicians should be alert for possible medial-sided chondrosis associated with a PCL tear in order for a complete and accurate diagnosis during examination [31]. Overall, meniscal tears and articular cartilage damage occur as a result of delaying the time of surgery after initial injury or residual posterior laxity of the knee following PCL reconstruction [31]. Of the 13 patients who presented with chondrosis

at the time of surgery as described above, 41% of the patients treated within a year of the initial incidence displayed chondrosis, while 75% treated after 1 year displayed chondrosis [31]. Based on this point, it can be concluded that delaying surgery can be detrimental to the overall health and objective outcomes of the PCL deficient knee joint.

Treatment

Since the PCL is highly vascularized, it is capable of intrinsic healing [26]. Historically, the majority of isolated PCL tear treatments have been non-operative, although new anatomic reconstruction techniques have pushed physicians toward opting for surgical intervention [9]. PCL reconstruction (PCLR) is normally indicated for grade III PCL tears when associated with multiligament injury or with concomitant repairable meniscal body or root tears [32]. The DB technique requires reaming two femoral tunnels and one tibial tunnel, replicating the attachment points of both bundles anatomically [32]. SB (ALB reconstruction) or DB PCLR can be performed, although DB PCLR is reportedly more anatomical and objectively restores the native biomechanics of the knee joint [9] (Fig. 8.5).

Isolated PCL tears have been documented to increase medial compartment contact pressures, thereby increasing the risk of meniscal damage and progression of OA [29]. Additionally, analysis of non-operative treatment outcomes of isolated PCL tears indicates high rates of OA [31, 33]. At 7 years of follow-up, 23% of patients with isolated PCL tears had arthritic progression, with 11% of all patients developing moderate-severe OA. At 14 years of follow-up, the prevalence of OA increased to 41% in the same patient group [33]. This literature implies that long-term outcomes of non-operative treatment may present good functional and subjective scores; however, this method can be considered to be unfavorable in deterring the progression of osteoarthritis over an extensive amount of time [33].

SB PCLR can be performed by either using transtibial or tibial inlay techniques since both methods produce similar outcomes [9]. IKDC outcome scores of isolated PCL injuries treated by the transtibial technique indicate 75% of patients had normal or nearly normal subjective function, while posterior knee laxity improved from a range of 8.4–12.3 mm, preoperatively, to a range between 2.0 mm and 5.9 mm, postoperatively [31]. However, the study concluded that overall knee function was not completely restored [31]. Additionally, Hermans et al. reported that 60% of knees had evidence of OA, but posterior knee laxity was significantly worse compared to injured knees treated nonsurgically (4.7 mm vs. 2.1 mm, respectively) [31]. A long-term follow-up (average 9.2 years) of SB PCLR procedures found that 92% of patients who had chondrosis associated with the initial injury presented mild to moderate cartilage defects [31]. In non-chondrosis-associated injuries, SB PCLR greater reduces the progression of OA relative to non-operative approaches [31]. However, residual posterior laxity is a common problem associated with SB PCLR treatment and could possibly lead to altered kinematics, contact pressures, and subsequent arthritic development [31].

Theoretically, since the two bundles of the PCL work in a codominant manner, nonanatomic SB PCLR could not restore native knee kinematics. Therefore, it is believed that DB PCLR could prevent the onset or progression of cartilage damage by improving both biomechanics and stability. Clinical outcome analyses of DB PCLR have reported significantly improved IKDC subjective outcome scores [30]. Furthermore, side-to-side posterior translation is significantly reduced, ranging between 0.9 mm and 3.2 mm, with the higher range occurring in multiligament injured knees [34]. The tibial inlay procedure has been reported to produce similar results, because side-to-side posterior translation improves to a range between 2.6 and 5.1 mm, postoperatively [34]. DB PCLR reduces posterior knee laxity in comparison with SB PCLR techniques, successively restoring the knee more closely to native biomechanics and improving long-term patient outcomes [32]. However, long-term objective outcomes have yet to be reported.

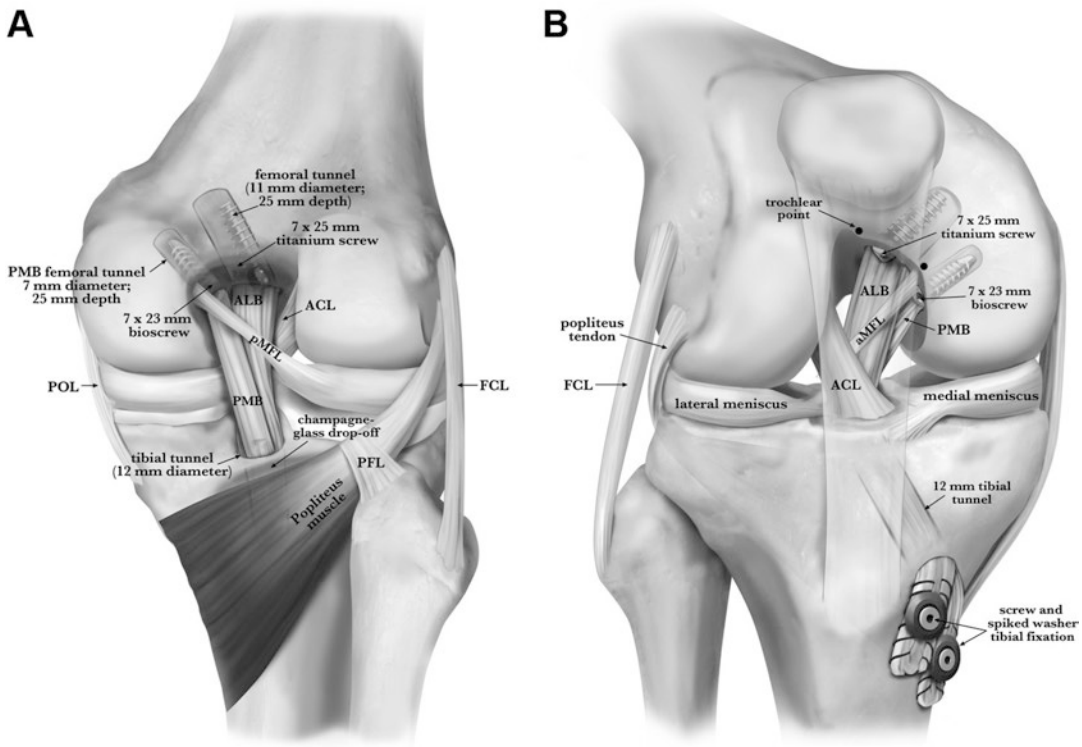

Fig. 8.5 (**a**) Posterior and (**b**) anterior view illustration of the anatomic double-bundle (DB) posterior cruciate ligament reconstruction (PCLR) depicting the anterolateral bundle (ALB) and posteromedial bundle (PMB) grafts with regard to the size, shape, and location of the femoral and tibial tunnels. Other ligaments depicted include FCL, fibular collateral ligament; PFL, popliteofibular ligament; pMFL, posterior meniscofemoral ligament; ACL, anterior cruciate ligament; POL, posterior oblique ligament. (Reprinted from Wijdicks et al. [42]. With permission from SAGE Publications, Inc.)

Biologic Future

Methods for approaching treatment of OA have more recently shifted toward biological interventions, rather than surgical procedures, from the recent appraisal of biologic treatments that can be harvested and used to improve the healing process [10, 35]. Common biologics used in orthopedic applications include platelet-rich plasma (PRP), mesenchymal stem cells (MSCs), and bone marrow aspirate concentrate (BMAC) [36]. PRP and MSCs have shown in previous literature to be helpful in stimulating the healing of numerous knee injuries, while the treatment for mild OA by BMAC has shown the potential for future applications [35, 36]. Some recent studies have published supportive data in advancement of treating knee injuries via biologics, but this approach remains a controversial topic in orthopedics because literature also exists showing the lack of benefit from these respective biologic treatments. Much like the inability of the ACL to undergo healing (restoration of functional stability) with nonsurgical treatment following rupture, the management of knee injuries could improve greatly from biological support to supplement an anatomical surgical reconstruction [35] (Table 8.3).

Platelet-Rich Plasma

PRP has the potential to enhance tissue healing from several growth factors that can serve as chemoattractants and stimulators of cell proliferation

Table 8.3 Major components of PRP and selected contents/releasate[a]

Component	Contents/releasate
Platelets	
Alpha granules	Growth factors (e.g., PDEGF, PDGF, TGFβ1, IGF1, bFGF, PDAF, PF4, EGF, VEGF, CTGF, HGF, SDF1α), hemostatic factors (e.g., factor V, vWF, fibrinogen), angiogenic factors (e.g., angiogenin, VEGF), antiangiogenic factors (e.g., angiostatin, PF4), proteases (e.g., MMP2, MMP9), necrotic factors (e.g., TNFα, TNFβ), and other cytokines
Dense granules/ bodies	ADP, calcium, serotonin
Lysosomes	Lysosomal enzymes
Plasma	Proteins (e.g., albumin, fibrinogen, globulins, complement, clotting factors), electrolytes (e.g., sodium, chloride, potassium, calcium), hormones (e.g., estrogens, progesterone, androgens, IGF1, ACTH, HGH), biomarkers (e.g., osteocalcin, CD11b, protein C)
Leukocytes	
Neutrophils	Cytokines (e.g., IL4, IL8, TNFα), proteases, bactericidal molecules, lysozymes
Eosinophils	Cytokines and growth factors (e.g., VEGF, PDGF, TGFα, TGFβ, ILs), plasminogen
Basophils	Histamines, proteases, heparin, leukotrienes
Monocytes	Cytokines and growth factors (e.g., IL1, IL6, FGF, EGF, PDGF, VEGF, TGFβ)
Erythrocytes (minimal numbers)	ATP, nitric oxide, hemoglobin, and free radicals

Adapted from LaPrade et al. [35]. With permission from SAGE Publications, Inc.

[a]*ACTH* adrenocorticotropic hormone, *ADP* adenosine diphosphate, *ATP* adenosine triphosphate, *bFGF* basic fibroblastic growth factor, *CTGF* connective tissue growth factor, *EGF* endothelial growth factor, *HGF* hepatocyte growth factor, *HGH* human growth hormone, *IGF* insulin-like growth factor, *IL* interleukin, *MMP* matrix metalloproteinase, *PDAF* platelet-derived angiogenesis factor, *PDEGF* platelet-derived endothelial growth factor, *PDGF* platelet-derived growth factor, *PF* platelet factor, *SDF* stromal cell-derived factor, *TGF* transforming growth factor, *TNF* tumor necrosis factor, *VEGF* vascular endothelial growth factor, *vWF* von Willebrand factor

Table 8.4 Biologics for the treatment of ligament injuries: targeted areas for future research and barriers to clinical implementation

Targeted areas
The use of biologics to augment the healing of autografts and allografts for ligament reconstruction, specifically graft-tunnel healing and graft maturation
Further basic science investigation of biologic augmentation of graft-tunnel healing and graft maturation to direct the development of clinical studies
Imaging modalities to objectively evaluate graft healing in reconstruction and the effect of biologic therapies
Feasibility of ACL repair and the optimal criteria for targeted ACL repair
Comparative laboratory studies on scaffolds, cells, and growth factors
Barriers
Reliance on predominantly preclinical studies to support biologic augmentation
Heterogeneity in characteristics of biologic therapy as well as patient population with ligament injury

Adapted from LaPrade et al. [35]. With permission from SAGE Publications, Inc.

including transforming growth factor (TGF)- ß, platelet-derived growth factor, insulin-like growth factor, and vascular endothelial growth factor (VEGF) [35]. PRP can be effective due to the growth hormones present. One study by Anderson et al. found improvement in healing of the bone-tendon interface and pullout strength of ACL grafts following administration of bone morphogenetic protein (BMP-2) [37].

However, PRP may also contain inflammatory cytokines and matrix metalloproteinases (MMPs) that could increase tissue damage and deter from its potential benefits [35]. TGF-ß1, which is present in PRP, may negatively affect articular cartilage, and while VEGF has previously been noted to promote angiogenesis (tissue healing), it negatively affects articular cartilage healing [35]. In addition, the downregulation of desired effects could potentially be altered by the presence of leukocytes or by concentration levels, further acting as a negative feedback loop dependent on higher platelet presence [35] (Table 8.4).

Mesenchymal Stem Cells

MSCs, or otherwise known as medicinal signaling cells, affect tissue regeneration either by the indirect stimulation of angiogenesis, inflammation limitation, and recruitment of local tissue-specific progenitors or by direct differentiation into damaged cell types [35]. The use of growth factors with MSCs is increasing due to its latter ability to differentiate into bone, fat, muscle, and cartilage while simultaneously creating a regenerative microenvironment promoting musculoskeletal regeneration [38]. The capacity of growth factors to promote cellular proliferation, migration, survival, and differentiation along with angiogenesis promotion is important for concomitant application with biologics such as MSCs and future directions of biologics (LaPrade 2016 biologics). With one study finding promising results for the treatment of tendinopathy in race horses via MSCs relative to the control group, respective recurrence rates of 27% and 56%, many questions remain unanswered regarding its clinical outcomes in humans [39] (Fig. 8.6).

Bone Marrow Aspirate Concentrate

BMAC has gained much ground in popularity due to it being one of the few methods available for delivering stem cells, as the US Food and Drug Administration (FDA) does not require approval for this treatment method [as of this writing] [36]. BMAC contains growth factors including platelet-derived growth factor, TGF-ß, and BMP-2 [36]. In addition to the benefit of stem cells, these growth factors may assist in the regeneration and preservation of cartilage and have previously been shown to have anti-inflammatory and anabolic effects on injected tissue [36]. Studies reporting outcomes on cartilage defects of the knee from BMAC are few, but the outcomes are seemingly good to excellent [36]. A study by Gobbi et al. treated a cohort of patients with a hyaluronan-based scaffold soaked in BMAC and, relative to a control group, found that patients with small chondral defects (mild OA) reported significantly better IKDC and KOOS scores, although these score improvements didn't represent the patients with large chondral lesions [40]. In conclusion, mild OA seems to be more effectively treated by BMAC than patients with greater severity of OA.

Conclusion

The main focus of this chapter is to stress the importance in proper diagnosis and treatment of isolated and complex ligamentous injuries, more specifically emphasizing anatomic reconstruction. Aside from the prevalence of ACLRs to be performed via the SB technique (as the ACL is anatomically composed of two bundles), anatomic restoration is the most important factor in reducing the incidence of OA. This further leads

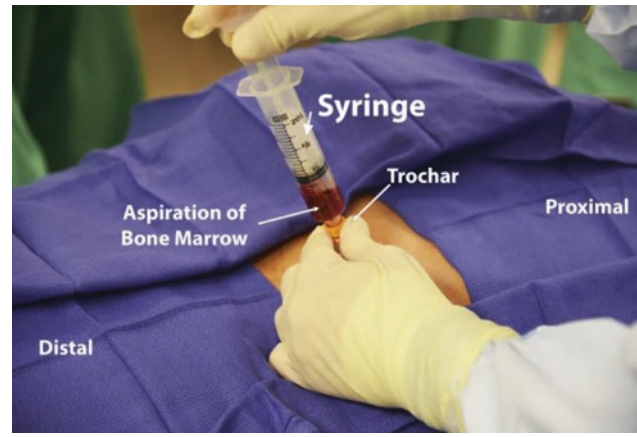

Fig. 8.6 Bone marrow aspirate harvesting as bone marrow aspiration needle inserts into the cancellous bone of the iliac crest. Depicted sample is obtained on the left posterior superior iliac spine. (Reprinted from Chahla et al. [43]. With permission from Elsevier)

into the ability to address multiligamentous injuries in their entirety, as failure to diagnose and, subsequently, treat concomitant injuries, and will fail to restore native anatomic and kinematic characteristics of the knee. The absence of treatment leads to the altered contact stresses of the tibiofemoral joint that results from variable conditions of ligamentous laxity, which further instigates degenerative changes of articular cartilage. Biologic treatment options show promising results, although the data remains fairly inconsistent. In the near future, anatomic surgical management with supplemental biologic treatments could not only drastically improve healing qualities of ligamentous knee injuries but also preserve or even regenerate articular cartilage of the tibiofemoral joint.

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