The ACL-Deficient Knee

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Editors

The ACL-Deficient Knee

A Problem Solving Approach

Springer

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Foreword I

Twenty-five years have passed since we published the first edition of The Crucial Ligaments and a much expanded 2nd edition was published in 1994. Drs. Vicente Sanchis-Alfonso and Joan Carles Monllau now offer The ACL-Deficient Knee – A Problem Solving Approach. They support their text, and the work based on the fact that the ACL "is an injury that has not been completely solved" and that "problem resolution" is a more constructive and logical approach than "closed compartment" presentation. Indeed, they are absolutely correct.

The strengths of this new, fresh, and much needed contribution to the discipline of knee surgery are many. Foremost – an acknowledgement that "we are not there yet" – 50 % of primary repair ACL surgery patients develop osteoarthritis, and further in Section 3, the authors clearly address the formidable complications of our current surgery. The authors are to be complimented on the unique approach to this conundrum through the use of problem resolution rather than the traditional didactic compartments.

The editors have assembled an international panel of distinguished authors who present problem resolution in 3 sections and 33 chapters. In addition, the text comes with a collection of step by step surgical technique videos that will be accessed via an online link.

The organization and content of the chapters reflect the combined experience, seniority, and wisdom of the editors and the authors. This is evidence-based medicine at its best.

This text, The ACL-Deficient Knee, is noteworthy and needed. Every student of knee care and knee surgery will find new information, new principles, and will further enhance and advance our care of the knee.

The beneficiaries of this evidence-based text are the patients and those who will follow and will someday lead.

Colorado, USA — John A. Feagin Jr. M.D.

Foreword II

Treatment ACL Injuries: Still an Unsolved Clinical Problem?

In 1955, I performed my very first ACL operation. Unfortunately, now 57 years later, we are not that much wiser when it comes to the ACL injuries than we were then. We still do not know which graft is the best one to use for an ACL reconstruction. We are still discussing whether we need a single or a double graft. We still do not agree on the rehabilitation and at what time we can allow the athletes to go back to sports. And worst of all, the results of the ACL reconstructions are not that much better (or not better at all) than they were in the 1970s in spite of arthroscopic technique and thousands of scientific studies.

In 1965–1966, the late Lennart Broström and myself performed our first patellar tendon reconstructions for old ACL injuries. Fortunately, we had not read Kenneth Jone's paper about ACL reconstruction with the patellar tendon (because his suggested technique is very "unanatomical"). Nor did we know about Brückner who was performing a similar procedure at the same time but published it in a small east-German journal, that we did not even know the existence of. The stimulus for Lennart Broström was to perform a similar operation in the knee as the technique he had developed for reconstruction of the anterior talofibular ligament of the ankle. Nor did we know about pivot shift. My first contact with pivot shift was at an AOSSM course in Snowmass, Aspen, Col., USA, in 1973 when Victor Frankel, M.D. demonstrated pivot shift on his own wife, who had sustained an ACL injury.

Should then all ACL injuries be treated surgically? No, professional athletes should be treated surgically. Leisure time athletes and nonathletes with pivot shift should be informed that if they give up sports, they can live well even with their unstable knee. If they want to continue with "pivoting sports," they need surgery. Unfortunately, ACL injuries are often combined with injuries to the joint lines. Some authors maintain that one gets these irrespective of treatment. For me, a reconstruction of the ACL in order to obtain a stable knee has been a way of preventing the pivot shifts that I have seen can destroy the joint lines.

Since 1965, I have performed many hundred ACL reconstructions. Due to my age, I have now given up surgery, but I am still following the discussions about ACL injuries and the treatment options. I am really surprised over that most orthopedic surgeons in my own country – Sweden – have abandoned the patellar tendon graft and gone over to use the hamstrings for ACL reconstructions. Since

there are no real proofs that the hamstring tendons are any better than the patellar tendon, my feeling is that it is the industry that has persuaded the doctors to change from patellar tendon grafts to hamstring grafts. The surgical instruments used for a hamstring ACL reconstruction and for securing those grafts are much, much more expensive than the simple instruments you need for a patellar tendon reconstruction. Although I have been preaching the need for good randomized clinical trials since 30–40 years, there are very few good such studies performed. One good such study (that unfortunately is seldom quoted) is the Swedish study by Heijne and coworkers. They compared patellar tendon reconstructions with hamstring reconstructions in a "double" randomized study. Besides comparing the two different surgical techniques, they also randomized the patients to either aggressive rehabilitation (an early start of open chain exercises 4 weeks postoperatively) or a later start (12 weeks postoperatively). Everybody would probably guess that the hamstring reconstructions with early start of open chain would be the best group. It was not. The patellar tendon reconstructions with late start of open chain were the best ones. My feeling is that when the enthusiasm over the hamstring reconstructions has subsided in a couple of years' time, the patellar tendon reconstructions will come back again in Sweden. There are some types of sport where the hamstring grafts definitely should be avoided – downhill skiing for instance. All downhill skiing is done in internal rotation of the lower leg. As soon as a ski rotates outward, you fall. In skiers, one should therefore avoid using two internal rotators like the hamstrings for ACL reconstruction as Steadman and his group in Vail, Colorado, USA, has pointed out. It is possible that we will also find out that different sports need different grafts.

Since I have been so engaged in the history of ACL reconstructions, of course I also have some dreams for the future. I believe that in 10 years time we will not be discussing what graft we should use. When a child is born, we will take stem cells from the umbilical cord and let them grow under tension and under sterile conditions. They will then develop tendocytes and a "neo-ligament." I believe that all professional football players will have 2–3 sterile deep-frozen autologous tendon grafts in their deep freeze. We will implant one of these with arthroscopic technique and use growth factors to speed up the healing. Not every orthopedic surgeon will perform these operations; only a small group of very talented ACL surgeons will perform them. Their hands will be "instrumented" and a robot will perform the operations anywhere in the world. This has already been done for cardiac surgery and will become common also in orthopedics.

Finally, I hope that in the future, we will be able to promise ACL-injured athletes a 95 % chance of becoming normal after ACL surgery. Today, it is difficult to promise them more than a 70 % chance of becoming normal again. It is therefore my hope that this excellent book could change this.

Stockholm, Sweden Ejnar Eriksson M.D., Ph.D.

Preface

This book reflects our deep interest in knee pathology, particularly that of the anterior cruciate ligament (ACL), and emphasizes the great importance we give to the concept of subspecialization, which is the only way to confront the deterioration and mediocrity of our specialty, orthopedic surgery, and to provide our patients with better care. In line with the concept of subspecialization, this book necessarily required the participation of various authors.

We are aware of the fact that several monographs about ACL injuries have been published. Therefore, why are we going to publish a new book about the ACL-deficient knee? The answer is obvious, because it is a very frequent injury. The annual incidence of primary ACL reconstructions is 35 cases per 100,000 inhabitants. If we only consider a high-risk population (age group between 16 and 39 years old), the incidence goes up to 80 cases per 100,000 inhabitants. In the USA more than 100,000 ACL reconstructions per year are performed, and in Spain, more than 15,000. But the main reason we have decided to write this book is because it is an injury that has not been completely resolved, despite the good or excellent surgical treatment results, and if we measure them by return to elite sports, then it is almost 95 %. In fact, if surgical treatment results are measured by the capacity of surgery to prevent the development of osteoarthritis in the knee, we can be sure that the problem has not yet been resolved, since more than 50 % of patients with an isolated ACL tear that has been operated develop an osteoarthritis in a long-term follow-up. Therefore, until we are able to refine the surgical treatment, injury prevention should be the priority of our studies. Therefore, we are facing a very frequent injury that is far from being completely resolved.

In this book, we approach the ACL-deficient knee from a different perspective that is unlike the previous classical one. The common approach is the analysis of closed compartments, anatomy, biomechanics, physical findings, imaging techniques, surgical treatment, and rehabilitation. Our approach is completely the opposite. We are focused on problem analysis and problem solving, besides analyzing the possibility of prevention. Therefore, in each chapter, the biomechanics, anatomy, etc. that are relevant to the topic are reviewed. There are chapters where highly specialized surgical techniques are presented (v. gr. double-bundle reconstruction or meniscal transplant). These chapters are written by internationally renowned specialists who are pioneers in the topic analyzed. In this book, we will also address the characteristics of ACL tears in children. We are finding a growing number of injuries in children, due to the increase of sports at early ages.

In this book, we will deal will the ACL-deficient knee in three sections. In the first section, we will analyze the current status and real controversies that exist nowadays in the approach and treatment of the ACL-deficient knee. In the second section, we will present different case scenarios that a surgeon treating ACL injuries could encounter and how to solve each one of them (the problem and the solution). In the third section, the complications of the treatment will be analyzed, as well as how to prevent them and how to treat them (can we do better?). At the end of each chapter, future research, and the take home messages are summarized, with an evidence level of each recommendation whenever it is possible (evidence-based medicine). For this reason, at the beginning of the book, there is a reminder of the basic concepts of evidence-based medicine (How Can we Use Evidence-Based Medicine to Guide our Practice?). We should never forget the achievements of our surgical forefathers, and this is the reason why at the forefront of the book we evaluate the ACL-deficient knee from ancient history to the twenty-first century. Finally, another interesting aspect of this book is the collection of step by step surgical technique videos that will be accessed via an online link that will allow the knee specialist to perform the technique presented by the author.

This book is addressed to orthopedic surgeons specialized in knee surgery, specialists in sports medicine, rehabilitation specialist MDs, and physiotherapists. This book obviously does not attempt to replace the classical monographs, even so we believe it can complement them. We trust that the reader will find this work useful, and consequently, that it will be indirectly valuable for patients.

Spain Vicente Sanchis-Alfonso, M.D., Ph.D.
Spain Joan Carles Monllau, M.D., Ph.D.

Acknowledgments

We have had the privilege and honor to count on the participation of outstanding specialists who have lent prestige to this monograph. We thank all of them for their time, effort, dedication, kindness, as well as for the excellent quality of their contributing chapters. All have demonstrated generosity in sharing their great clinical experience in a clear and concise form. We are in debt to you all. Personally, and on behalf of those patients who will undoubtedly benefit from this work, thank you.

Last but not least, we are extremely grateful to both Springer-Verlag in London for the confidence shown in this project, and to Mr. Karthik Periyasamy and his production team from SPi Global (Chennai, India) for completing this project with excellence from the time the cover is opened until the final chapter is presented.

Vicente Sanchis-Alfonso, M.D., Ph.D.
Joan Carles Monllau, M.D., Ph.D.

Historical Aspects on Surgery for Anterior Cruciate Ligament Deficiency

Dedication:
I dedicate this work to the loving memory of my late mother Karin Christa and father Franz-Josef whose loss one cannot comprehend and who will be missed forever.

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Synopsis

Our understanding of the clinical implications and surgical remedies of injuries to the anterior cruciate ligament (ACL) has seen remarkable changes since Robert Adams observed the first confirmed case of an ACL rupture in 1837. High morbidity and mortality associated with surgery delayed efforts to repair the torn ligament until the end of the nineteenth century. Suture repair however yielded unpredictable results. The era of ligament reconstruction began with Grekov and Hey Groves in the early parts of the twentieth century, but their knowledge and achievements were not uniformly appreciated at the time. A period of startling ingenuity followed, which created an amazing variety of different surgical procedures often based more on surgical fashion than an indication that continued refinements were leading to improved results. It is hence not surprising that real inventors were forgotten, good ideas discarded, and untried surgical methods adopted with uncritical enthusiasm only to be set aside without further explanation. Over the past 100 years, surgeons experimented with a variety of different graft sources. Synthetic graft materials enjoyed temporary popularity in the misguided belief that they were stronger and more durable. Until the 1970s, ACL reconstructions were formidable procedures, often so complex and fraught with peril that they remained reserved for a chosen few. Advancements in arthroscopy techniques and instrumentation have improved surgical reliability and reproducibility and established ACL reconstruction as a procedure within the realm of most surgeons' ability.

Prologue

Writing a historic review bears the danger of creating an uninspiring list of chronological events which incite little enthusiasm with the reader. The author has hence made the conscious decision to focus on key events and circumstances over the past two millennia that have proven to be of significance in the progression of this particular field of surgery. Anyone who yearns for a more elaborate review of the historic events is referred to other publications [196]. The reader should bear in mind that information obtained through reviewing historical papers is mainly based on case reports and observational studies, with the great majority representing no more than a reflection of a surgeon's personal experience. Longer-term follow-up studies are scarce and controlled trials simply unavailable. This historic review of the surgical advances in the treatment of ACL deficiencies portrays how evolving knowledge combined with often controversial concepts and ideas has shaped our current understanding of ACL reconstruction.

From Ancient Greece to the 20th Century: The Age of Conservative Management

The history of the surgery for the anterior cruciate ligament (ACL)-deficient knee is also the history of the discovery of the ligament's function, the recognition of its injury pattern, and the development of reliable methods in assessing and diagnosing ACL injury. Although Hippocrates (460–370 BC) acknowledged the disabling signs associated with distortion of the knee, he was unaware of the underlying cause of such ailment [87]. We owe the discovery of the cruciate

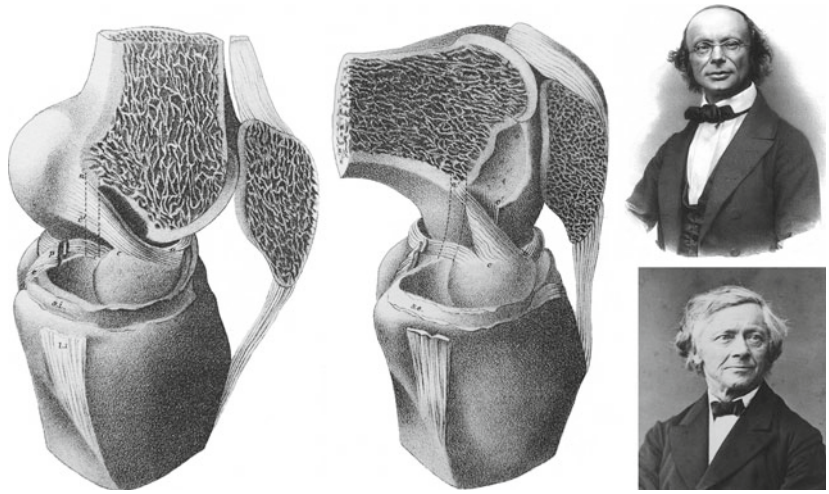

Fig. 1 Drawings taken from "Mechanik der menschlichen Gehwerkzeuge" published by the Weber brothers in 1836. These are this first illustrations to show the ACL to consist of two distinct fibre bundles with in dependant tension pattern. Wilhelm Weber (*top right*) was a Professor of Physics in Göttingen whilst his brother Eduard (*bottom right*) was Professor of Anatomy in Leipzig (Image of Eduard Weber courteous of Universitätsbibliothek Leipzig, Drawings with kin permission of Springer Science, Berlin [226])

ligaments and their name to Claudius Galen of Pergamon (131-201 BC) who devoted much of his life to the study of anatomy mostly though dissection of the deceased [68]. Over the following 2,000 years the ACL led a relatively uncharted existence. This changed in 1836 when Wilhelm (1804–1891) and Eduard Weber (1806–1871) published their treatise "Mechanik der menschlichen Gehwerkzeuge" which became a milestone in the description of anatomy and function of the cruciate ligaments [226]. The two brothers demonstrated that the ACL consists of two functionally independent fiber bundles with independent tension pattern, which are twisted during knee flexion (Fig. 1). They also realized that sectioning of the ACL resulted in abnormal forward movement of the tibia, thereby providing an early description of the anterior drawer sign. In 1858 the anatomist Karl Langer of Vienna (1819–1887) confirmed earlier findings made by the Weber brothers and provided an advanced description of the kinematic behavior pattern of the cruciate ligaments [127].

Clinicians of the eighteenth century began to raise awareness of the functional disabilities associated with distortion of the knee but failed to make the connection with rupture of the ACL. William Hey (1736–1818) described the sensation of the "pivot shift" when he observed that "The knee joint is not infrequently affected with an internal derangement of its component parts, and this sometimes in consequence of trifling accidents. The defect is, indeed, now and then removed as suddenly as it is produced, by the natural motions of the joint without surgical assistance" [84]. Sir Astley Cooper of London (1768–1841) called it a "partial luxation of the thigh-bone from the semilunar cartilages," while Joseph-François Malgaigne (1806–1865) considered the sudden subluxation of tibia on femur to be due to abnormal relaxation of the cruciate ligaments [2, 33]

Robert Adams of Dublin (1791–1875) first described the distressing signs of "giving way" in a patient as a "Sudden sense of weakness … followed by

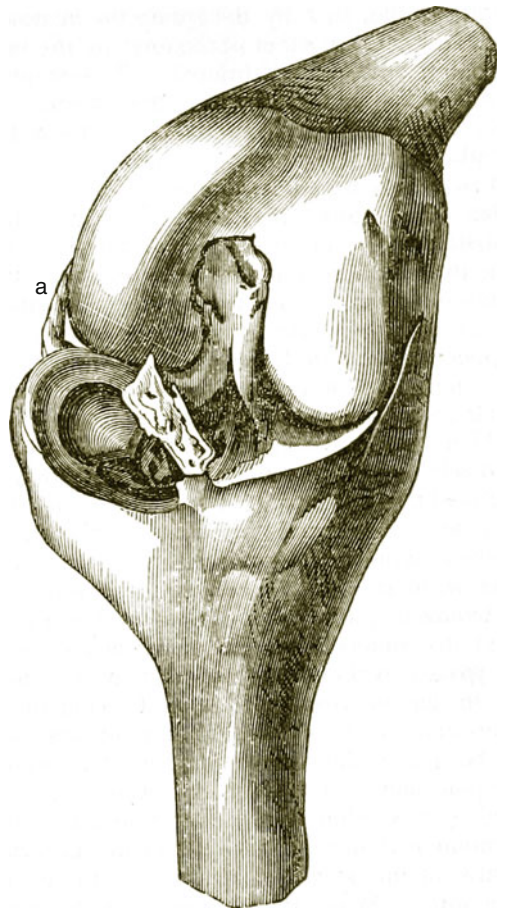

Fig. 2 Robert Adams of Dublin provided the first record of a torn cruciate ligament (avulsion injury), which he observed in 1837 [2]

some effusion of synovial fluid into the joint" [2]. He also provided us with the first description of a proven ACL injury, although it is likely that many more such injuries had occurred before then, but failure to recognize clinical signs and the absence of reliable assessment tools prevented their discovery. In 1837 Adams observed the case of a drunken 25-year-old man who injured his knee wrestling and died 24 days later. Autopsy of the knee revealed that the knee had become septic and that the ACL had torn off the tibia with a portion of bone still attached to the ligament (Fig. 2). Adams did consider it "not improbable that in sprains of the knee joint, the interior of the articulation is occasionally injured; that the crucial ligaments are stretched; and that some of their fibres give way occasionally, breaking in their centres, or detached by their extremities from the bone."

In 1845 Amedeé Bonnet of Lyon (1809–1858) published his "Traité des maladies des articulations," describing some of the essential signs indicative of acute ACL rupture: "In patients who have not suffered a fracture, a snapping noise, haemarthrosis, and loss of function are characteristic of ligamentous injury in the knee" [17]. Bonnet advocated conservative management for ligamentous injuries and suggested application of cold packs in the acute stage [18]. Through his own experiments, he was aware of the detrimental effects of

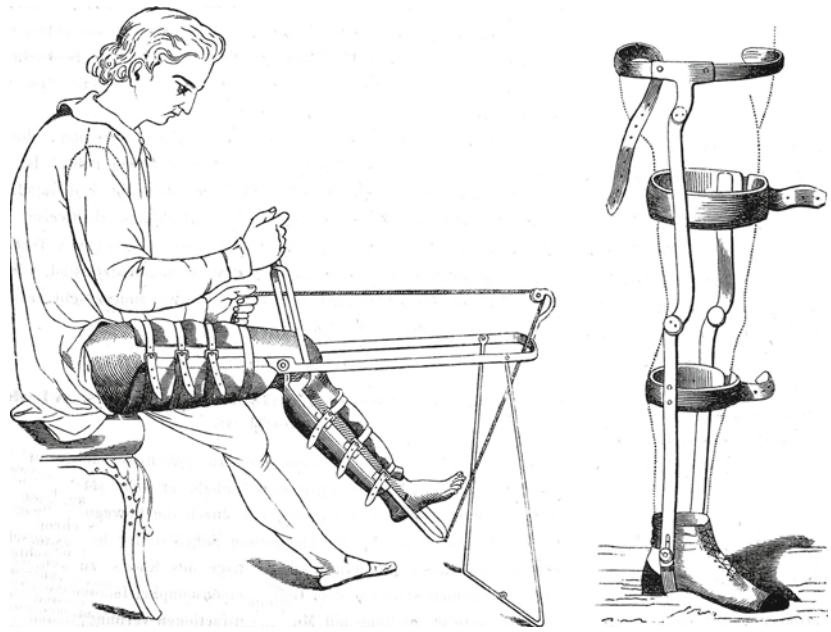

Fig. 3 Amedeé Bonnet's patient-operated movement apparatus to prevent stiffness following internal knee derangement (*left*). Knee brace to enable patients with chronic instability to remain ambulatory [18]

prolonged immobilization on articular cartilage and hence encouraged early motion exercises using a motion apparatus and sliding frames (Fig. 3). For patients who continued to suffer from instability, he suggested wearing of a long-leg hinged brace. Sadly, Bonnet's ideas and suggestions received little recognition beyond French borders.

In 1850 James Stark of Edinburgh (1811–1890) reported some of the disabling signs of ligament rupture he had observed as "… something gave way with a snap in the left knee; when raised, she found she had lost all command over the leg" [208]. He treated both of his patients conservatively, but despite 3 months of immobilization and a further 10 months using a semi-rigid brace, neither regained normal knee function.

Toward the end of the nineteenth century, clinicians started to perform cadaver experiments with zest to better understand the mechanism of ligament failure. It was soon recognized that the ACL most commonly tore off the femoral insertion unless it became avulsed with a fragment of bone off the tibia [18, 44, 90]. In 1876 Leopold Dittel of Vienna (1815–1898) published on the examination results of a number of knee specimens [44]. Although he noted that ACL tears can occur in isolation, he also recognized the common association between ACL injury, damage to medial collateral ligament, and medial meniscus, structures which Galeazzi later incorporated in his concept of the "central cruciate meniscal capsular complex" (Fig. 4). Erwin Payr (1861–1946) and Willis Campbell of Memphis (1880–1941) confirmed Dittel's findings through clinical observations [26, 179]. Although Campbell described this injury pattern "terrible triad," it was the term "unhappy triad" coined by Don O'Donoghue of Oklahoma (1901–1992) in 1950 which became a household name and synonymous with this injury pattern [172].

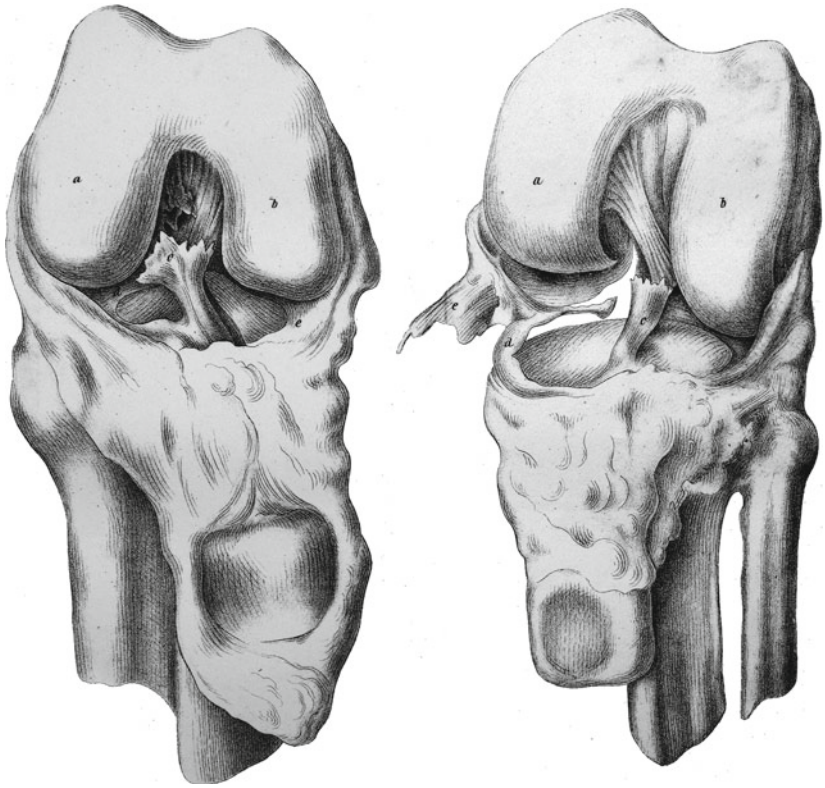

Fig. 4 Drawings of two knee specimens prepared by Leopold Dittel following his motion experiments published in 1876. The *right* image is depicting the common injury pattern of ACL, medial collateral ligament, and medial meniscus, later described by O'Donoghue as "unhappy triad". Letters on drawing refer to a=medial femoral condyle, b=lateral femoral condyle, c=ACL, d=medial meniscus, e=medial collateral ligament [44]

Albert Trillat later described the injury pattern of "pentade malheureuse interne" which included additional damage to PCL and lateral meniscus [218].

In 1875 Georgios Noulis of Athens (1849–1919) presented his thesis entitled "Entrose du genou" to the medical faculty of the University of Paris [168]. It contained the first detailed description of what today is known as the Lachman test, and was based on his observation that anterior displacement of the tibia was most noticeable when he positioned the leg near full extension. Stirling Ritchey rediscovered the value of Noulis's findings in 1960 [188]. The eponym was attributed to the test in 1976 by Joseph Torg in appreciation of his mentor John Lachman (1956–1989) [216]. Torg popularized its value in assessing ACL function by providing a biomechanical rationale regarding the test's improved diagnostic accuracy over the anterior drawer test. The latter had for a long time been considered the investigation of choice despite Palmer's and Lenggenhager's discovery that significant anterior subluxation cannot occur in isolated ACL tears without injury to external supporting structures [130, 177]. The test's value however was not called into question until evidence on its low sensitivity was revealed through investigations conducted by Jack Hughston of Columbus (1917–2004) and Sten-Otto Liljedahl of Stockholm (1923–1982). Both researchers were able

to show that the test was positive in just 1/3 of patients with proven ACL deficiency [96, 131].

By the late 1870s, clinicians had gained a sound knowledge of the clinical signs and symptoms associated with injuries to the ACL which Paul Segond of Paris (1851–1912) summarized as "strong articular pain, frequent accompanying pop, rapid joint effusion and abnormal anterior-posterior movement of the knee on clinical examination" [199] He also described the so-called Segond fracture, which he rightly believed to be "… pathognomonic of torsion of the knee in internal rotation and slight flexion of the lower leg and which is associated with rupture of the anterior cruciate ligament."

In 1927 Bruno Pfab described in detail the blood supply to cruciates and menisci [182]. Our knowledge of the functional unit of ACL and PCL in safeguarding normal rolling and sliding motion of femur on tibia was further enhanced through the work of the anatomists Hermann von Meyer (1815–1892) and Hermann Zuppinger (1849–1912) of Zürich, Hans Straßer of Bern (1852–1927), and Rudolf Fick of Innsbruck (1866–1939) [58, 156, 210, 239]. In the following decades, further studies on the functional anatomy of the ACL confirmed its role as the primary anterior stabilizer and secondary rotatory stabilizer of the knee [1, 22, 167]. By the end of the twentieth century, the orthopedic community had thus acquired a sophisticated understanding of the functional behavior of the ACL and the detrimental effects associated with its deficiency.

Direct Ligament Repair

During the nineteenth century, conservative management remained treatment modality of choice as open surgery was considered grave and generally reserved for life-threatening conditions. The aim was to get the patient back to work, while little emphasis was placed on establishing normal function or a possible return to recreational activities. Patients were generally immobilized for several months, and although most patients showed acceptable stability, few regained their preoperative mobility. Even after the introduction of Lister's antiseptic method, surgeons showed reluctance in embracing surgery for a condition as obscure as ligament disruption. This era was described by Edgar Bick as a time "when the [knee] joint was considered a matter beyond the pale of the ordinary rules of surgery" [14].

In 1900 William Battle (1855–1936) published the successful result of an open ACL repair using silk sutures [12]. Arthur Mayo-Robson of Leeds (1853–1933), however, had performed a similar procedure in a 41-year-old miner 5 years earlier but did not publish his case until 1903 [150]. When reviewed 6 years later, the patient considered his leg "perfectly strong," and Mayo-Robson remarked, "He walks well without a limp and can run. No abnormal mobility whatever present. Extension to the straight line is perfectly free. Flexion is somewhat limited."

By 1913 Hubert Goetjes of Cologne was able to trace a total of 23 published cases of ACL rupture and added 7 of his own [74]. He presented a deep understanding of the effects of cruciate deficiencies and gave a comprehensive account of the ligament's function and biomechanics. Goetjes recommended direct repair of all acute and chronic cases affected by abnormal knee

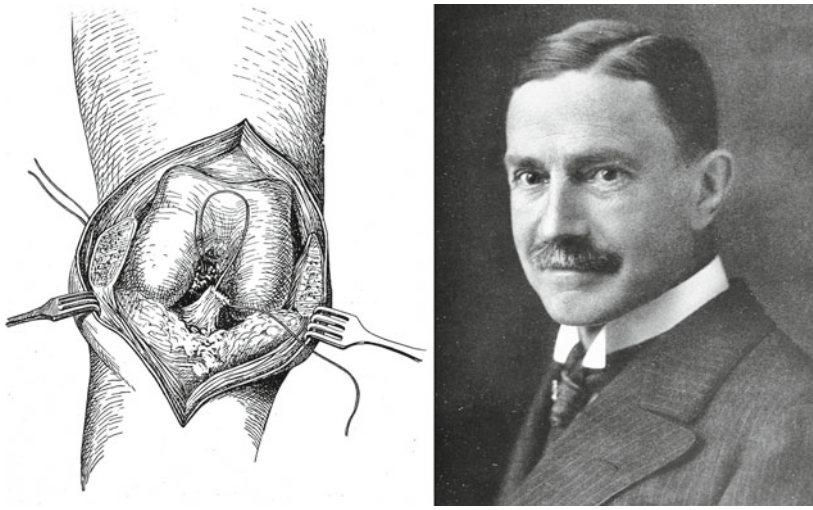

Fig. 5 ACL repair technique presented by Georg Perthes of Tübingen (*right*) in 1927 using a patella-splitting approach. The ligament remnant was reattached to the femur with a transcortical aluminum-bronze wire (With kind permission of Hüthig Jehle Rehn, Heidelberg [181])

function and became the first surgeon to suggest examination under anesthesia when the clinical diagnosis was uncertain.

The results of ACL repair however remained unpredictable. Robert Jones (1857–1933) expressed disbelief that suture repair would yield advantage over plaster immobilization when he remarked that "… stitching the ligaments is absolutely futile. Natural cicatricial tissue … is the only reliable means of repair" [108]. Jones's view was echoed by Ernest Hey Groves (1872–1944) who commented that "… in all my cases the ligaments have been so destroyed … that direct suture would have been utterly impossible" [85]. Critics of surgical intervention like Constantine McGuire also believed that repair did not yield any benefit other than a conversion from a state of instability to one of joint stiffness, created through prolonged immobilization [140].

Georg Perthes (1869–1927) offered an improved repair technique by connecting a wire loop to the ligament remnant which he secured via transfemoral drill holes (Fig. 5) [181]. He reported excellent results with up to 4 years of follow-up in three patients. Perthes thought it was wrong to consider ACL repair only once patients became affected by ongoing instability and expressed concern that "the level of knee laxity and associated symptoms of swelling and discomfort are likely to increase with time." He suggested examining patients as soon as pain and swelling had subsided and to repair all complete tears. Pfab provided further evidence on the suitability of this technique, when he observed complete reconstitution of the ACL following Perthes' repair in sheep [183]. In response to the often insufficient length of ligament remnants, Erwin Payr of Leipzig (1861–1946) designed a procedure that was essentially a partial ACL reconstruction [179]. A fascia loop was threaded through a semicircular tunnel, positioned at the femoral origin of the ACL, and sewn against the tibial ACL stump (Fig. 6).

In 1938 Ivar Palmer of Stockholm (1897–1985) published his treatise "On the Injuries to the Ligaments of the Knee Joint," a detailed study on anatomy,

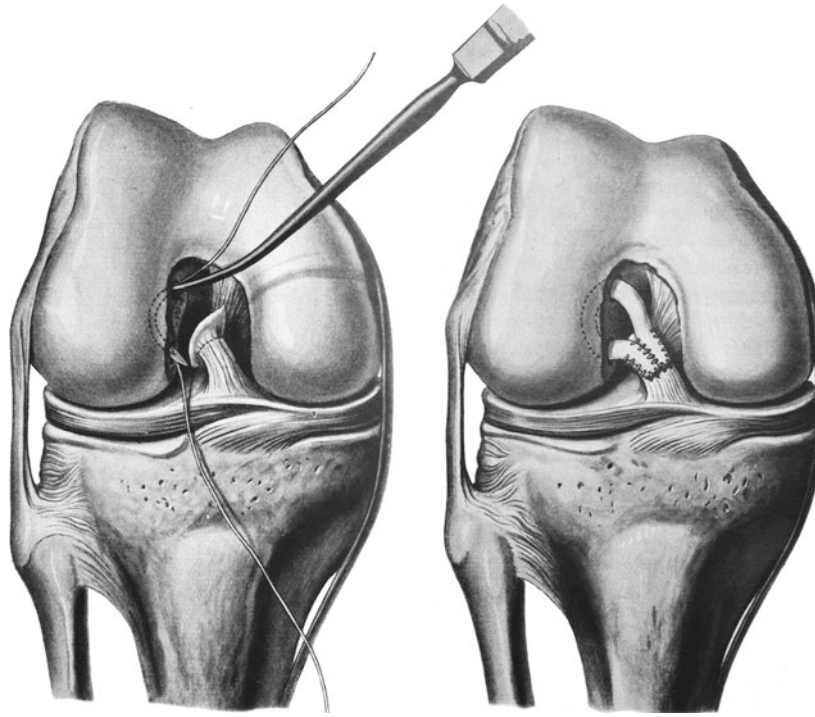

Fig. 6 Erwin Payr's technique published in 1927 to repair the proximally torn ACL with a fascia lata loop anchored against the lateral wall of the intercondylar notch (With kind permission of Springer Science, Berlin [179])

biomechanics, pathology, and treatment [177]. Like Perthes, he advocated that "the golden opportunity is the early operation … when it is generally possible to restore anatomic conditions." Palmer, a proponent of the Perthes' repair technique, also saw potential benefits in repairing both ACL bundles separately.

In the early 1950s, O'Donoghue, a key figure in orthopedic sports medicine, published his experience of treating 22 athletes, revealing that surgery within 10 days of injury offered the best chance of a complete recovery [172, 173]. In his view "the rate of success [of reconstruction] is not sufficiently high to warrant the attitude that acute ruptures of the anterior cruciate need not be repaired under the misapprehension that the ligament can be satisfactorily reconstructed at a later date if the patient has sufficient disability. On the other hand, after successful repair of an acute rupture I have no hesitation in recommending return to active athletics, including football." Through emphasizing the need for early intervention if return to sport activities is desirable, O'Donoghue gave ACL surgery an unexpected boost in the USA. In 1965 Liljedahl presented 18-month follow-up results of 33 patients who had undergone acute ACL repair with "all but three of their knees were completely stable and had a full range of motion" [131].

Suture repair continued to be practiced into the 1980s and was supported by good clinical results published by David MacIntosh and John Marshall [142, 145]. Both devised a variation on the Perthes' technique with sutures being passed behind the lateral femoral condyle in a so-called over-the-top repair. In 1976 John Feagin of New York presented his 5-year results of 32 army cadets

who had undergone direct ACL repair [57]. Although initially 84 % did well and returned to sporting activities at 5 years, almost all patients suffered some instability and two-thirds experienced pain. Feagin concluded that "long-term follow-up evaluations do not justify the hope … that anatomic repositioning of the residual ligament would result in healing." His views were shared by Werner Müller who believed that "success in these cases may well have been due to extensive adhesions among the intra-articular folds, greatly reducing joint play and restraining anterior translation while still permitting recovery of knee motion in flexion-extension" [163]. Superior results achieved with ligament reconstruction compared to ligament repair sealed the fate of primary suture repair, which was all but abandoned by the end of the twentieth century [46, 53].

Pioneers of ACL Reconstruction

Clinicians eventually realized that a number of patients with chronic knee laxity suffered ongoing and debilitating instability despite previous attempts of conservative or surgical management. Hey Groves expressed disenchantment with the standard of treatment of ACL injuries at the time when he wrote, "while the frequency and importance of this injury is becoming more widely known, there have not been any corresponding advances in the method of treatment … a rigid plaster or leather cast to be worn for a year, followed by a hinged apparatus represents the generally accepted method" [85]. In 1913 Paul Wagner wrote a thesis entitled "Isolierte Ruptur der Ligamenta Criuciata" in which he suggested the use of fascia to reconstruct the ACL when the ligament was so badly damaged that repair was impossible [222].

Erich Hesse, surgical assistant to Ivan Grekov of St Petersburg (1867–1934), reported in 1914 on a 40-year-old man who dislocated his knee and tore the ACL [82]. Grekov used a free fascia graft, routed through drill holes in the femur and stitched against the ligament remnants, achieving a knee that was functioning "exceptionally well with no side to side laxity."

Although we know that Max zur Verth of Hamburg (1874–1941) replaced ACLs with proximally based fascia lata before 1917, details of his surgical technique and outcome remain unknown [89]. On 25th of April 1917, Hey Groves reconstructed his first ACL at Bristol General Hospital, using fascia, which he detached from Gerdy's tubercle and "threaded through new canals bored in femur and tibia" [85]. Leaving the tendon attached to the muscle was believed to maintain the tendon's blood supply and nutrition. Hey Groves was aware that proper knee joint function could only be reestablished if the reconstructed ligament graft is placed in the exact anatomic position of the original ACL "in contradistinction to a mere passage of new ligaments across the joint" [86]. He also recognized the importance of graft obliquity as "any new ligament which is used to replace them should be given this oblique direction, even in an exaggerated degree, because an anterior ligament will be efficient in preventing anterior tibial displacement in proportion to its obliquity." It took however, more than 80 years before the mechanical principle behind the notion of graft obliquity to facilitate improved rotational stability received wider recognition [135, 198].

In 1918 Alwyn Smith of Cardiff (1884–1931), who reported on nine cases treated with the Hey Groves' technique, criticized its incomplete nature "as it

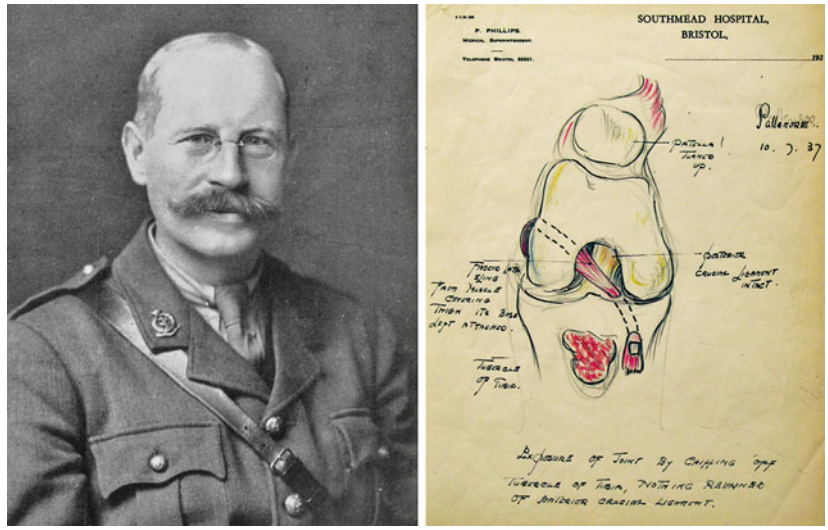

Fig. 7 Photograph of Ernest William Hey Groves taken in full uniform in 1916 (From (1941) *Br J Surg* 24:165–167, with kind permission of John Wiley & Sons, Hoboken). Original drawing by Hey Groves produced in 1937, depicting his revised ACL reconstruction technique (author's archive)

does not attempt to strengthen in any way the internal lateral ligament, so that the new fascial strip has to bear the entire strain of abduction of the knee as well as of anterior sliding and internal rotation" [207]. Smith obviously encountered a more complex injury pattern with involvement of the medial structures. In his technique, he described using distally based fascia routed through femoral and tibial tunnels and folded upward across the medial joint space to strengthen the MCL. Smith also described using massage and electrical stimulation to prevent quadriceps atrophy.

Hey Groves like Smith also switched to distally based fascia as he found that a proximally based graft only provided a limited length (Fig. 7) [86]. In 1919 he conveyed his experience of 14 cases, of which "None were made worse, 4 showed no benefit, 4 benefitted to some degree, 4 were cured and 2 were only operated 6 months ago [but] promise to be successful." Compared to his predecessors, Hey Groves recognized the association between ACL deficiency and anterolateral tibial subluxation when he commented that "In active exercise, when the foot is put forward and the weight of the body pressed on the leg, then the tibia slips forward; sometimes this forward slipping of the tibia occurs abruptly with a jerk ...." In 1972 Robert Galway and David MacIntosh of Toronto used this phenomenon to devise the "pivot-shift test", thus creating a sensitive assessment tool to identify ACL incompetence [70]. During the 1980s Roland Jakob of Berne refined the test by developing a reproducible grading system to classify type and degree of various laxities [*]. Donald Slocum, Ronald Losee, and Jack Hughston (jerk test) described alternative assessment methods to reproduce anterolateral subluxation, all of which essentially represented variations of

*Jakob RP, Stäubli HU, Deland JT. Grading the pivot shift. Objective tests with implications for treatment. J Bone Joint Surg. 1987;69[Br]:294–299.

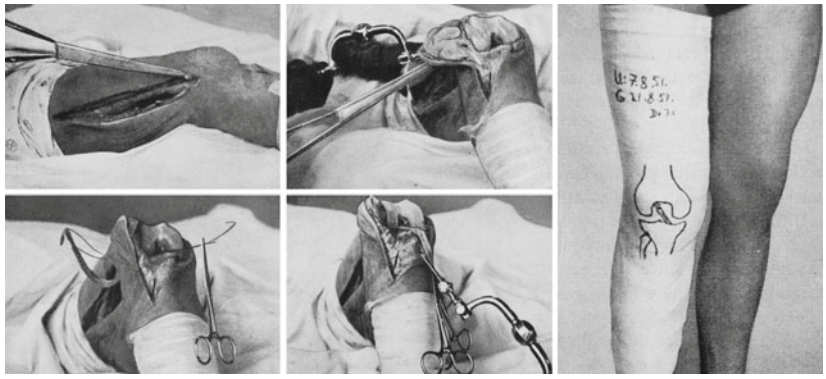

Fig. 8 Contemporaneous intraoperative photographs showing an ACL reconstruction procedure according to Hey Groves performed by Bernard Janik of Vienna in the early 1950s. These images highlight the extensive exposure needed to perform this surgery at the time (With kind permission of Walter De Gruyter, Berlin [102])

the pivot-shift phenomenon [97, 137, 206]. In 1981 Jakob introduced the "reverse pivot-shift test" to assess and diagnose posterolateral instability [**].

In 1927 Maurice Horan reported on a well-healed ligament in a knee which he excised 5 years following a Hey Groves reconstruction [91]. In 1938 Palmer was able to examine the knee of a patient who had died of a pulmonary embolus just 10 weeks after receiving a "Hey-Groves plasty" [177]. To Palmer's amazement, the graft had already become synovialized, and vessels and connective tissue had started to invade from the periphery. Max Lange of Munich (1899–1975), who had used Hey Groves' technique since the late 1930s, reviewed 50 of his cases in 1957 and observed excellent results in 82 % following early reconstruction and in 62 % when surgery was delayed [69, 125].

Despite the excellent work of these early pioneers, the debate over the following 50 years was less over primary repair versus reconstruction but whether any procedure should be performed at all [149]. The mood was captured by Timbrell Fisher (1888–1967) who believed that "operations should be reserved for cases who suffer grave functional disability, which persist in spite of increasing the power of the quadriceps, and other thigh muscles, or the wearing of a well-planned and accurately fitting mechanical support" [59].

Although ACL reconstruction was a formidable procedure (Fig. 8), proponents of surgery like Leroy Abbott of San Francisco (1890–1965) believed that "The application of a splint or plaster cast until such time as the lesion is judged to have healed satisfies the attendant, if not always the patient. Rest and fixation, although sound in principle … often prove disastrous in those patients in whom the supporting ligaments of the knee have been severely damaged" [1]. The 1930s also saw evidences emerge, as referred to by Hans Burckhardt of Essen (1879–1965), that the ACL-deficient knee is "exposed to gradual degeneration due to malfunctioning of its internal guiding system" [25].

[**]Jakob RP, Hassler H, Stäubli HU. Observations on rotatory instability of the lateral compartment of the knee. Experimental studies on the functional anatomy and the pathomechanism of the true and the reversed pivot shift sign. Acta Orthop Scand [Suppl]. 1981;191:1–32.

Choice of Graft Materials

Fascia Lata (Iliotibial tract)

Fascia remained a popular choice of graft for the best part of the twentieth century [36, 50, 98, 102, 187]. In 1927 Charles Eikenbary of Seattle (1877–1933) reported on using free fascia graft implanted through a medial parapatellar approach [50]. He thereby avoided complications associated with patellar tendon detachment or patellar division, which were still the standard methods to facilitate knee exposure at the time [85, 187, 207, 211].

First clinical results on the survival of free fascia grafts, which up to this point were believed to disintegrate as a result of being deprived of their blood supply, were provided in 1929 by Wilhelm Jaroschy of Prague (1886–1938) [103]. Heinz Simon, his assistant, later observed an increased incidence of degenerative changes in 3 out of 12 patients following ACL surgery but was uncertain whether this was related to the operation. Simon nevertheless demanded that tunnels are to be positioned at the ligaments' native attachment sites [202].

William Cubbins of Chicago became key promoters of the Hey Groves procedure in the USA [36, 37]. Few surpassed his enthusiasm when, in 1937 he and his colleagues exhumed the body of a deceased who had been buried for 3 weeks and on whom cruciate reconstructions had been performed a year earlier. Based on their clinical experience, they concluded that best results are obtained either through acute ligament repair or in the chronically unstable knee through ACL replacement.

In 1937 Frank Strickler of Louisville championed intra-articular reconstruction augmented with a lateral extra-articular substitution using a continuous loop of distally based fascia [211]. Tibial and femoral tunnel were positioned centrally within the joint, creating a vertically aligned graft, believed by Strickler to "work equally well in either rupture of the anterior or posterior cruciate ligament." In his experience, "about 6 months from the date of surgery, these patients have a good functioning, serviceable joint."

In 1940 Frederick Tees of Montreal offered a modification on the Hey Groves technique, by routing the graft via the tibia through the lateral femoral condyle before anchoring it against the fibular head [214]. Tees believed that reinforcing the lateral ligament would help to stabilise the joint, thereby introducing the idea of lateral extra-articular augmentation. In 1963 O'Donoghue suggested a similar variation, but instead of attaching the tendon to the fibula head, he folded it upward to repair the defect in the fascia [174]. In 1978 John Insall of New York (1930–2000) presented the "bone block ilio-tibial band transfer," a procedure based on Nicholas's and Minkoff's "iliotibial band pull-through" technique, first used at Lennox Hill Hospital in 1971 [98, 165]. Insall detached the central portion of the fascia lata with its osseous insertion from Gerdy's tubercle, rerouted the graft over the top of the femoral condyle into the joint and screwed the bone block to the tibial plateau. Insall was well aware that it would be "impossible to duplicate the original anatomy exactly with any form of graft," but his clinical results nevertheless showed that "although the results of the postoperative anterior drawer test are disappointing if one hopes to restore the knee to normal, the improvement in the patients' functional capacity is quite dramatic…and

most of these patients were engaging in strenuous sports without brace protection."

Meniscus: The Misguided Sacrifice

The treatment of choice for a torn meniscus was its removal, and since it was known that meniscal tissue consisted of avascular fibrocartilage nourished by synovial fluid, it appealed as an almost ideal substitute for the ACL [224].

In 1917 zur Verth replaced the ACL of a sailor with the torn lateral meniscus, which he left attached posteriorly, and sutured against the ligament remnants [89]. Although meniscus never gained widespread popularity, it was nevertheless considered by many to be a suitable ACL replacement [32, 133, 166, 230]. Their opinion is reflected by Bengt Tillberg who, after having performed the surgery on 43 patients, concluded that "The use of a meniscus for the reconstruction of either cruciate ligament is considered to be simple, safe and effective" [215].

Max Lange had experimented with meniscal tissue graft in the early 1930s but remained critical upon its use. He upheld the view that meniscal tissue was "functionally unsuitable to replace a ligament" as it was primarily designed to withstand compression rather than tension and shear [125]. In histological studies, Lange was able to confirm cystic degeneration of meniscal implants and concluded that "a degenerative meniscus appears to be too poor to be considered for reconstruction, whilst a healthy meniscus would appear to be too good" [69, 125].

Knowledge of the importance of the meniscus, consequences of its removal, and reports on clinical failures gradually prompted a shift in opinion [93, 143, 224]. This was led by publications of Hughston in 1962 who recognized the contribution of the meniscus to knee stability and those of Peter Walker in 1975, who defined the role of the meniscus in the force transmission across the joint [94, 223]. By the end of the 1980s meniscus was finally abandoned as grafting material.

Extensor Retinaculum and Patellar Tendon

Mitchell Langworthy of Spokane/WA (1891–1929) is reported to have been the first surgeon to replace the ACL using part of the ligamentum patellae [50]. Langworthy never published on his method and suffered an untimely death when he became the victim of a bullet from an unhappy patient in his private practice in 1929.

In 1928 Ernst Gold presented the case of a 27-year-old lady, who had torn her ACL skiing 2 years earlier [75]. Gold achieved a good result by using a distally based strip of extensor retinaculum and patellar tendon, which he passed through a tibial tunnel, and secured against the PCL. In 1932 zur Verth reported on the treatment of chronic ACL-deficient knees with a pedicled section of patellar tendon [240]. Arnold Wittek of Graz (1871–1956) adopted the "zur Verth" technique and presented 16 successfully operated cases in 1935 [231].

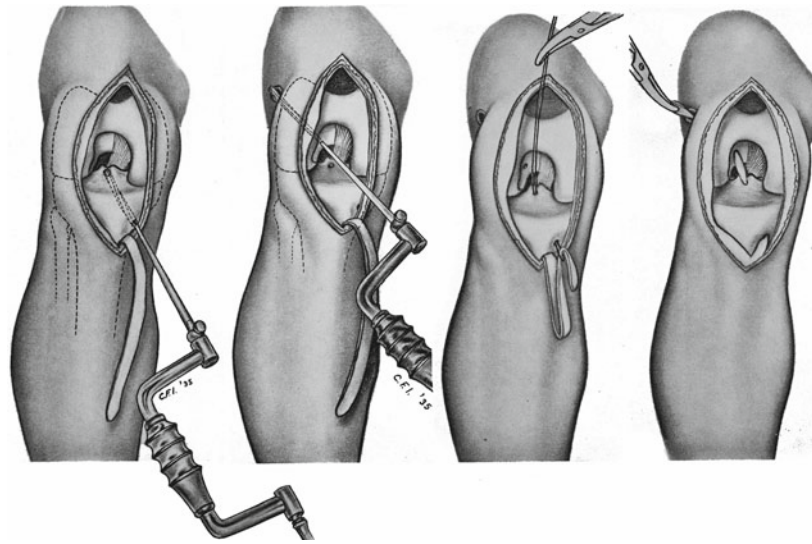

Fig. 9 Illustrations taken form Willis Campbell's publication on knee ligament repair published in 1936, showing the use of pedicled extensor retinaculum and patellar tendon in reconstructing the ACL (With kind permission of Elsevier, Philadelphia [26])

In 1936 Campbell, who coined the term "giving way" in summarizing the distressing signs of knee instability, described the use of pedicled extensor retinaculum containing "very strong tendinous tissue from the medial border of the quadriceps and patellar tendons" (Fig. 9) [26]. Campbell, like Smith, promoted combined reconstruction of ACL and MCL in cases of "unhappy triad" [27].

In 1963 Kenneth Jones of Little Rock suggested a reconstruction technique which he "considered simpler and more physiological than those previously described" [106]. He used the pedicled central third of the patellar tendon which he passed "beneath the fat pad" into the joint. To overcome problems of insufficient graft length, Jones "placed [the femoral tunnel] in the intercondylar notch just posterior to the margin of the articular cartilage." This resulted in an extremely nonanatomical graft position, contradicting his earlier claims and forcing Jones to concede that "Anatomical normalcy of the structure is, by the nature of the situation, beyond expectation." Two-year results were nevertheless promising, but when Jones reviewed 83 of his patients in 1980, almost 30 % were lacking confidence and suffered residual symptoms [107]. In the USA, the principle of ACL reconstruction with patella tendon became synonymous with the Jones procedure and known as such.

Modern biomechanical understandings and the principle of the "four-bar-linkage" have since revealed that anterior positioning of the femoral tunnel away from its native insertion would, as shown by Werner Müller, increase tension forces within the ligament graft in proportion with knee flexion (Fig. 10) [21, 153, 162].

In 1966 Helmut Brückner of Rostock described the use of the medial third of the patellar tendon [24]. To overcome problems of insufficient graft length, which had forced Jones to compromise on the femoral tunnel position, Brückner routed the tendon strip through a tibial tunnel, thereby essentially shortening the distance between graft attachment and entry into the joint. This allowed Brückner

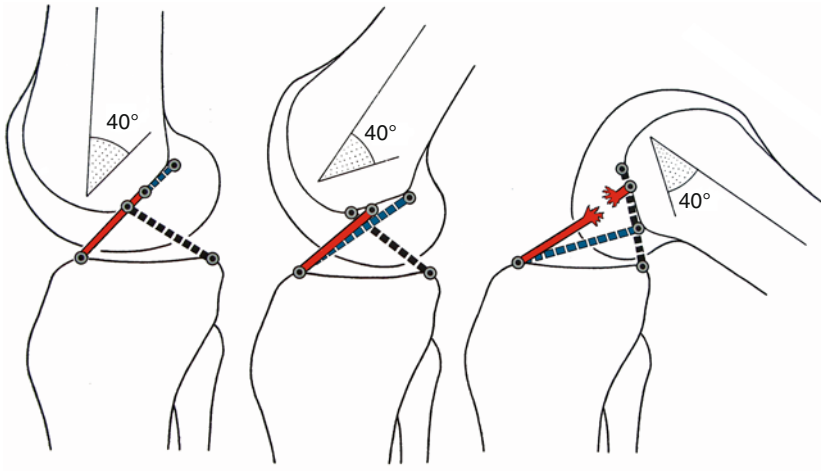

Fig. 10 Werner Müller's interpretation of the detrimental effect of malpositioning of the femoral tunnel, based on the "four-bar-linkage" model, first developed by Hermann Zuppinger of Zürich in 1904 and later refined by Straßer and Menschik (With kind permission of Springer, Berlin [162])

to position a blind-ending femoral tunnel close to the anatomic footprint. By 1969 he had performed 35 reconstructions, 90 % of which regained normal stability and 25 % experienced minor discomfort after strenuous activities [184]. The Brückner technique remained relatively unknown at first but received wider attention through Lennart Brostöm of Stockholm who modified Brückner's original procedure by pulling the proximal graft into a decorticated groove and securing it with transfemoral sutures [23]. Clinical results of 72 patients were published by Eriksson in 1976, 80 % of whom were stable at 1 year [55].

Critics of using the medial third of the patellar tendon argued that it would create changes in patellar kinematics resulting in patellar maltracking and subsequent degeneration [147, 229]. In 1974 Artmann and Wirth of Munich started to experiment with free bone-patellar tendon-bone graft (B-PT-B) taken from the central portion of the patellar tendon as it allowed for the femoral tunnel to be freely placed in its most anatomic position without being compromised by insufficient graft length [10]. Although Brückner had already reported on using a free graft in 1966 (Fig. 11), he initially reserved this technique for cases where the ipsilateral patellar tendon was compromised through previous surgery [24].

William Clancy of Madison/WI, moved from pedicled medial third to free patellar tendon graft in the 1980s and became a major proponent of this technique in the USA [30, 31]. John Marshall and associates of New York chose a different approach with their "Quadriceps tendon substitution" technique published in 1979 [145]. They harvested the patellar ligament, the prepatellar expansion, and part of the quadriceps tendon as a single graft, passed through a tibial tunnel, and looped "over-the-top" of the lateral femoral condyle. In 1976 Kurt Franke presented his experience of 79 ACL injuries, most of which were treated with a free B-PT-B graft according to Brückner [62]. He followed his patients over an 8 year period, and despite 5 cases of graft rupture, the functional results were "highly satisfying", and the majority of patients went back to high-level sporting activities.

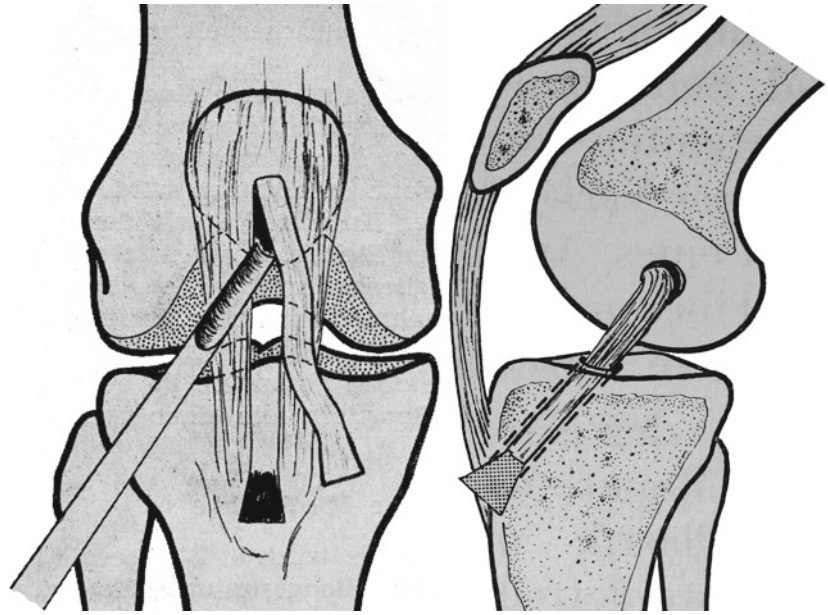

Fig. 11 ACL reconstruction with free central 1/3 patellar tendon graft and press-fit tibial fixation first described by Helmut Brückner in 1966 (With kind permission of Springer Science, Berlin [24])

Kenneth Lambert and the group of Noyes investigated potential benefits of vascularized tendon grafts in the 1980s, but clinical and experimental studies by Tomas Drobny of Zürich failed to show any advantage over free tissue grafts with regard to revascularization, tissue integration, and biomechanical properties (Drobny TK, 2012, personal communication) [45, 121, 178]. The merits of patellar tendon were further endorsed by Eriksson in Europe and Clancy and Shelbourne in the USA, and by the end of the 1990s, patellar tendon had become the most popular graft source in ACL surgery [30, 55, 200].

Quadriceps Tendon

Mindfulness of the potential morbidity associated with harvesting patellar tendon prompted some surgeons to experiment with alternative sources [3, 169, 194]. In 1976 Robert England of Jackson/WY reported on a patient who was scheduled for acute ACL repair, but upon arthrotomy, the ACL was found to be absent [54]. England elected to use a free quadriceps graft which he secured with transcortical sutures according to Perthes. Pleased with the patient's outcome, he repeated the procedure successfully in three further patients. Walter Blauth started using quadriceps tendon for chronic ACL deficiency in 1981 [16]. In the USA, John Fulkerson became the key promoter of quadriceps tendon which he considered to be superior to any other graft source [66]. Although quadriceps never gained the same level of popularity as patellar or hamstring tendon, it has nevertheless remained a suitable alternative in the revision setting or when other graft sources are compromised [42].

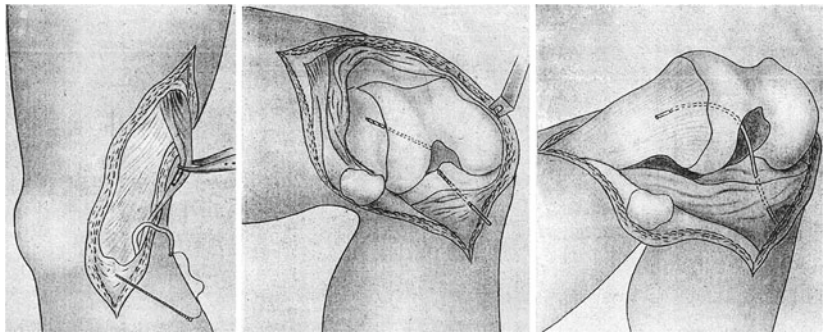

Fig. 12 In 1934 Riccardo Galeazzi of Milan presented his ACL reconstruction technique with an anatomically placed distally pedicled hamstring graft (semitendinosus) [67]

Hamstring Tendons

In 1927 Alexander Edwards of Glasgow suggested an operation he had performed on a cadaver whereby both cruciate ligaments were replaced with the proximally based hamstring tendons [48]. He was not concerned with anatomic reconstruction, since he used a single femoral tunnel drilled through the medial femoral condyle and two tibial tunnels placed in the anterior aspect of the tibial spines.

In 1934 Riccardo Galeazzi (1866–1952) pioneered anatomic ACL reconstruction with hamstrings, utilizing semitendinosus tendon which he left attached to the pes anerinus (Fig. 12) [67]. Patients were immobilized in a cast for 4 weeks and remained partially weight bearing for 6 weeks. All three patients in his series fared well but follow-up was short. Galeazzi's brilliant idea however remained unnoticed.

Harry Macey of Rochester/MI (1905–1951) presented a simplified version of the Galeazzi technique in 1939 but never reported on any clinical cases [139]. The knee was exposed via an S-shaped lateral parapatellar approach while the hamstring tendon was severed through a small stab incision at its musculotendinous junction thereby reducing surgical trauma.

In 1950 Kurt Lindemann of Heidelberg (1901–1966) developed the concept of "dynamic reconstruction" by attempting to take advantage of the stabilizing effect of the muscle-tendon unit, a principle first explored by Hey Groves in 1917 [132]. Lindemann utilized proximally based gracilis tendon, which he directed via an opening in the posterolateral capsule into a tibial tunnel (Fig. 13). At 2 years, all of his six patients had returned to work and maintained normal knee function.

In 1956 Robert Augustine of Madisonville/KY, unaware of Lindemann's publication, suggested an almost identical procedure using gracilis [11] He believed in the dynamic effect of the operation to "stabilise the tibial plateau on the femur in conjunction with the PCL when the hamstrings are contracted." DuToit of Pretoria used the Lindemann procedure extensively during the 1960s, and most of his patients returned to vigorous sporting activities [47]. In his opinion, the preservation of proprioceptors and attachment to active muscle would facilitate tension in the transferred graft to be maintained.

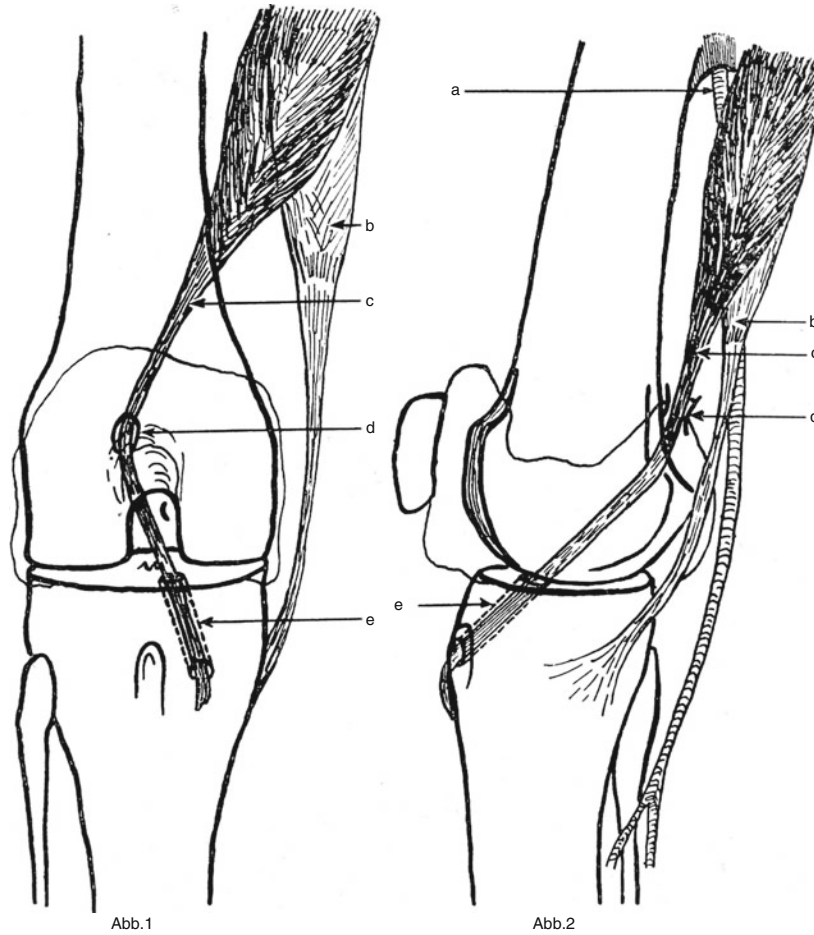

Fig. 13 Kurt Lindemann of Heidelberg introduced the concept of "dynamic ACL reconstruction" in 1950, believing that the gracilis muscle/tendon unit would actively stabilize an ACL-deficient knee. Letters on drawing refer to: a = politeal artery, b = original position of gracilis muscle, c = altered position of gracilis, d = entry point of tendon through posterior capsule, e = tibial canal. (With kind permission of Springer Science, Berlin [132])

Robert Merle d'Aubigné of Paris (1900–1989) adopted the principles of the Galeazzi/Macey technique in the 1950s using pedicled semitendinosus, while gracilis was passed through a transfemoral tunnel, to reinforce the MCL [155]. Max Lange, although satisfied with his results achieved with fascia, switched over to hamstrings in the mid-1960s as the operation "required less exposure and dissection therefore reducing surgical trauma." He also believed in the merits of medial capsular reefing for most chronic cases with significant laxity [125, 126]. The 1970s saw a renewed interest in pedicled hamstrings as graft source led by James McMaster of Pittsburgh and Kenneth Cho of Washington DC [29, 151].

James Horne and Chris Parsons of Toronto expressed concern about possible abrasion of the tendon graft at the femoral tunnel entry site and proposed for the graft to be positioned "over-the-top" of the lateral femoral condyle in a more "anatomical line" [92].

In 1973 Karl Viernstein (1920–2011) and Werner Keyl of Munich recruited both gracilis and semitendinosus tendon introducing the double-strand technique [219]. Brant Lipscomb of Nashville brought the concept of using both hamstrings to a wider audience in the early 1980s, but their technique soon became challenged by the introduction of the four-strand hamstring reconstruction offered by Marc Friedman of Los Angeles [64, 134]. Comparative studies eventually confirmed equivalence in terms of clinical outcome between hamstrings and other autologous graft sources [8, 88, 189].

Xenografts and Allografts

Allograft reconstruction of the ACL was an attractive proposition as it avoided the need of graft harvest and associated donor site morbidity. Although Eugene Bircher of Arau (1882–1956) and Italian Micheli successfully experimented with kangaroo tendon, xenografts remained a rare choice and never gained any real popularity [15, 158]. The use of human allografts was first reported by Konsei Shino in 1986 [201]. When he reviewed 31 of his patients after a minimum follow-up of 2 years, all but one had been able to return to full sporting activities. The use of allograft has since achieved widespread popularity particularly in the USA despite a temporary setback in the 1990s following fears of viral disease transmission [79, 160].

Synthetics: Hankering for the Ideal Graft

Themistocles Gluck of Berlin (1853–1940), pioneer of joint arthroplasty, successfully bridged tendon defects with plaited catgut in 1881 [72]. Fritz Lange of Munich (1864–1952), who had successfully used silk for the treatment of paralytic feet in 1895, first suggested silk as prosthetic ligaments to treat "wobbly knees" in 1903 [122]. In 1907 he reported on four cases of ACL deficiency, which he stabilized with extra-articularly placed "artificial ligaments made of silk" augmented with hamstring tendons (Fig. 14) [123]. The silk was slowly surrounded by fibrous tissue, and Lange praised the "wonderful ability of the silk to produce fibrous tissue under functional stress," a finding confirmed through histological investigations by Max Borst of Würzburg (1869–1946) a few years earlier [19]. Lange's grandson Max achieved clinical success by utilizing silk augmented with fascia in ACL reconstruction which he reported in 1932 [124]. Lange was mindful that joint stability could not be achieved by silk alone, which he saw merely as a scaffold providing initial strength while inducing a process of ligament healing and regrowth.

In 1913 Edred Corner of St Thomas in London (1873–1950) tried to replace a torn ACL with two interlaced loops of silver wire, but the wire broke after the patient started to mobilize [34]. Karl Ludloff of Frankfurt (1864–1945), used a strip of fascia wrapped around a thick central silk suture to replace the ACL in a 23-year-old farmer in 1927 [138]. He was meticulous in trying to place both tunnels at the center of the anatomical footprints of the

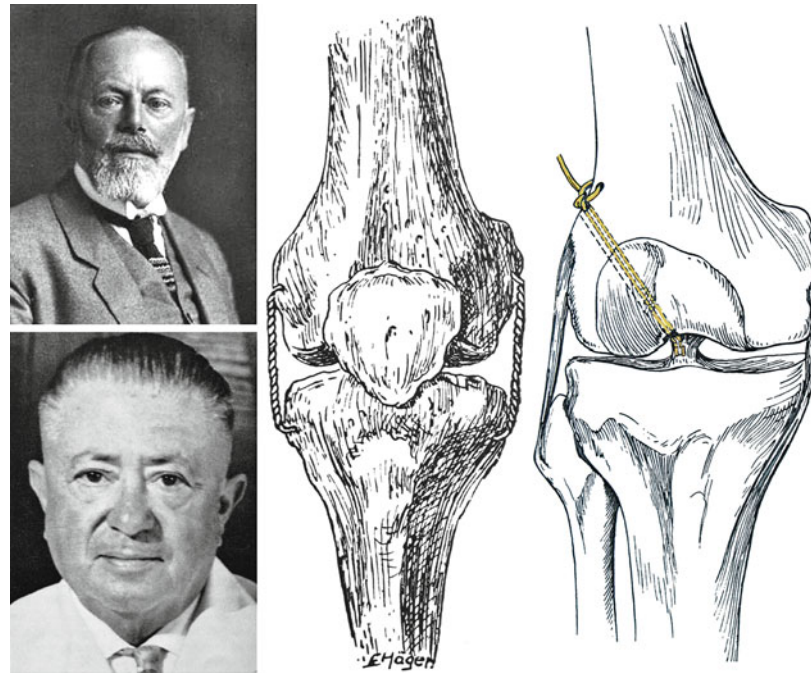

Fig. 14 In 1903 Fritz Lange (*top left*) started using silk sutures as extra-articular augmentation to treat chronic knee instabilities. His grandson Max (*bottom left*) introduced the technique of partial substitution/reconstruction of the torn ACL with "Hydrargyrumoxyzyanat-Seide" in the late 1920s. (From: Vulpius O, Stoffel A (1913) Orthopädische Operationslehre. Enke, Stuttgart [221])

ACL and kept tunnel diameters small enough to obtain a tight-fitting graft. Ludloff refrained from any form of graft fixation as he believed that the graft should be allowed to establish equilibrium of tension. He encouraged early mobilization, and the patient was walking on the 25th day. When reviewed at 5 months, he had resumed his duties as a farmer and presented minimal loss of flexion and a negative anterior draw.

The second half of the twentieth century saw a myriad of different synthetic ligament graft materials appear. In 1949 Rüther reported disappointing results following the implantation of a synthetic ACL made of Supramid®, a polyamide derivative [193]. Olav Rostrup started using Teflon® and Dacron® grafts in 1959 [191]. He saw synthetics primarily as augmentation devices to support fascia or tendon and felt that the synthetics used are "not the ideal material" and hence did "not recommend its wide-scale or indiscriminate use." In 1973 Proplast®, a porous Teflon® graft claiming to offer enhanced fibrogenic properties, became one of the first synthetic graft materials to receive FDA approval, but clinical performance was disappointing [233].

Richard Wilk and John Richmond of Boston reviewed 50 patients with Dacron® ligament grafts in 1993 and recorded a significant deterioration in ligament failure rate from 20 % at 2 years to 37.5 % at 5 years [227]. Equally devastating results were reported from Sweden by Wolfgang Maletius and Jan Gillquist. In their 9 year results they recorded 44% of graft failures, whilst only

14% of patients maintained acceptable stability [144]. The Stryker Inc. finally discontinued the Dacron® ligament device in 1994. David Jenkins of Cardiff experimented with flexible carbon fiber in the 1980s [105]. Carbon was thought to act as a temporary scaffold, encouraging the ingrowth of fibroblastic tissue and collagen production. Clinical results however were overshadowed by foreign body reaction and tissue staining through carbon fragmentation [192].

In the late 1970s, Jack Kennedy of London/ON (1917–1983) introduced the LAD®, a ligament augmentation device made of polypropylene [111]. Kennedy developed the concept of "load sharing," which arose from observations that biological grafts are affected by temporary degeneration and loss of strength before being fully incorporated. The LAD® was hoped to protect the biological graft during this vulnerable phase [113]. Lars Engebretsen of Oslo conducted a large randomized controlled study in the 1980s to assess the merits of the LAD® compared to acute repair and reconstruction [53]. He enrolled 150 patients into the three treatment arms and produced follow-up results of up to 16 years. Both acute repair and repair with the LAD® provided for failure rates of up to 30 % which discouraged the authors from recommending the use of this ligament augmentation device [46].

Various other synthetic ligament grafts, including Gore-Tex®, PDS®, Eulit®, and Polyflex®, were introduced during the same period [101]. Awareness of the potential biological and biomechanical shortcomings of using a single type of synthetic material also prompted attempts to combine materials of favorable characteristics like it was done with the ABC (Activated Biological Composite) ligament. Clinical long-term performance of most of these materials, however, was characterized by fatigue failure as in vivo functional stresses exceed their biomechanical properties [186]. Reports on complications like chronic synovitis, osteolysis, foreign body reaction, and poor incorporation into host bone finally sealed the fate of synthetics, a trend Ejnar Eriksson had already anticipated in 1976 by stating that synthetics are "like shoestrings, they eventually break" [56, 203, 232].

Extra-articular Procedures: Treating Functional Disabilities

Even before intra-articular reconstructions were attempted, surgeons had already started to experiment with simplified extra-articular procedures designed to control patients' disabilities [71, 123]. The rationale behind such efforts was encapsulated by Henry Milch of New York (1895–1964) when he expressed the notion that "a torn ACL left little if any disability whilst the medial or tibial collateral ligament is of the utmost importance in the stability of the knee" [159].

The first account of an extra-articular procedure was published in 1907 by Fritz Lange who successfully placed silk sutures across the joint space in an attempt to treat disabling knee laxity (Fig. 14) [123]. Encouraging results of free tendon transfer by Kirschner and Davis persuaded Knut Giertz of Stockholm (1876–1950) in 1913 to attempt stabilising the knee of a 13-year-old girl who had lost her cruciates as a result of septic arthritis [41, 71, 114]. He augmented both collateral ligaments with sections of fascia, and the child regained good function albeit with slight restrictions in motion.

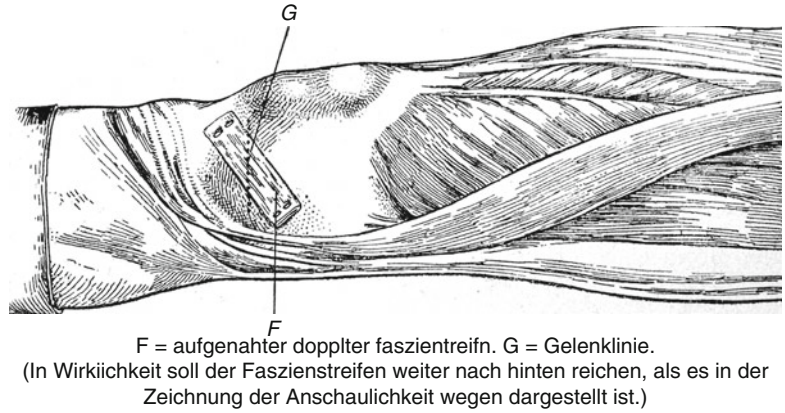

Fig. 15 Extra-articular stabilization with obliquely placed fascia strip across the medial joint space according to Hermann Matti of Bern (With kind permission of Springer Science, Berlin [148])

In 1918 Hermann Matti of Bern (1879–1941) published his paper entitled "Replacement of the torn anterior cruciate with extra-articular free fascia graft," where he describes the application of an obliquely placed doubled-up fascia strip across the medial joint space (Fig. 15) [148]. A number of similar procedures focusing on strengthening of the MCL and anteromedial capsule were introduced over the following 20 years [13, 20, 149]. In 1947 Emil Hauser of Chicago (1897–1981) proposed placing pedicled strips of patellar and quadriceps tendon in a crisscross fashion onto the anteromedial capsule to treat ACL or PCL deficiencies [80]. In 1957 Merle d'Aubigné advocated his "plastie osteo-ligamentaire," an opening wedge tibial osteotomy positioned above the distal MCL attachment for the treatment of ligament laxities [155].

In 1963 Arthur of Cape Town (1907–1989) conveyed, "If we consider that the cruciate ligaments act as check-straps which prevent anteroposterior movement of the tibia on the femur and that resulting instability after rupture of these ligaments is due to the absence of these check-straps, then the only logical course of treatment is anatomic replacement. On the other hand, if the cruciate ligaments are guide ropes which keep the tibia in its normal helicoid track on the medial condyle of the femur, it is possible to replace this function by extra-articular tendon transplant" [81]. Helfet made a case for the latter, and his views were echoed by Arthur Ellison (1926–2010), who in comparing the knee with a wheel believed that "it is easier to control rotation of a wheel at its rim than at its hub" [52]. The debate hence gradually moved away from focusing primarily on restoring anatomy by ways of reconstructing damaged ligament structures toward a treatment approach that tried to address functional disabilities.

The concept that instability was caused by abnormal rotation about the long axis of the tibia was introduced by Donald Slocum and Robert Larson of Eugene/OR in 1968, citing as the usual cause, an injury to the medial capsular ligament complex [204]. The clinical picture became known as "anterior medial rotatory instability" and sparked the development of a myriad of extra-articular procedures most notably the "pes anserinus transfer" and the

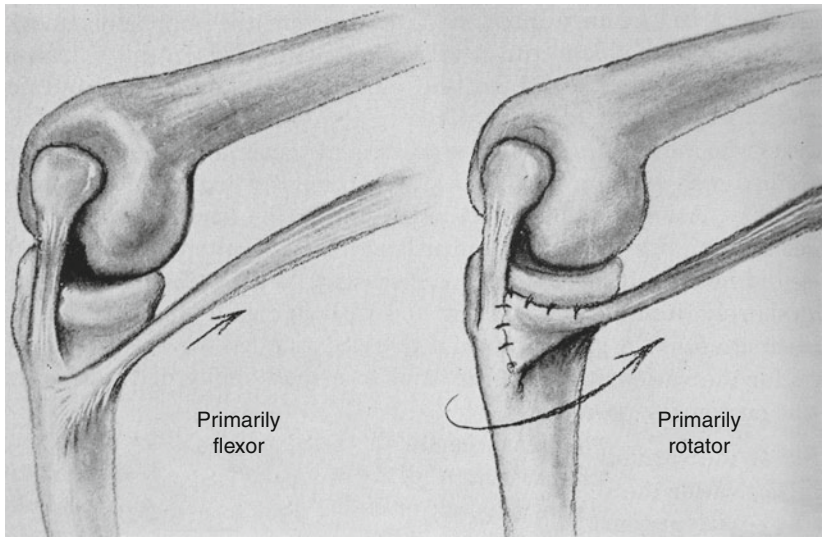

Fig. 16 "Pes anserinus transplantation" introduced in 1968 by Donald Slocum and Roger Larson of Eugene for the treatment of anteromedial rotatory instability [205]

"five-in-one repair" (Fig. 16) [95, 164, 175, 205]. Slocum and Larson's discovery however was not new. In 1893 Johann Hönigschmied of Klagenfurt had already reported on the propensity of increased external rotation following medial capsular injuries he had created in cadaver experiments [90]. In 1928 Hans Tretter of Graz expressed a similar opinion when he concluded that "The condition of the capsular structure is vitally important in limiting the degree of rotatory knee movements" [217]. In 1953 Felix Merke of Bale suggested capsular reefing as a sole procedure for ACL deficiency to control tibial rotation, while Max Lange recommended it as an augmentation to "further improve the results of ACL reconstruction" [125, 154].

Anatomical and clinical studies by Kennedy and Fowler and the establishment of the "pivot shift phenomenon" as pathognomonic for ACL deficiency, prompted Hughston to incorporate these findings into his "anterior lateral rotatory instability," or ALRI, theory [70, 97, 110, 112]. Despite its linguistic complexity, ALRI simply described the clinical appearance of an isolated ACL injury. It became a buzz word in orthopaedic circles in the 1970s, and a proficient examiner was held in high esteem when he produced a decisive pivot shift.

Marcel Lemaire of Paris (1918–2006) recognised the physical disability associated with the pivot shift. He subsequently created his "transposition musculo-aponéurotiques"; a laterally based extra-articular procedure utilizing a pedicled fascia strip reinforced with nylon and secured against the lateral epicondyle (Fig. 17) [128]. He later dropped the nylon stent, using a loop of fascia routed through a bony tunnel and folded back onto Gerdy's tubercle [129]. In 1975 he reviewed 328 of his patients, rating 87 % as having a good result [129]. Lemaire was aware that, although his procedure was ill equipped to effectively reduce anterior drawer, it controlled elements of rotational laxity and abolished the pivot shift, which in clinical practice appeared sufficient to allow patients to resume sporting activities.

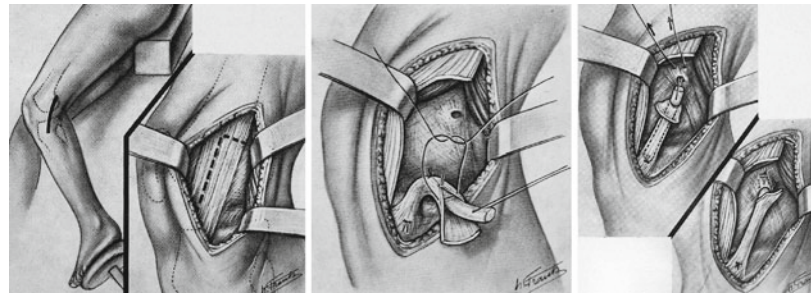

Fig. 17 "Transposition musculo-aponéurotiques" by Marcel Lemaire of Paris first presented in 1967. The procedure was designed to reduce disabling symptoms associated with tibial subluxation [128]

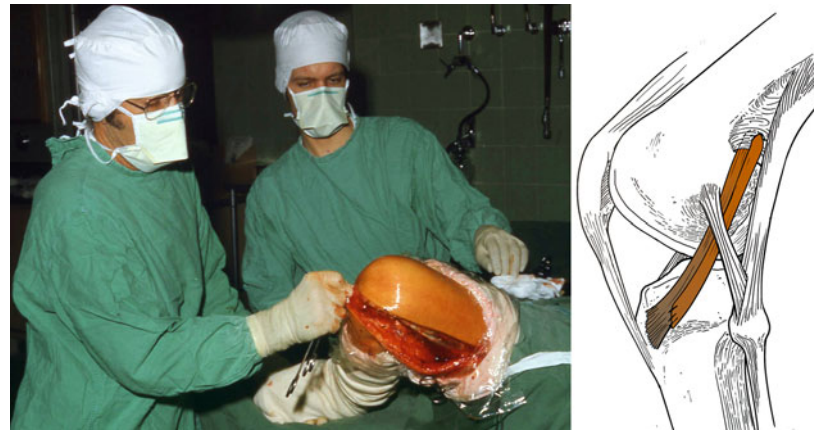

Fig. 18 David MacIntosh of Toronto (*far left*) performing his "lateral substitution reconstruction" in the early 1970s (Photograph courtesy of David Dandy, Cambridge)

In 1971 MacIntosh and Galway devised the "lateral substitution reconstruction," which became known as the "MacIntosh tenodesis" (Fig. 18) [70, 141]. Compared to Lemaire's revised technique, the tendon loop was placed beneath the LCL and routed through the intermuscular septum. In cases of significant laxity, MacIntosh suggested a combined reconstruction with a pedicled fascia sling placed "over-the-top" of the condyle, into the intercondylar notch and through the tibial tunnel to exit at Gerdy's tubercle, a procedure not dissimilar to Hey Groves' earlier technique. A variety of other substitution procedures designed to control anterolateral subluxation, notably those of Trillat (1972), Ellison (1975), and Losee (1978), became popular around the same time [51, 52, 137, 217].

By the 1980s, clinicians had created a classification of all variations of knee instabilities, appropriate tests to define them, and a plethora of surgical remedies to treat them [43, 100, 162]. Critics of the notion of rotatory laxities like David Dandy of Cambridge believed that with regard to the pivot shift phenomenon, "undue emphasis was being placed on tibial rotation, as the

concept did not fit the facts." The introduction of a system of rotatory, straight, and combined instabilities administered in Dandy's view "a coupe de grăce to Slocum and Larson's original simple idea [and resulted in] a jungle of jargon and biomechanics that helps only those who profess to understand it" [39] (Dandy DJ, 2011, personal communication).

Although most extra-articular procedures diminished or obliterated pivot shift and Lachman manoeuvres in the short term, repairs gradually stretched out and led to unsatisfactory results [61, 112, 225]. In a landmark paper, Kennedy reported in 1978 on 52 patients following extra-articuar stabilization with only 47 % achieving good to excellent outcome [112]. Similar results were observed by Warren and Marshall, who concluded that "as a general rule, extra-articular surgery without attention to the cruciate ligaments will often result in failure" [225]. By the late 1990s, surgeons began to realize that efforts to stabilize an ACL-deficient knee had to involve the central pivot, and attention turned again toward the reconstitution of the anatomy [7, 8, 30, 169, 212, 237].

Double-Bundle Reconstruction: Replicating the Native ACL

Ludloff was aware of the complex tension pattern within the ACL and suggested in 1927 that "reconstitution to relatively normal function would require the new cruciate ligament to consist of two separate bundles" [138]. Palmer had already performed double-bundle ACL repairs in the 1930s, claiming good results, but his technique failed to find wider acceptance [177].

Viernstein and Keyl pioneered double-bundle ACL reconstruction with a distally based semitendinosus and gracilis graft in 1973 [219]. According to their technique, both tendons were routed via a single tibial tunnel into two separate femoral tunnels and sutured together at the exit (Fig. 19). By placing the femoral tunnels within the anatomic footprints of the native ACL, the graft appeared to emulate the twisting of the native ACL bundles during flexion. Up to this point, traditional single-bundle reconstruction techniques had aimed to replace the anteromedial bundle, thereby predominately restoring anteroposterior laxity. With the addition of a posterolateral bundle, Viernstein and Keyl were hoping to address any remaining elements of rotational laxity.

In the early 1980s Werner Müller introduced his "anatometric" double-bundle reconstruction for which he used free patellar tendon graft [162, 163]. The graft emerged from a single tibial tunnel and was divided proximally. The posterolateral leg, which incorporated the bone block, was placed intraosseously, while the anteromedial leg was lowered into a trough in the "over-the-top" position, thereby bringing it closer to its anatomical origin (Fig. 20) (Müller W, 2012, personal communication). Blauth started using free double-bundle quadriceps graft in 1981, dividing the proximal tendon into two strands, with one placed transfemorally and the other "over-the-top." By 1984 he had performed the procedure on 53 patients with good overall results [16].

In 1983 William Mott of Jackson/WY published his "Semitendinosus Anatomic Reconstruction," creating double tunnels in both tibia and femur through which he placed a free semitendinosus graft [161]. In 1990 Jean-Louis Meystre of Lausanne reported 77 % good to excellent results with his technique

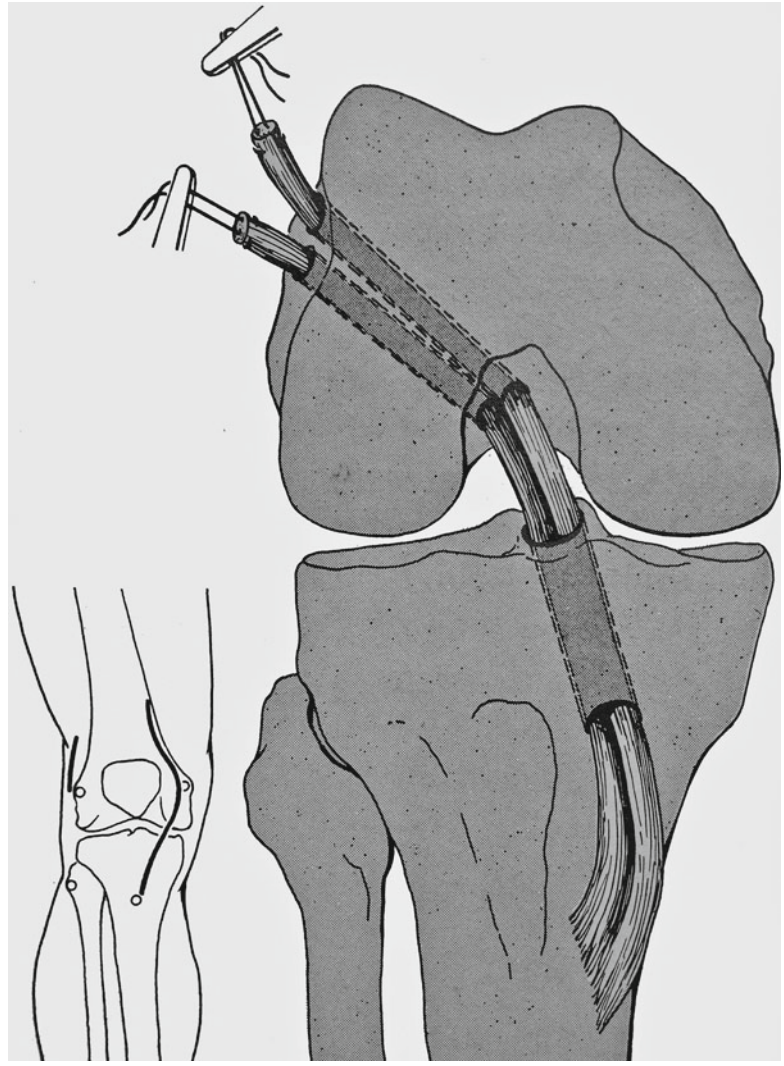

Fig. 19 Illustration of the first double-bundle ACL reconstruction as performed by Karl Viernstein (1920–2011) and Werner Keyl of Munich in 1973. The procedure required an open two incision technique with a medial para-patellar approach (left) (With kind permission of Urban & Fischer, Munich [219])

of semitendinosus double tibial and single femoral tunnel reconstruction [157]. Bradley Edwards and associates compared single bundle with three different double-bundle techniques in vitro which revealed that the most physiological graft conditions are obtained when using dual tibial/dual femoral tunnels [49]. More recently, selective bundle reconstruction in cases of partial ACL ruptures has been performed [170].

In 1997 the group of Freddie Fu of Pittsburgh highlighted significant variations in force distribution between the two ACL bundles, prompting the investigators to suggest that reconstruction principles would have to focus on the role of both bundles if in situ forces of the native ACL are to be reproduced (Fu FH, 2011, personal communication) [195]. The same investigators

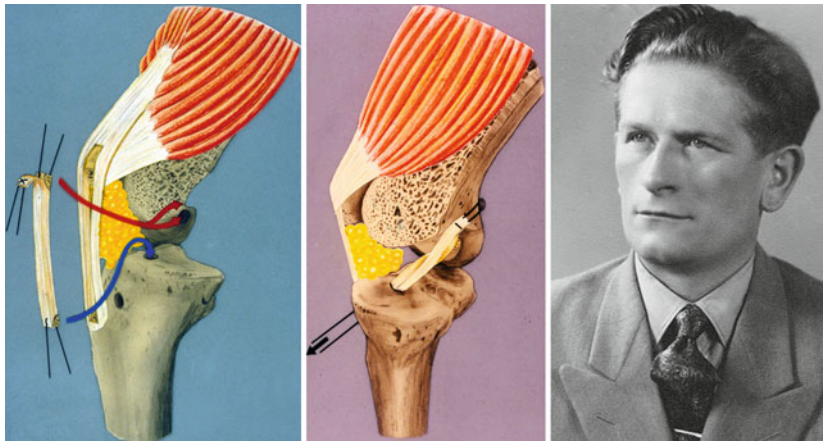

Fig. 20 Werner Müller of Bale (*right*) devised his "anatometric" double-bundle reconstruction in the early 1980s. Division of the proximal aspect allowed the graft to better cover the femoral footprint of the ACL, with the AM bundle being placed "over-the-top" in a 4-mm trough (Illustrations adapted from and courtesy of Tomas Drobney, Zürich)

indicated in an in vitro study that double-bundle reconstruction has the ability to more closely resemble physiological knee kinematics with respect to translation and rotation [234]. More recently, the groups of Kondo and Aglietti observed improved levels of stability and function with double compared to single-bundle reconstruction [4, 115]. It is hoped that such improvements may translate into a reduction in the prevalence of osteoarthritis, but whether proposed benefits will outweigh the increased surgical complexity and trauma associated with this technique remains unclear to this day [73].

The Concept of Isometry and the Variations Thereof

In 1911 Rudolf Fick described in detail the tension pattern of the two ACL bundles, with the "upper medial bundle" being tightest in extension and the "lower lateral bundle" tightest in flexion [58]. His discovery that some ACL fibres are tensioned at all times was later misconstrued to support the idea of graft isometry.

The functional complexity of the motion controlled by the cruciate ligaments indicated that a ligament could not be placed at liberty within the joint. Alfred Menschik of Vienna used Zuppinger's concept of a "four-bar linkage" to develop a mechanical system based on mathematical principles in which he tried to explain that the spatial arrangement between ACL to PCL represents an inextricable relationship which works in a kind of "stepless transmission" [153, 239]. This created the biomechanical basis of graft isometry, a concept centred on the notion that the ideal ACL graft is isometric, either in parts or in the mechanical summation of its parts, thus showing little or no change in distance of linear separation during flexion and extension [35, 120, 171]. Isometric placement of the ACL inferred that a full range of knee motion should be achievable without causing irrevocable ligament elongation.

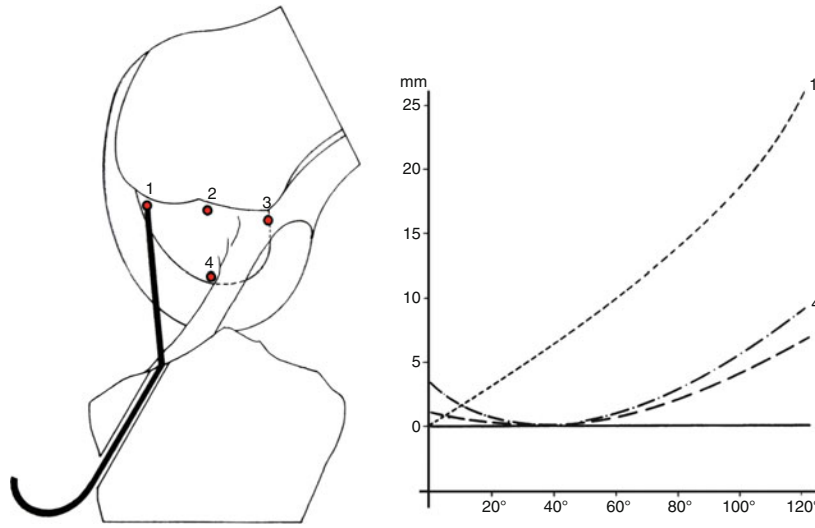

Fig. 21 Experimental study on the definition of isometric attachment points of the ACL by Artmann and Wirth in 1974. Changes in distance between tibial attachment and various points on the lateral wall of the intercondylar notch (*left*) are demonstrated on the *right* (With kind permission of Springer Science, Berlin [9])

Reproducing the ACL bundles and their tension pattern with a single tubular graft composed of parallel fibers posed difficulties, and surgeons were generally unsure where to best place tibial and femoral tunnels within the ligament's functionally important fan-shaped footprints. DJ Cowan of London believed that "from the multiplicity of its actions it would be difficult to produce a new ligament of the complexity of the normal anatomical arrangement of the anterior cruciate ligament" [35]. Surgical orientation was usually accomplished through bony landmarks like the lateral intercondylar ridge located immediately anterior to the femoral attachment of the ACL. It was described as the "resident's ridge" by Clancy since it is commonly mistaken for the "over-the-top" position by inexperienced surgeon in training [65, 104].

In an experimental study performed in 1974, Artmann and Wirth were able to define isometric points within the ACL origins (Fig. 21) [9]. This required the femoral tunnel to be placed within the posterosuperior portion of the anatomic footprint, close to the "over-the-top" position, while location of the tibial tunnel appeared far less critical. Based on these results, Artmann und Wirth concluded that reconstruction of the ACL should aim to replace the anteromedial bundle as it is the more isometric of the two, a finding later confirmed by other investigators [152, 171, 180].

The surgical precision required to achieve these goals demanded better instrumentation. The first specific femoral drill guide was presented by Palmer in 1938, incorporating the basic features of most modern aiming devices [55, 83, 120, 177]. In 1987 Dale Daniel (1939–1995) and Richard Watkins of San Diego developed the tension Isometer® to define points of equidistance for isometric graft placement [40]. The clinical application of isometers was at best difficult and hence became superseded by offset guides providing more reliable and reproducible tunnel positioning [60, 197].

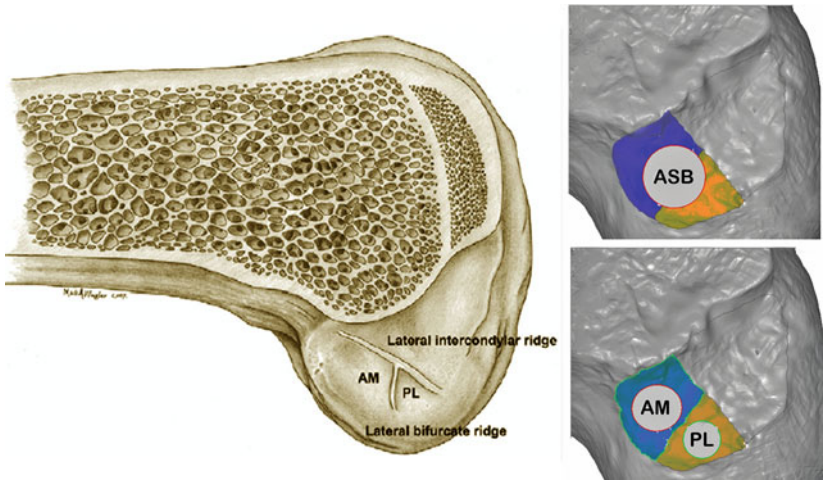

Fig. 22 "Anatomic double-bundle concept" according to Fu and associates based on the anatomic insertion sites of the native ACL (*left*). Three-dimensional laser scan image indicating best graft placement for anatomic single-bundle (*ASB*) or double-bundle (AM & PL) reconstruction (With kind permission of Elsevier, Philadelphia; laser images adapted from and courtesy of Carola van Eck, Pittsburgh [65])

Pierre Chambat of Lyon observed that the majority of ACL fibers are positioned posterior to their isometric points. He believed that these fibers should not be ignored as they display "favourable non-isometry," contributing to the rotational stability of the knee near extension [28]. In 1988 Friederich and O'Brien conceived the notion of "functional isometry" in recognition that "only a limited number of fibres can directly interconnect isometric points" [63]. According to Müller, these fibers are the first to become taut and "supported by [non-isometric] tissue fibres that become tense when the laws of biomechanics demand a greater fibre potential to supply the necessary mechanical strength" [163] (Müller W, 2012, personal communication). He believed isometry to be "too narrow and rigid a concept," and conceived the paradigm of "anatometry," thereby defining a workable compromise between isometric and anatomic graft placement.

By the 1990s, the wider surgical community began to appreciate that the concept of graft isometry was an elusive one, which if achievable, would create unphysiological conditions [6, 63, 119]. Traditional reconstruction techniques were unable to fully restore normal knee kinematics and were hence thought to be responsible for the relatively disappointing clinical results and the high prevalence of arthritis long term [109, 136, 213, 234]. Wirth and Artmann, who had assessed knee joint kinematics before and after ACL reconstruction in 1973, stressed the importance to precisely reproduce the anatomic origin and insertion when placing the graft if abnormal rolling and gliding motions are to be avoided [228].

Not surprisingly, the beginning of the twenty-first century has seen the reemergence of the philosophy of anatomic ACL reconstruction, aiming at the functional restoration of native ACL dimensions, fiber arrangements, and insertion sites, a concept Palmer, Ludloff, Wirth and Hughston had already

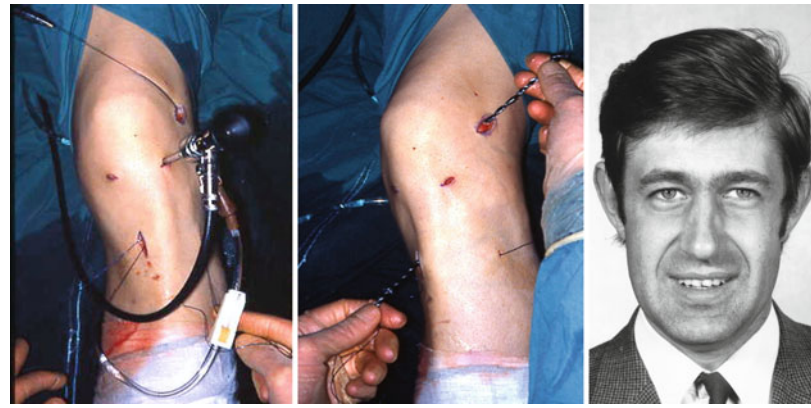

Fig. 23 First arthroscopically assisted ACL reconstruction performed by David Dandy in 1980 using a composite carbon fiber graft (Photographs courtesy of David Dandy, Cambridge)

championed in previous decades. Kazunori Yasuda and Freddie Fu recently created the "anatomic double bundle concept" which seeks replication of the native ACL anatomy by placing tunnels at the center of the ligament's native femoral and tibial insertion sites, independent of whether single or double-bundle reconstruction techniques are used (Fig. 22) [235, 236, 238]. Biomechanically, anatomic single- or double-bundle graft placement promises to provide improved rotational control when compared with nonanatomic reconstruction techniques [116].

Arthroscopically Assisted ACL Reconstruction: This Final Frontier

Prior to the advent of operative arthroscopy, Frederick Tees of Montreal (1940) and Willy König of Hannover (1950) had already performed transarticular reconstruction of the ACL without opening of the joint, either by relying on anatomical landmarks or on radiographic control for tunnel positioning [117, 214]. Arthroscopy to assess for internal knee derangements was first suggested by Danish clinician Severin Nordentoft in 1912 and Swiss surgeon Bircher in 1922 but did not gain wider appeal until the pioneering work of Robert Jackson of Toronto (1932–2010) [99]. On the 24th of April 1980, David Dandy performed the first arthroscopically assisted ACL reconstruction at Newmarket General Hospital in England using a carbon fiber prosthesis augmented with a MacIntosh tenodesis (Fig. 23) [38] (Dandy DJ, 2011, personal communication). Although Dandy reported good results with this technique at 1 year, he believed this to be due to the extra-articular reconstruction rather than the carbon fiber ACL graft, which in his experience often disintegrated over time (Dandy DJ, 2011, personal communication).

In those early days, arthroscopic ACL reconstruction was still relatively complex and challenging as neither sophisticated instrumentation nor camera and monitor units were available. Initially, the procedure required a

two-incision technique, one to facilitate graft harvest and tibial tunnel preparation and another to position a "rear-entry-guide" for "out-side-in" drilling of the femoral tunnel [39]. The introduction of arthroscopic drill and offset guides in the early 1990s allowed for simplification of femoral tunnel preparation, making a posterolateral incision unnecessary [197]. In 1988 Friedman performed the first arthroscopically assisted reconstruction with a four-strand hamstring graft and was followed by Tom Rosenberg of Salt Lake City who, in 1994, pioneered arthroscopic double-bundle ACL reconstruction [64, 190]. By the turn of the century, the technique of arthroscopically assisted ACL reconstruction had become firmly established as the "gold-standard" and a procedure within the realm of most surgeons' ability [78].

Graft Fixation: The Weakest Link

Traditionally, most grafts were either sutured against periosteum or secured with transosseous wires or suture material. Hey Groves used ivory nails to secure his fascia grafts against the tibial bone in the 1920s and 1930s (Fig. 7) [85, 86]. Wittek first employed intra-articular screws for graft fixation in 1927, while Simon reported using a nickel nail in 1931 [202, 230]. Fred Albee of New York (1876–1945) believed that graft fixation was the main mode of failure and in 1943 suggested the use of bone wedges to create an interference fit between tendon and tunnel [5]. Augustine promoted aluminum "boat nails" for extra-articular fixation of hamstrings in the late 1950s [11]. In 1966 Brückner reported the use of patellar tendon graft harvested with a triangular bone block from the tuberosity which he press fitted into the tibial tunnel thereby avoiding additional fixation material [24]. Hans Pässler of Heidelberg later adopted a fixation-free technique for soft tissue grafts by knotting the ends [176]. Jones secured the proximal bone block of his patellar tendon graft by means of a Kirschner wire "drilled across the femoral tunnel and into the opposite femoral condyle" [107]. This technique received wider attention with the Transfix® device for the suspension of hamstrings designed by Donald Grafton and Eugene Wolf in 1998 [77].

Aperture fixation with AO screws was originally described by Kenneth Lambert of Jackson/WY in 1983. With this technique he was able to achieve an "interference fit, whereby it [the screw] actually engages both the side of the bone block and the screw hole in a more or less cogwheel fashion" [121]. Like Albee before him, Masahiro Kurosaka believed that the "mechanically weak link of the reconstructed graft is located at the fixation site." He designed the first designated "interference screw" in 1987, which gave rise to the development of a plethora of ligament fixation devices [118, 146]. The 1990s also saw the introduction of biodegradable implants [209]. In 1992 Leo Pinzcewski and Gregory Roger of Sydney introduced the RCI® screw, the first "soft" threaded interference screw, suitable for the use of both soft tissue and bone-tendon graft fixation [185]. In 1994 Ben Graf, Tom Rosenberg and Joseph Sklar introduced the Endobutton®, a universal ligament suspension device that anchors itself against the femoral cortex at the tunnel exit [76]. Despite concerns about disadvantages of suspensory compared to interference/aperture fixation, clinical results between the various fixation methods have not differed significantly [146].

Epilogue

The number of injuries to the ACL has risen exponentially, since the days when only a fall from a horse could send its rider into early retirement due to an unstable knee. High-speed travel and an ever increasing enthusiasm for sports are to be blamed for this development. From a healthy skepticism toward surgery in the nineteenth century to an ever increasing plethora of operative solutions, simplified by a myriad of surgical aids and implements, we have come a long way. The treatment of the ACL-deficient knee has seen many changes since Adams described the first clinical case of an ACL rupture 175 years ago. Arthroscopic ACL reconstruction has since become a standard procedure for almost every knee surgeon, but are we in danger of becoming complacent? It is essential that all of us continually review our own results and carefully assess the values and merits of new techniques and technologies in order to offer the best treatment to our patients. In all of this, we should not forget the old truism in Jack Hughston's advice that "no knee is so bad that it cannot be made worse by surgery."

It is intriguing to review the pioneering work of Hey Groves, Smith, and Palmer as it anticipated many of the modern ideas on graft obliquity and anatomic reconstruction. Many advancing ideas have been dismissed, or forgotten only to be rediscovered, often without extending credit to the original inventors. We should hence not lose sight of the achievements of our surgical forefathers and be encouraged to become familiarized with the historical developments as it may assist us in the pursuit of, what Ivar Palmer called, "the restoration of the physiological joint".

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Evidence-Based Medicine: How Can We Use It to Guide Our Practice?

Why Is Evidence-Based Medicine Needed?

In the last decades, the production of scientific biomedical articles has grown exponentially. Nowadays, we have around 25,000 medical journals that publish more than 2,000,000 articles per year, around 2,000 per day. However, their methodological quality is highly variable, generating contradictory results.

The practice of medicine has always been based on clinical experience and reasoning based on physiopathologic knowledge. To obtain information regarding the best treatment, the doctor referred to the opinion of experts, to his/her own experience, or to physiopathological arguments about the disease. At the beginning of the 1990s, a group of epidemiologists and clinicians from the McMaster University in Canada headed by G. Guyatt admitted the limitations of this type of practice and established the postulates of evidence-based medical practice (EBM) [6]: (1) Clinical experience and the development of a clinical instinct are necessary as well as crucial for a competent doctor, but are not enough. We have to exercise caution when attributing value to information that has not been obtained and evaluated in a systematic fashion because there is a high risk it can lead us to error, (2) physiopathological mechanism knowledge is necessary but not sufficient to guide in clinical practice, and (3) understanding certain principles, methods, and rules of scientific verification is necessary to correctly interpret the literature about causality, diagnostic tests, treatment strategies, and prognosis.

EBM is a strategy which implies that the decisions about patient care are made, adjusting all the valid and relevant information, integrating it with clinical experience and with the patient's preferences. In recent years, much has been said about the "paradigm change" that appearance of EBM has meant. EBM is only the integration of the scientific method to obtain the best clinical information to deal with a specific clinical case. EBM is a self-directed process based on problem-based learning. To help the physician in this process, EBM established four steps: (1) Convert our information needs in questions to be answered, (2) find the best evidence about the specific

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Table 1 Make a list with the most important terms that describe the problem, interventions, and outcomes

P	I	C	O
Problem of interest	Intervention which is considered	Comparison with placebo or other intervention	Outcome of clinical interest
ACL repair OR ACL Arthroscopy OR ACL reconstruction	Low weight heparin OR Enoxiparin OR Dalteparin OR Nadroparin	Placebo	Deep vein thrombosis OR Pulmonary embolism

Connect the synonyms with OR and the different components of the question with AND. A good search should not have more than three connectors, and sometimes the C box may be left empty

question, (3) evaluate critically the validity and usefulness of that evidence, and (4) apply the obtained result in our clinical practice.

In this chapter, we offer a short summary of the steps that can help the readers understand and integrate the contents of this book in their ordinary clinical practice.

How to Ask Effective Questions?

In our daily clinical practice, we frequently have doubts about how to diagnose or to treat a specific patient. The first step to solve the uncertainty that a case can generate is to correctly identify the problem we are trying to solve. The following search for information will be much easier if we learn an effective strategy to identify the problem. We do this by asking ourselves a correct clinical question that can be answered.

Clinical questions can be divided into general and specific ones. General questions normally have an initial interrogative adverb: what, how, when, and where? They are the most frequent questions when we begin our professional practice. When we become more expert, our information needs are more specific, and we tend to ask more specific questions than general ones. However, the need for general questions never disappears in spite of our growing clinical experience on a subject.

Specific questions have a double advantage over general ones. On one hand, they assist the mental process of delimiting the clinical problem, and on the other hand, are more susceptible to an efficient answer search in different databases and evidence-based resources.

When facing a clinical problem, it is very useful to ask a specific question with four components summarized in the acronym **PICO** (**P**roblem, **I**ntervention, **C**omparison, and **O**utcome) (Table 1). Elaborating a question with this system requires thinking and understanding the thought process the experienced doctor implicitly does every day.

- *Problem.* The problem to be solved has to be defined in a precise manner, but only using the information relevant to define patterns. Even if

each patient is unique, diseases and, therefore, patients can be classified in patterns. Common sense, previous knowledge, and experience will guide us in describing the problem and highlighting its most relevant aspects.

- *Intervention*. The treatment, diagnostic test, or risk factor that we are considering must be carefully defined according to the type of information we need.
- *Comparison*. In the information search about a treatment, we must compare the intervention with a placebo or with another standard treatment that is common for that condition. If it is a question about a diagnosis, the comparison must be with another test that can be considered a "gold standard."
- *Outcome*. Here we will state clearly the relevant variable that we want to obtain or modify. We have to observe the final variables that are clinically important.

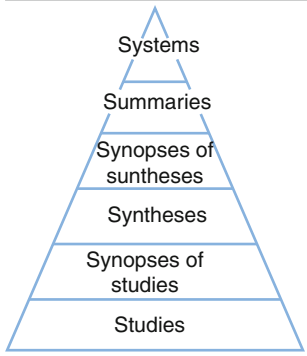
The specific questions usually come up when we are with a particular patient and are mostly to be questions about diagnosis or treatment. The PICO format can also be used to ask questions about prognosis, etiology, prevention, and financial analyses.

How and Where to Search for the Evidence?

Every day, new knowledge in medicine appears and requires a daily effort to keep updated. This knowledge is found in articles published in medical journals and constitutes the foundation on which the medical knowledge is built. The amount of medical articles in Medline is 12 million from 1966 to 2012 and growing. Approximately 8,000 every week and 400,000 articles every year are published in 5,000 biomedical journals. Obviously, it is impossible to stay updated reading all the articles, even only of one specialty. However, it is traditionally the first information search, and it can sometimes be difficult and extenuating because of its immense size and because most of what is published has a poor methodological quality. The search system PubMed is a project developed by the National Center for Biotechnology Information (NCBI) and the National Library of Medicine (NLM). We will briefly describe a simple search strategy to help us find the information we need.

Search in PubMed. Once the clinical question in the PICO format is established, we must find the keywords to define each of the elements of the question. It is useful to look for synonyms using a thesaurus MeSH. We write the keywords and synonyms separated by the boolean connector OR for each of the components in the PICO question. We perform an independent search for each of the components of the question, and the results are grouped in a new search using the boolean connector AND. In most cases, it will give a good number of citations that can be easily reviewed in order to find the best ones to answer our question. If the number of results is too high, we can limit the search extension using limits by study type or other available filters.

Table 2 The 6S model [5]



Systems: Computerized decision support
Summaries: Clinical Practice Guidelines, Evidence based textbooks
Synopses of Syntheses: Abstracts of Systematic Reviews
Syntheses: Systematic Reviews
Synopses: Abstract of highquality studies
Studies: Original Journal articles

Despite Medline's popularity to find specific medical information, it is not very useful because of the time it consumes and the skills it requires regarding critical reading to distinguish between what has value and what does not have. To facilitate this task, several pre-appraised resource databases have appeared, selecting only those studies with high methodological quality. They are also frequently updated, so the evidence provided is perfectly valid. To establish a hierarchy of these sources, Haynes developed the "4S" model that has evolved to the "6S" model [5, 10] (Table 2). In the ground floor, we can find the original *studies* and their *synopses* (short descriptions of some individual studies, such as those found in evidence-based journals). In next levels, there are *syntheses* (systematic reviews like the Cochrane's reviews) and the *summaries of syntheses*. Above them, *summaries* that integrate the best available evidence of previous studies to develop clinical practice guidelines (e.g., Clinical Evidence, National Guidelines Clearinghouse) and, at the summit of the model, the *systems*, in which patient´s individual characteristics are automatically matched with the best updated evidence, the clinician may thus manage it by using informatics decision support systems. When using model 6S, the search begins at the highest possible level. The use of pre-appraised resources increases the probability of searching through updated, high quality, and efficient evidence.

Types of Studies

Case series. The evolution of a group of patients is shown after a certain treatment without comparing it to a control group. This type of design is more likely to have a bias that tends to magnify the effect of the intervention. It can be useful for the initial evaluation of a new treatment in order to verify its safety.

Cross-sectional study. It measures the prevalence of risk factors or outcomes in a group of patients at a point in time. This design can only demonstrate association but not causality. However, a cross-sectional study is cheap and easy to perform and is often the initial approach in a clinical investigation. For example, a study that evaluates patients with anterior knee pain after an ACL reconstruction, with the intention of identifying the risk factors involved in the development of this complication.

Case–control study. The groups to be compared are established based on the final result, meaning the disease or symptom is present or not. Once the effect has been observed, the presence of risk factors or intervention factors is analyzed for each group. This type of design is the most common in the medical literature, although it is subject to bias that tends to magnify the effect of the intervention or the risk factor. However, it has the advantage of being cheap and not too time-consuming. It can also analyze multiple risk factors in one condition. For example, a study performed in a sample of patients with ACL reconstruction that compares those who have anterior knee pain with those who do not retrospectively analyzes the risk factors in each group (graft, lack of extension, etc.).

Cohort study. The groups to be compared are identified depending on the presence of a risk factor or if they have undergone an intervention. At this moment in time, the final result is unknown, and both groups are observed for a period of time to learn about the phenomenon that we are studying. This type of study is normally prospective, but it is possible to have a retrospective cohort if the final result has been reached, and it has been researched by analyzing medical files of samples where the event has already occurred. Cohort studies are superior to case–control studies since they are less likely to be biased. However, they are more expensive to perform, and some cases may be lost during follow-up. For example, a study that compares knee rotational stability in a group of patients with single-bundle ACL graft reconstruction with a group with double-bundle ACL reconstruction without a randomized allocation.

Randomized clinical trial. It is an experiment where subjects are assigned to one group or another randomly. In one group, the therapeutic intervention is performed, and the other group receives placebo or the usual treatment. To assign randomly allows each of the groups to be similar, the only difference being receiving or not receiving the studied variable. It is the ideal design type to learn about the effects of the treatment because it is more strict and less likely to be biased. It is considered the gold standard to learn about the effect of a therapeutic intervention. However, it is expensive and difficult to perform. Sometimes it is difficult to perform because of ethical limitations, especially regarding surgical interventions. The conclusions of a randomized clinical trial are very reliable (good internal validity), but sometimes their generalization to other patients is difficult (external validity) because they have strict inclusion criteria and because of how rigid the intervention is. For example, a group of patients with an ACL injury is randomized to receive either a single-bundle ACL reconstruction or a double-bundle ACL reconstruction.

Systematic review. It is a study where all the previous studies about a specific medical intervention have been systematically gathered. The search and gathering of the studies must follow a very strict methodology so that no study is missed. The studies included must follow certain quality criteria previously stated by the researchers. A *meta-analysis* is a statistical analysis that combines and integrates the results of several independent studies from a systematic review, therefore obtaining a large sample of patients. The quality of a systematic review and its meta-analysis depends on the type of studies included. When these studies are randomized clinical trials, the conclusions of the meta-analyses are of the highest level of evidence.

Level of Evidence

The goal of medical research is to learn about the truth; therefore, we must aim for precise and valid measurements. The elements that threaten our measurements are the random error and the systematic error. *Random error* is inevitable and part of the nature of any human activity because of its variability. Reducing random error is known as accuracy and can be achieved by increasing the sample studied. *Systematic error* is produced directly by the study's own characteristics. The absence of a systematic error is known as *validity*. The certainty of the results is known as *internal validity*. *External validity* is when the results can be generalized and applied to other patients outside the study. Obviously, internal validity is necessary for a study to have external validity. Internal validity of a medical study is threatened by systematic error that is called *bias*. They cause an incorrect estimate of the associations between exposure and disease. The most important biases are selection bias, information bias, and those caused by confusion factors. *Selection bias* is a systematic error caused during the recruitment and follow-up of the studied subjects. It is a frequent problem in case–control studies and retrospective cohort studies where the final event of interest has already occurred. The selection of the control group and the experimental group can be influenced by external noncontrolled factors that can make both groups noncomparable. *Randomizing* the selection for both groups is the technique used to minimize this type of bias. *Information bias* is a systematic error in the measurement of the studied variables. This distortion in the measurement can cause an erroneous classification of the subject at the beginning of the study or during follow-up because of an error in the measurement of the results. *Confounding factor bias* happens when an association between a variable and an event is observed in a study, and this association is not real; it is caused by an unevaluated third factor, which acts as a confounding factor. All studies can be influenced by confusing factors, and randomizing tends to reduce this confusion effect by distributing any possible confounding factors equally in both groups. Information and selection biases cannot be overcome by data analyses; however, a confounding bias can be controlled by using regression techniques. Depending on the presence of more or less systematic errors in the design study, a level of evidence has been established. There are different classifications developed by different institutions, all very similar (Table 3).

How to Critically Evaluate Evidence?

The third step in the practice of EBM is critically evaluating the articles we have found, with which we want to answer a specific clinical question. We should analyze three aspects of the study: its validity, its importance, and its applicability. The *validity* of the study refers to the trustworthiness or how close to the truth the results are. It will depend on the type of study and how it was developed. The *importance* refers to the magnitude of the findings and if these are important in the course of the disease. There are different ways to quantify these changes that can help or confuse us when making a decision.

Table 3 Levels of evidence and grades of recommendation

	Treatment	Prognosis	Diagnosis
Level I	High-quality randomized controlled trial	High-quality inception cohort	High quality prospective cohort with adequate gold standard
	Systematic review of Level-I randomized controlled trials	Systematic review of Level-I studies	Systematic review 2 of Level-I studies
Level II	Lesser-quality randomized controlled trial	Retrospective cohort	Retrospective cohort with adequate gold standard
	Prospective cohort study	Untreated controls from a randomized controlled trial	Systematic review of Level-II studies
	Systematic review of Level-II studies	Systematic review of Level-II studies	
	Outcome research		
Level III	Case–control study		Non consecutive cohort (without proper "gold" standard)
	Systematic review of Level-III studies		Systematic review 2 of Level-III studies
Level IV	Case series	Case series	Case–control study
			Poor reference standard
Level V	Expert opinion based on physiology, bench research or "first principles"	Expert opinion based on physiology, bench research or "first principles"	Expert opinion based on physiology, bench research or "first principles"

Grade A	Consistent level 1 studies	Body of evidence can be trusted to guide practice
Grade B	Consistent level 2 or 3 studies *or* extrapolations from Level 1 studies	Body of evidence can be trusted to guide practice in most situations
Grade C	Level 4 studies *or* extrapolations from level 2 or 3 studies	There is some support for recommendation but care should be taken in its application
Grade D	Level 5 evidence *or* troublingly inconsistent or inconclusive studies of any level	Evidence is weak and recommendation must be applied with caution

Adapted from Oxford Centre for Evidence-Based Medicine (www.CEBM.net)

Lastly, *applicability* refers to the capacity of using the results for our patients after establishing clinically relevant benefits as well as risks. For this task, different strategies have been designed to help us to critically evaluate articles [16] (Table 4).

Evaluating Validity of an Article About a Treatment

Has the Question of the Study Been Clearly Defined?

First of all, we must identify the goal of the study. Besides making sure it will respond to our specific information needs, it will indicate the validity of the obtained results. If a lot of data are collected with no specific criteria, we may

Table 4 Checklist to evaluate the validity, importance, and applicability of a trial

Appraising validity of the study
Primary criteria
Was the objective of the study clearly defined?
Was the assignment of patients to treatment randomized?
Was the allocation of patients concealed?
Was the followup of patients complete?
Were all patients analyzed in the groups to which they were initially randomized?
Secondary criteria
Were patients, clinicians and reviewers kept blind to treatment?
Were the groups similar at the beginning of the study?
Apart of the intervention, were the groups treated equally?
Appraising importance of the study
What is the magnitude of the treatment effect?
How precise was the estimate of the treatment effect?
Appraising appliability of the study
Are the patients covered by the trial similar enough to your population?
Were all clinically important outcomes considered?
Are the benefits worth the harms and costs?

Adapted from www.caspinternational.org)

find significant differences in some of them which do not depend on the intervention but on the sample variability itself. Also on occasion, the authors find that their study does not provide positive results when all the subjects in the sample are analyzed. They do however find small differences analyzing smaller subgroups of the sample without having calculated the strength of the study for these smaller groups. This phenomenon should make us question the validity of the study because the result variable itself has variability within a certain range under the law of chance if it is not correctly controlled.

Have the Compared Groups Been Formed Randomly?

Randomizing is the best process to make both compared groups more similar. This way, any differences observed in the results will be because of the intervention, and not because of the presence of other prognostic factors (known or unknown). As we mentioned previously, the results of a study are compromised by confounding factors that frequently cannot be identified. Random assignment, for example, by flipping a coin, to form an intervention group and a control group lets chance equally balance the existence of prognostic factors in both groups. If one prognostic factor was predominant in one of the groups (e.g., the seriousness of a disease), the effects of treatment could be exaggerated, canceled, or even counteract the real effects of the treatment. Generally in clinical studies, when randomizing is not used in the compared groups, the effects of the intervention tend to be magnified [8, 9, 17].

Frequently, studies select patients in succession as they come to the office. If we send the first patient to a group (where the coin indicated) and the second patient to the other group, and so on, we will obtain two groups with the same number of subjects, and we will mistakenly think we are randomizing

well. In this case, researchers know to which group each patient will be assigned; this causes bias in patient selection. This selection bias is prevented by *allocation concealment*.

We should pay attention to some details that can help us make sure that the allocation is correct. Initially we would think that a random allocation could distribute all patients evenly in both groups; however, this does not always happen because of the laws of chance. If we flip a coin 50 times, the odds of getting heads or tails 25 times each is only 11 %. If we flip it 60 times, the odds of getting 30 and 30 is 10.3 %, for 80 times it would be 8.9 %. It is amazing to find in the literature so many studies with small samples (under 100 patients) in which simple random allocation has assigned the same number of patients in each group. This should make us be suspicious of improper allocation concealment. Those randomized trials that do not preserve allocation concealment tend to overestimate the treatment effect up to 40 % compared to those with adequate randomization [17]. Therefore, if we see a very large effect in a RCT without allocation concealment, we can suspect that the results are reflecting a biased allocation rather than the real treatment effect.

Complete Follow-Up and Intention to Treat Analysis

All the studies have losses to a variable degree. A *sensitivity analysis* is useful to find out if these losses invalidate the result of the study. This consists of assuming the losses in the treated group have not gone well and losses in the control group have gone well. If this does not change the result, those losses can be accepted.

On other occasions, some patients assigned to one group do not receive the allotted treatment for different reasons (the patients withdraw, it is not possible to apply the treatment, or he/she changes to the control group). Even if it seems to the contrary, patients should be evaluated depending on what arm they have been assigned, and not on the real treatment received. This is known as the *intention to treat analysis*; it causes less bias than an analysis by treated cases, which tends to magnify the effect of the intervention [19].

Has the Blind Design Been Followed with Regard to Patients, Clinicians, and Researchers?

Ideally, patients, clinicians, and researchers should not know what group each patient belongs to. The fact that each one of them knows what treatment was received can alter the perception of the obtained result; this is information bias. The impact of the blinding on the validity of a study is less than what randomization has, but it can be important if the final result measures subjective criteria like pain and disability. Non-blind studies tend to magnify the effect of the intervention in almost a third of this effect, both in general medical studies [8, 17] and in orthopedic surgery [15].

The technique with which the received treatment is hidden is called *masking*, and therefore, the group the subject belongs to cannot be identified. On certain occasions, it is not possible to mask a treatment, especially in studies that include surgical procedures or physical therapy, because of technical and ethical reasons. Single blind is when one of the participants, patients, or investigators does not know the treatment received. Double blind refers to the

masking of both patients and clinicians, and triple blind when the evaluator is also blinded, as well as the patients and the clinicians who perform the treatment.

For the patient, this masking of the received treatment helps reduce the effect of placebo when the results are evaluated. The placebo effect is caused by the patient expectation or because of suggestion. All the medical interventions (pharmacological, surgical, or physical therapy) can have a placebo effect, but this effect is particularly strong with surgical procedures.

Regarding researchers, the masking also enables both groups to receive the same treatment throughout the entire study because the clinicians in charge cannot tell what group the patient belongs to. Researchers might feel tempted to closely follow the patients who receive the treatment researched, for example, closely following side effects or a special interest in a positive result.

In the trials about surgical techniques, on some occasions, the patient can be blinded. However, it is obviously impossible to blind the surgeon; in these cases, it is recommendable that the researcher be a different person [13, 14]. If a surgeon asks the patient about the result of the operation, the patient tends to say he/she is better than he/she really is because he/she wants to please his/her surgeon, plus the surgeon tends to perceive the results as better than they really are. This cognitive dissonance is another phenomenon that makes the surgeon's opinion not be very reliable [7, 11]. It is a principle established in experimental psychology that says that if one states firmly that something is true (e.g., a treatment that you have always performed), then cognitive shortcuts take place to evaluate the experience with ones beliefs. If you use one particular operating procedure, you will end up believing that what you do every day really works.

In the orthopedic literature, correct masking of at least one of the relevant actors (patient, clinician, or researchers) only takes place in less that half of the studies [3].

The concept of masking and allocation concealment may appear to be the same initially, but they are not. Masking refers to not knowing what group the subject belongs to once he/she has been included in that group, in order to avoid the information bias. Allocation concealment however tries to reduce selection bias, and it can always be performed, while masking is not always possible.

Evaluating the Importance of the Results

Once we have decided that the study is trustworthy, we can determine if it is worthwhile to continue reading to know the importance of the results. The importance is determined by the *magnitude* and by the *accuracy* of the results.

What Is the Magnitude of the Results?

Sometimes results are shown in continuous variables like the degree of pain or the degree of disability measured by a scale. The comparison is showed as mean differences. However, clinical studies usually show their results as

binary variables (healing or not, infection or not, union or pseudoarthrosis, tumor recurrence or not) and can be presented in different ways.

Let us see an example: You are going to operate on a 32-year-old male with a closed patella fracture. You are worried about the infection risk, and you want to reduce the chance of infection by giving him an antibiotic. You find an article that evaluated the effectiveness of antibiotic prophylaxis with ceftriaxone in the surgical treatment of lower limb closed fractures [2]. The study seems valid because it is a double-blind randomized clinical trial in a large sample (2,195 patients: 1,105 ceftriaxone and 1,090 placebo), followed for 120 days, with a small amount of withdrawals and intention to treat analysis. After follow-up, 36 patients (3.6 %) in the ceftriaxone group had a superficial or deep infection compared with 79 patients (8.3 %) in the control group ($p < 0.001$).

- *Relative risk (RR)* is the quotient between the risk in the treated group and the risk in the control group. In our example, the RR would be 3.6 %/8.3 % = 0.47, meaning the risk of infection is reduced in those who receive the antibiotic compared with those who receive placebo because the quotient is under 1. The relative risk can be more intuitively seen using the quotient between the larger and smaller RR, 8.3 %/3.6 % = 2.3. The risk without antibiotic is 2.3 times higher than with it.
- *Absolute risk reduction (ARR)* is the simple difference between the risk in the control group and in the treated group. In our example, 8.3 % – 3,6 % = 4,7 % or 0.047. Meaning, out of 100 patients with treatment, almost five infections will be prevented. ARR gives smaller figures, which is why it is less used since it gives clinicians the impression of smaller effect.
- *Relative risk reduction (RRR)* is the quotient between the absolute risk reduction (risk without treatment – risk with treatment) and risk without treatment. In our example, RRR is 4.7 %/8.3 % = 0.57 or 57 %, meaning that an absolute risk reduction of 4.7 % represents a reduction of 57 % with regard to not receiving treatment. The RRR is the most normal way of presenting results because the figures are high and it gives results in relative terms. By doing this, we lose the reference of the base risk without treatment which can lead us to overestimating the real clinical impact.
- *Number needed to treat (NNT)* is the number of patients who should receive the treatment so that one of them will obtain a benefit (or prevent an adverse event). It is calculated as the inverse of the ARR. In our example, NNT is 1/0.047 = 21. We need to treat 21 patients in order to prevent infection in one of them. The lower the NNT value is, the bigger the treatment effect is. This way of expressing the magnitude of the treatment's effect is more useful for the clinician because it enables him/her to compare the magnitude of the beneficial effect with its adverse effects.

Most of the studies express results in relative reduction risk because they give the impression of a bigger effect, and naturally, this is the way the pharmaceutical industry presents their results in order to impress the doctors. However, RRR cannot differentiate the effects of the treatment when it is calculated in patients with different prevalence of the adverse outcome. Let us suppose that ceftriaxone also produces a RRR of 57 % in infections in arthroscopic surgery. The risk of infection in knee arthroscopy is very low,

where a study found three infections in 2,261 arthroscopies without antibiotic [1]; therefore, 3/2,261 = 0.0014 or 0.14 %. We can calculate its ARR by knowing the RRR and the risk without treatment (RRR = ARR/risk without treatment). Therefore, 0.57 = ARR/0.0014 and ARR = 0.57 × 0.0014 = 0.0008. Now we can calculate NNT = 1/0.0008 = 1,250. So we can see that although the RRR is 57 %, we have to treat 1,250 patients in order to avoid one of them being infected. The figure of NNT gives a better picture of the real impact of a treatment in clinical practice and may also help to evaluate the benefits and harms by quantifying them. It would be preferable for the studies to present their dichotomic results in NNT or at least show the data that will allow us to calculate it.

How Accurate Are the Results?

Clinical studies collect results from a sample that represents part of the patients with that condition. The results are close to the "real value" that would be obtained if all the population had been studied. In our previous example, each estimation (RRR, ARR, NNT) is close to the "real value"; however, if we repeated this study with other patients, we would get similar results, but not identical. We would prefer to know the whole population's "real value" than the mean value obtained. Since studying the whole population is not possible, we can try to find in what interval this "real value" is with a certain probability. The *confidence interval (CI)* is a range or interval in which the population's "real value" will be with a generally established probability of 95 %. This means that if we repeat the study 100 times, the result would be within the CI range 95 times. The CI gives more information than the *p value* because it evaluates the accuracy with which the result has been estimated. The narrower the CI is, the more accurate it is. If it is large, it provides little information since the "real value" can be situated at any point. The $p < 0.05$ corresponds with a CI range in which the 0 is not included (when evaluating the differences in the mean of the absolute risks or NNT since 0 means there are no differences in the comparison of values). When evaluating relative risks, if the differences are significant, the CI will not include the value 1 (because 1 means that there is no increased or reduced risk).

The statistic significance (represented by the p value) tells us if we can be sure (normally with a probability of 95 %) that both compared groups are different. It tells us the probability that the obtained result is not due to chance. But it does not inform us about the magnitude of the differences between both groups. As clinicians what we need is to reduce our uncertainty by knowing if the effect of the intervention is relevant for our patient, and here is where the CI can help. For example, in the study we reviewed, we saw that the preoperative antibiotic significantly reduced the infection rate with a RRR of 57 % with a CI between 36 and 70 % and a NNT of 21 with a CI between 15 and 39. We can see that the range of the CIs do not include 0, and therefore, the differences are significant. We can also see that the high end of the CI of the NNT is 39 and should decide if this value is clinically relevant. If we accept it as clinically relevant, we can be sure that it will be useful to give our patients antibiotics. If we decide this high end is too high or is clinically irrelevant, the study will not help us much even if it does show significant differences.

On the contrary, a study that has given negative results (without significant differences) can also be useful if we look at its CI. For example, if for a condition in which there is no valid treatment, we find a study comparing an intervention with placebo that shows no significant differences, we could consider the IC. If the IC includes the 0 close to the lower value of the IC (for instance IC −0.5 to 25), we could decide to use that intervention because the "real value" of the intervention is within the IC.

Can the Results Be Applied to Our Patients?

Clinical trials are performed in a selected population with certain inclusion and exclusion criteria, which is why we should be cautious when generalizing the results. Clinical trials show the mean effects of the treatment in that population, but this effect can vary in other populations if the characteristics are different. We must therefore check to see if the characteristics of our patients match those of the studied population, and if they do, then we can confidently apply the results.

Sometimes our patients will show signs that can make us suspect a higher or lower risk than the mean risks of the patients included in the study. Even so, the study can still be useful. An important advantage of the NNT is that it enables us to estimate the benefit of a treatment in a particular individual patient. We should remember that the relative risk reduction (RRR) = absolute risk reduction (ARR)/risk in the control group (RCG), so the ARR = RRR × RCG. Since NNT = 1/ARR, we can replace NNT = 1/RRR × RCG. In a study, the RCG is the patient expected event rate (PEER). If our patient is like the average patient in the study, his/her PEER will be the same as the RCG of the study, and we can make calculations for our patient. For example, in the antibiotic prophylaxis study, the RCG = 0.083, and when using the antibiotic, we obtained a RRR of 0.57. Our patient with the patella fracture seems to have the same infection risk as the mean risk of the patients in the study; therefore, NNT = 1/RRR × PEER = 1/0,57 × 0.083 = 21, which is the same NNT value as the one in the study. But if our patient shows some sign that makes us suspect he has a higher or lower base risk, we can apply the results of the study using our PEER estimate. So, if our patient had diabetes or was elderly or immunosuppressed, the infection risk would increase the PEER to let us say 0.15 (this value can be found in other studies that quantify the risk factors). This way, our patient would have an NNT = 1/RRR × PEER = 1/0.57 × 0.15 = 9, and we could observe a greater impact of the treatment in our patient because he had greater risk for infection.

Have All the Clinically Important Results Been Taken Into Account?

Statistically Significant and Clinically Relevant

An important aspect for the applicability of the published results is to consider that statistically significant is not always the same as clinical importance. The term "statistically significant" has invaded the medical literature and is perceived as a quality label for the results. A p value <0.05 indicates

that the results have not been by chance. For example, a trial that compares the clinical results of ACL reconstruction using conventional single bundle or double bundle [12]. They reported significant differences ($p=0.025$) in the Lysholm score with a better function when using double bundle (Lysholm 90.9) than when using single bundle (Lysholm 93.0). Even if the difference is significant, a 2.1 improvement in the Lysholm score does not seem too clinically important for the patient and may not compensate for the costs and associated risks. In another example a study evaluated the analgesic effect of a continuous pump of local anesthetic after shoulder arthroscopy [4]. They reported significant differences ($p=0.003$) with less pain in those who received the infiltration with a difference of 0.6 (95 % CI 0.2, 1) in the visual analogue pain scale from 0 to 10 cm. Even if the difference is significant, a 0.6 cm improvement is pain doesn't seem too clinically relevant for the patient.

Surrogate Results and Clinically Relevant Results

In our final choice, what we really need to know is if a treatment improves those results that are important for the patients. Frequently, clinical trials have as a final variable result that we think can be relevant for the patient, but that by themselves are not. For example, a trial that compares the ACL reconstruction using anatomic double bundle with the traditional anatomic single bundle can show better rotational stability with double bundle, but something clinically important for the patient's outcome would be to reduce a future osteoarthritis. It is possible that a better control of rotational stability would have a correlation with reducing future osteoarthritis; however, through this study, we cannot know for sure if the double bundle prevents osteoarthritis of the knee in the long term. To base a decision on what is called intermediate results is the same as basing our decisions on physiopathological arguments.

Do the Benefits of the Treatment Outweigh the Costs and Possible Adverse Effects?

Lastly, the final choice has to be made, integrating the balance between benefits, risks, and costs. We have seen tools that allow us to quantify these parameters to limit uncertainty and to facilitate the choice. It is our clinical judgment and experience that each case will integrate the information from studies to offer our patients the best evidence available. Clearly, patients should actively participate in the decision-making process, taking into account their preferences and values.

Currently, cost is an important part of the medical care. Therefore, it is our responsibility to practice cost-effective medicine. However, we must note that cost-effectiveness should not be confused with cost savings. A quality cost-effectiveness analysis (CEA) should be performed under the recommendations of the Panel on Cost-effectiveness in Health and Medicine [18]. According to them, a CEA should be based on the long-term outcome of the procedure, instead of on the short-term outcome. Following our previous example of double-bundle (DB) ACL reconstruction versus single-bundle (SB) ACL reconstruction, it is clear that the DB technique significantly increases the cost of ACL reconstruction at short-term, and we could conclude that erroneously that DB is not cost-effective. In theory, the ultimately

potential advantage of DB ACL reconstruction is to reduce the incidence of knee osteoarthritis at long-term, decreasing long-term health costs and increasing quality of life. However, the long-term effectiveness and outcomes of anatomic DB ACL reconstruction have not been determined to date and therefore would be inappropriate to draw conclusions about cost-effectiveness of DB ACL reconstruction.

Take Home Messages

- Evidence-based medicine is an approach in clinical decision-making that combines physicians' training and experience with the best scientific evidence available while considering the patients values and preferences.
- EBM offers a number of tools and strategies that may help clinicians find, evaluate, and apply the best research evidence for the patients' care. It is eminently practical and patient centered. The best way to learn EBM methodology is by practicing it in our daily clinical setting.

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