Controversies in Orthopaedic Surgery of the Lower Limb

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Preface

Orthopedic surgery of the lower limb encompasses some of the most successful interventions in any surgical specialty. Hip and knee replacement are among the most clinically- and cost-effective procedures in medicine, and the evidence base for both is extensive. Despite, or perhaps because of this, there remain many controversial issues within orthopedic surgery of the lower limb. In this book, we have aimed to analyze the key questions in light of the most up-to-date evidence and in the context of the extensive experience of the authors of each chapter. The main objective of this book has been to look for the best option among many possible solutions to some important controversies.

In hip arthroplasty, we have addressed questions of implant fixation, bilateral surgery, approaches (in particular, the direct anterior approach), hip resurfacing, and the management of osteonecrosis; in the knee, we have explored the treatment of cartilage defects, anterior cruciate ligament (ACL) reconstruction, osteotomies around the knee, bilateral surgery, partial and total knee arthroplasty, the management of patients with metal allergies, and the management of important complications; periprosthetic fracture and infection. In the ankle, we have investigated the management of ankle arthritis with arthrodesis or arthroplasty, and the conservative and surgical management of Achilles tendon rupture; finally, we have analyzed the use of biomarkers in osteoarthritis.

Our aim as editors of this book has been to capture in a single volume the most important and current evidence base for clinical practice in this area, put into context by experts with extensive knowledge and experience in the field.

Madrid, Spain — E. Carlos Rodríguez-Merchán
London, UK — Alexander D. Liddle

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Total Hip Arthroplasty: Cemented or Uncemented?

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Ana Cruz-Pardos, Ricardo Fernández-Fernández, and Eduardo García-Rey

1.1 Introduction

Total hip arthroplasty (THA) remains one of the most successful and cost-effective surgical procedures and it has been considered the "*Surgery of the 20th Century*" [1]. The main goal of THA is to obtain pain relief and the restoration of normal hip function and biomechanics.

Over the last 60 years many THA designs have been developed, but it was in 1961 when J. Charnley revolutionized the management of the arthritic hip with the introduction of *"The Low Friction Arthroplasty"* with three key contributions: (1) the idea of the low friction torque arthroplasty; (2) the use of acrylic cement to achieve bone fixation; and (3) the use of a 22 mm femoral head that articulated with a high density polyethylene cemented cup as a bearing surface [2, 3].

Since then, many other cemented THAs have been developed. Due to poor implant designs, inadequate cementing techniques and a high rate of early loosening of these cemented implants (called as *"cement disease"*) [4], new uncemented THAs appeared at the end of the 70s [5].

Nowadays, both modern cemented and uncemented THAs have demonstrated excellent results at long-term follow-up. However, some controversies still remain: which is the best method of implant fixation, which of these implants perform better in certain situations and which of them has fewer complications. These latter issues will be addressed in this chapter. The optimal fixation method should be determined by clinical outcomes and survivorship [6]. Cemented fixation is less costly, requires a longer surgical time and may be associated with specific complications such as cement implantation syndrome [7]. On the other hand, uncemented fixation is faster to perform, but significant complications such as stress shielding, thigh pain, and periprosthetic fractures are also more common [8].

1.2 Cemented and Uncemented THA Design

The longevity of THA is influenced by the design of the implants; so, we are going to describe the most important concerns that have contributed to improve the clinical and the radiological results of THA.

1.2.1 The Cemented Cup

Nowadays the cemented cups retain many of the features designed five decades ago. It is commonly accepted that the "ideal cemented cup"

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must be all-polyethylene with three or four pegs or spacing pods on its outer surface and a circumferential flange. The spacers ensure a minimal and uniform cement mantle thickness of 2–4 mm around the cup and the circumferential flange provides an optimal pressurization and penetration of the cement into the bone. Pressurization of the acetabular cement has been correlated with a reduced risk of revision [9–12] (Fig. 1.1).

1.2.2 The Cemented Stems

Although the cemented stem can be considered according to its geometry, length, shape, cross-section, material, and surface, cemented stems are basically classified into two groups according to Shen and Huiskes [13–15] and how the stem transfers the load to the cement (Fig. 1.2).

(a) *¨Taper slip¨—"Forced closed"*: *Charnley, CPT (Zimmer, Warsaw. Indiana), Exeter (Stryker, Mahwah, New Jersey), C-stem (DePuy International Ltd., Leeds, United Kingdom)*
- Polished, collarless, and dual-or triple-tapered geometry.
- The cement is well fixed to the bone, allowing micromotion of the implant within the cement mantle. This micromotion protects the cement–bone interface from loosening. These stems show an initial migration of 0.9–1.4 mm during the first year.
- Under load, the taper in the cement converts axial forces into radially compressive forces at the bone–cement interface.

(b) *¨Composite—beam¨—"Shape-closed": Lubinus, Precoat Harris, Elite*
- Harris Philosophy [16]
- With a collar and roughened surface (matte, grit-blasted, or beaded) limiting distal insertion of the femoral stem into the cement mantle.
- Stronger and more rigid fixation between the stem and the cement, with no micromotion between implant and cement. The implant and cement act as a "composite beam."
- Forces are transmitted directly to the bone–cement interface and when debonding occurs, an early loosening and osteolysis are frequent.
- On the other hand, the collar may reduce stress shielding of the proximal femur, reduce the bending stress in the stem, and reduce the stress in the distal cement (Fig. 1.3).

Commonly accepted second- and third-generation cementing techniques are washing and drying of the femoral canal, pressurization of the cement into a distal plugged femoral canal, the use of a preheated stem with a distally centralizer to improve the quality and longevity of the cemented stems [17–20].

Rectangular and oval cross-sectional shapes are most commonly used because rectangular cross-sectional stems can cause stress risers. The surgical technique to prepare the femur also differs depending on the cross-section of the stems [21]. In summary, the issue of whether to use cemented polished or roughened stems is hardly debated among surgeons, and a variety of cemented stems with excellent long-term survivorship exists [15, 20–22].

1.2.3 The Uncemented Cups

Update five types of uncemented cups were described by Morscher [23] in relation to their shape/geometry: cylindrical, square, conical, ellipsoid, and hemispherical cups. Currently, hemispherical cups are the most widely used. These can be oversized hemispherical or non-hemispherical cups with an increased peripheral equatorial diameter. The most recent uncemented cups are made of titanium alloy or tantalum and achieve a biological fixation via roughened, wire mesh, or porous surfaces (range in pore size of 100–400 μm) with or without the addition of a calcium hydroxyapatite coating to enhance the fixation (Fig. 1.4). Although supplementary screw fixation can be employed, the use of

Fig. 1.1 Cemented cups: (**a**) all-polyethylene with three or four pegs or spacing pods on its outer surface and a circumferential flange. (**b**) Acetabular pressurizers

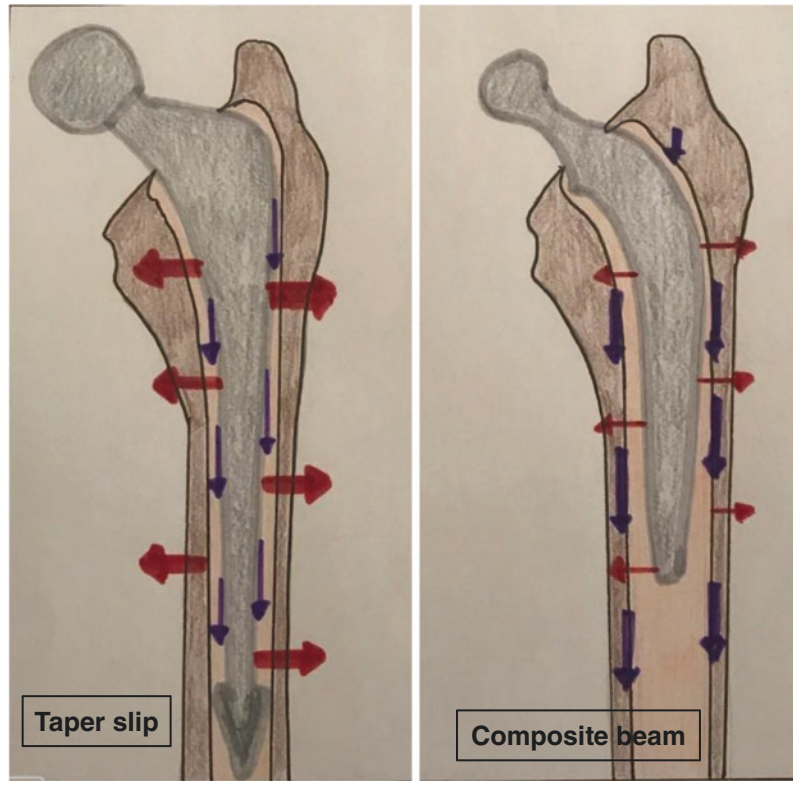

Fig. 1.2 Theories of cemented stem fixation. "Taper slip" (**left**): shear forces are transmitted to the prosthesis-cement interface where subsidence is avoided by compression of the cement–bone interface (red arrows). "Composite beam" (**right**): shear forces are directly transmitted to the bone–cement interface (violet arrows)

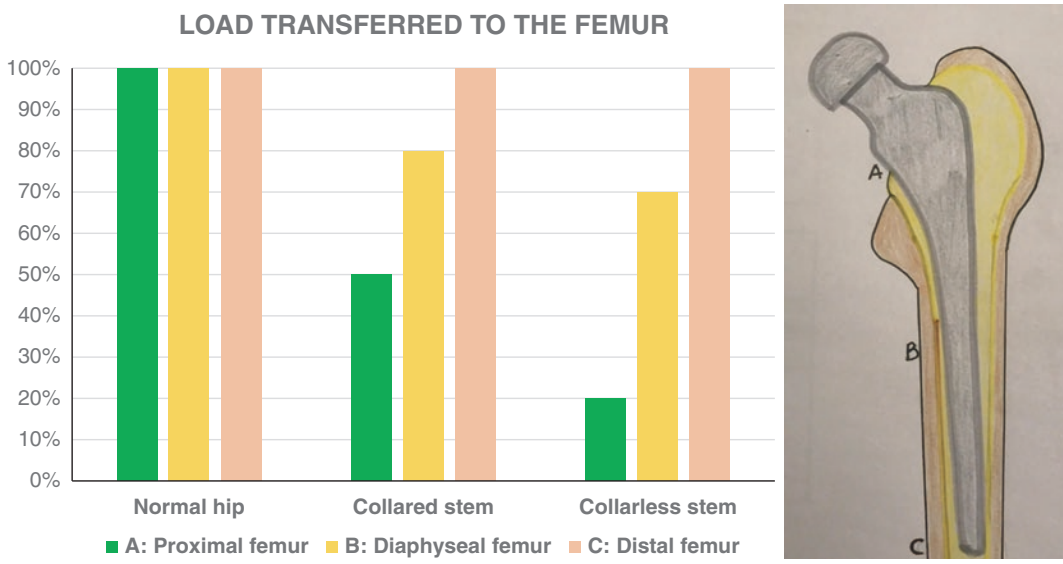

Fig. 1.3 Representation of load transferred to different parts of the femur in a normal femur and with a collared and collarless stem

screws-less fixation is increasing. Current cup designs enhance press-fit fixation and make this possible. To allow bone ingrowth of the cup (bone formation within the porous surface) there must be intimate contact between the surface of the cup and the bone, any motion between the cup and the host bone must be absent and, finally, the cup must have an optimal surface.

Fig. 1.4 Modern uncemented cups

1.2.4 The Uncemented Stems

The design of primary uncemented stems has developed since 1979. Cementless designs differ from one another in terms of geometry and the means of obtaining initial fixation [24].

- Ingrowth fixation: includes stems with a surface with sintered beads, fiber mesh, or a porous surface.
- Ongrowth surfaces are created by grit blasting or plasma spraying.

Table 1.1 Classification of cementless femoral stems designs [24]

Category	Type	Geometry	Location of fixation	Characteristic
Straight stems				
Tapered proximal fixation	1	Single wedge	Metaphyseal	Contact one plane: Medial-lateral
Tapered proximal fixation	2	Double wedge	Metaphyseal	Contact in two planes: Medial-lateral and anterior-posterior
Tapered proximal fixation	3A	Tapered, round	Metaphyseal-diaphyseal junction	Conical stem with proximal coated
Tapered distal fixation	3B	Tapered, round	Metaphyseal-diaphyseal junction and proximal diaphyseal	Conical stem with longitudinally splines
Tapered distal fixation	3C	Tapered, rectangular	Metaphyseal-diaphyseal junction and proximal diaphyseal	Rectangular section
Distally fixed	4	Cylindrical, fully coated	Diaphyseal	
Modular	5		Metaphyseal and diaphyseal	
Curved, anatomic stem	6		Metaphyseal	

Both types and surfaces can be enhanced by hydroxyapatite. All the coatings are circumferential and continuous. Titanium-aluminum-vanadium alloys are most commonly used in cementless femoral stem designs. According to their geometries shape and where fixation is obtained, six types of uncemented stem have been defined [24] (Table 1.1) (Fig. 1.5).

1.3 Results of Cemented and Uncemented THA

As has previously been mentioned in the introduction, there is still some controversy regarding the best method of fixation in THA. This is an issue that should be determined based on clinical outcomes and survivorship at long-term follow-up. Excellent long-term results of both cemented and uncemented THA have been reported in several studies. Table 1.2 shows the survivorship of the most commonly used primary cemented THAs [25–33] and Table 1.3 shows that of primary uncemented THAs [34–40].

The majority of these studies are retrospective, non-randomized, and only a few randomized controlled trials [5] comparing cemented and uncemented THA have been carried out. Therefore, national joint replacement registers with a large number of THAs and a long follow-up may be a more useful tool to highlight differences between cemented and uncemented THAs.

Registry data provide a vast amount of information regarding patient characteristics as well as their diagnosis, surgery-related information about the implant, and focus mainly on hip revision, outcomes, complications, mortality, etc. At present, there are registries in North America, Australia, New Zealand, and Europe (24 countries). Amongst these, the most popular are those from Sweden (SHAR), Finland, Norway, Australia (AOANJRR), and England-Wales-North Ireland (NJR). The Nordic countries, including Denmark, Sweden, Finland, and Norway pool their data in a single, complete register (NARA—Nordic Arthroplasty Register Association) [41]. Thanks to the long-term duration of these registries, indicators such as survivorship or implant-related complications can be documented.

After analyzing the data from the different registers, we can affirm the following [6, 8] (Table 1.4):

– Cemented fixation is preferred by Swedish surgeons. The 10-year survivorship analysis

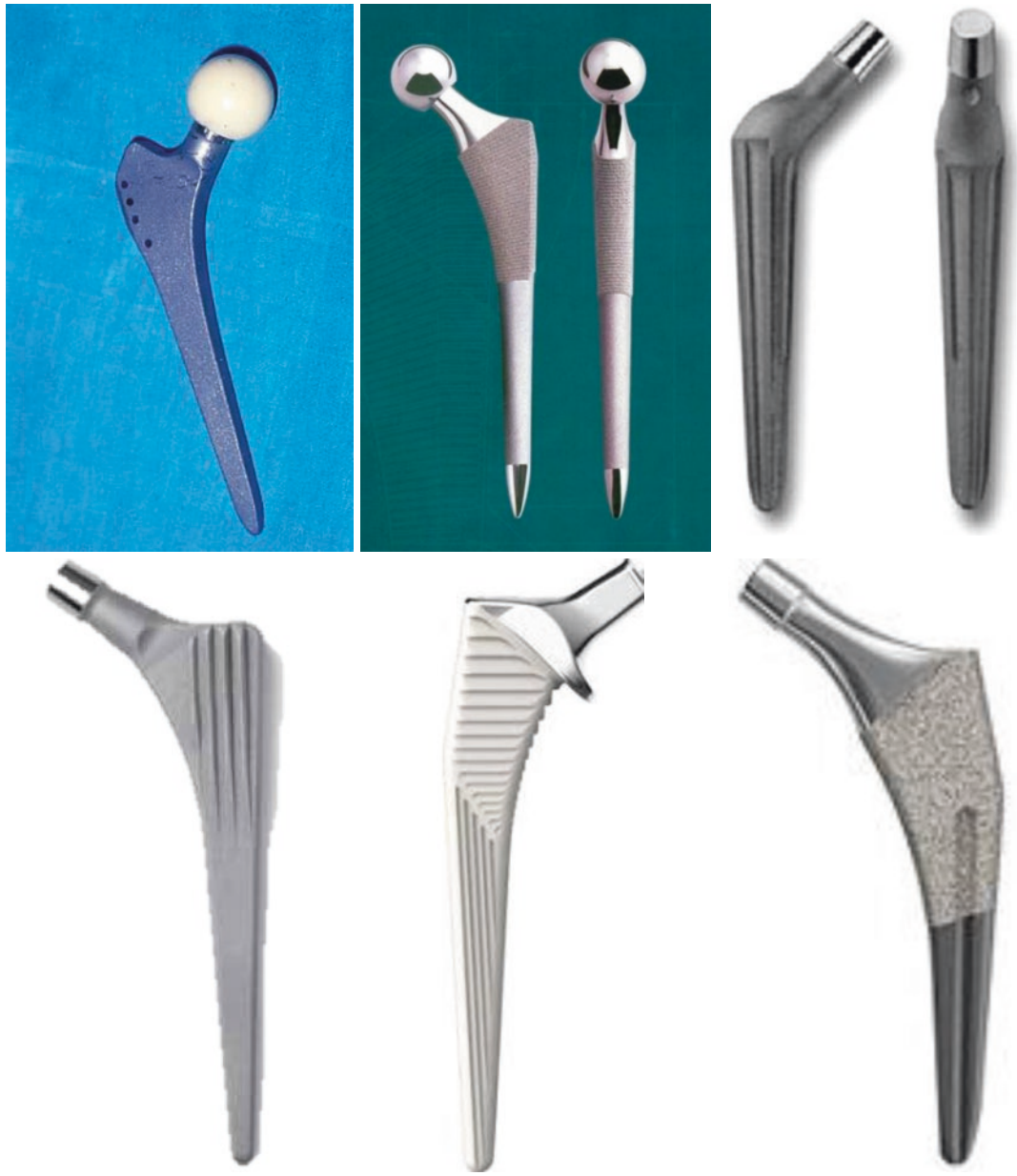

Fig. 1.5 Various designs of uncemented stems

showed that the revision rate of cemented implants is lower than other types of fixation. We do not whether this data will remain the same if patients are stratified by sex or age [42].

– In the Norwegian Joint Replacement Register, implant survivorship for the 1987–2018 period, after adjusting for age, sex, and diagnosis, uncemented fixation has a higher relative risk (RR) of revision compared to cemented fixation THA (RR = 1.25) and a RR = 0.83 when compared to reverse hybrid fixation ($p < 0.001$). If only the most modern implants are taken into account (between 2004 and 2018), no significant differences were found between cemented and uncemented

Table 1.2 Long-term clinical studies of cemented total hip arthroplasties

Author	Prosthesis	Number of hips (patients)	Mean age (years)	Mean follow-up (years)	Survivorship
Berry et al. [25]	Charnley	2000 (1689)	63.5	25	77.5% free of reoperation 80.9% free of revisión for any reason 86.5% free of revision for aseptic loosening
Hartofilakidis et al. [26]	Charnley	245 (205)	57	27	At 20 years: 80% free of revision for aseptic loosening At 30 years: 73%
Callaghan et al. [27]	Charnley	330 (262)	65	Minimum 30 years	Overall survival at 35 years: 78%
Warth et al. [28]	Charnley	93 (63)	42	Minimum 30 years	Overall survival at 35 years: 57.6%
Prins et al. [29]	Lubinus SPII	932 (829)	72	10	98.6% free of revisión for any reason 99.4% free of revision for aseptic loosening
Keeling et al. [30]	Exeter	130 (107)	41.8	22	74.9% for revision for all causes and 96.3% for revision of the stem for aseptic loosening or lysis
Westerman et al. [31]	Exeter	395 (374)	67.7	Minimum 10 years	At 13.5 years, survival rate for all-cause revision of the stem was 96.8% and all-cause revision was 91.2% With revision of the stem for aseptic loosening as the endpoint, this was 100%
Ling et al. [32]	Exeter original	433 (374)	66.8	30	The stem survival free from aseptic loosening rate was 93.5%. Revision for aseptic cup loosening was 76.5%
Carrington et al. [33]	Exeter original	325 (309)		15.7	The survivorship free from aseptic loosening at 17 years was 100% and 90.4% for the femoral and acetabular component, respectively

Table 1.3 Long-term clinical studies of uncemented total hip arthroplasties

Author	Prosthesis	Number of hips (patients)	Mean age (years)	Mean follow-up (years)	Survivorship
Cruz et al. [34]	Zweymüller-Alloclassic stem and a threaded cup	50 (44)	56.6	Minimum 25 years (25–27)	At 20 years: 84.1% free of revision for any reason, 95.9% free for stem aseptic loosening and 86.1 for the cup
Ateschrang et al. [35]	Bicontact stem	250(236)	58.1	22.8	A stem survival rate of 95.0% based on stem revisión for any reason
Sandiford et al. [36]	Furlong system	72 (60)	60	22.5	Overall survival at 22.5 years: 91.7%. Survival with aseptic loosening of the stem as endpoint was 100%
Evola et al. [37]	CSL Spotorno	92 (92)	59.6	24	At 23 years, survival rate for all-cause revision was 80.2%; and 95.1% free from revision of the stem for aseptic loosening
Vidalain [38]	Corail stem	347 (320)	63.3	20.9	96.8% free of revision for any reason for the stem and 84.4% for the cup
Kim [39]	PCA	131 (119)	48.4	19.4	The rate of survival after 20 years was 79% for the acetabular and 91% for the femoral component
Garcia Rey et al. [40]	Duraloc-Profile	73 (82)	56.8	23–26	The probability of not having component revision at 25 years was 83.2%

Table 1.4 Cumulative percent revision of some of the most common primary THA with 10-year data. Data from registries considering only primary diagnosis of osteoarthritis

Stem-Cup	Norwegian registry (2019)	AOANJRR (2019)	NJR (2018)
Charnley-Charnley	*N* = 1061 3.5%	*N* = 630 6.3% (4.4–8.9)	*N* = 10.324 3.8% (3.1–4.1)
Exeter-contemporary	*N* = 2214 3.4%	*N* = 2891 4.7% (3.9–5.7)	*N* = 77.380 2.3% (2.1–2.5)
Lubinus-SPI-II	*N* = 2922 3.5%		
CPT-ZCA		*N* = 829 5% (3.4–7.3)	*N* = 14.872 3.6% (3.1–4.1)
Corail-Pinnacle	*N* = 3100 2.9%	*N* = 43,071 5.2% (4.8–5.5)	*N* = 137.857 5.9% (5.7–6.2)
Summit-Pinnacle		*N* = 4684 3.4% (2.7–4.1)	
Accolade-Trident		*N* = 8573 5.6% (5.1–6.2)	*N* = 26.073 4.4% (4.0–4.9)
Alloclassic-Allofit		*N* = 5059 5% (4.4–5.7)	
Furlong-CSF		*N* = 4688 2.3% (1.9–2.8)	*N* = 22.253 2.9% (2.3–3.6)

AOANJRR Australian Orthopaedic Association National Joint Replacement Registry, *NJR* National Joint Registry (England-Wales-Northern Ireland)

fixation (cemented vs uncemented, RR = 1.05, $p = 0.213$). However, uncemented fixation has a higher relative risk (RR) of revision compared to cemented (RR = 1.25) and a RR = 0.83 if compare it to reverse hybrid fixation ($p < 0.001$) [43].

– In the entire NARA-hip dataset, cemented fixation is the most commonly used method of fixation, accounting for almost 60% of surgical interventions. Once again, differences between countries are quite marked. In Denmark, the hybrid technique is used in over 20% of hip operations, whereas in Norway the inverse hybrid technique accounts for 15%. The uncemented technique is employed in almost 50% of all hip operations in Denmark and Finland. Conversely, the cemented technique accounts for 80% of procedures in Sweden and 65% in Norway.
– The 15th annual report of NJR, published in 2018, registers a total of 992,090 primary THAs, among which 339,220 (34.2%) were cemented, 386,042 (38.9%) uncemented, 200,706 (20.7%) hybrid, and 25,929 (2.6%) reverse hybrid. Since 2012, the most salient feature is the marked increase in the use of hybrid primary THAs. The Kaplan–Meier analysis with a 12-year follow-up shows that all uncemented THAs have higher cumulative revision probability when compared to cemented and hybrid fixation (3.96% vs 7.55% and 4.45%, respectively) [44].
– AOANJRR report the data of 476,994 primary THAs. Up until December 2018, the use of uncemented fixation increased from 51.3% in 2003 to 62.8% in 2018 and cemented fixation has declined from 13.9 to 3.0% and hybrid fixation from 34.8 to 34.2% over the same period. If we only take into account the diagnosis of osteoarthritis, there is no difference in the rate of revision for cemented compared to hybrid fixation. Cementless fixation, however, has a higher rate of revision than hybrid fixation. Finally, cementless fixation has a higher rate of revision than cemented fixation for the first month following surgery but from then there is no difference [45].
– The New Zealand registry reports at 20-year analysis of data for the period between January 1999 and December 2018. There were 137,338 primary hip procedures registered, including 1877 resurfacing arthroplasties. Implant survi-

vorship analysis showed that the 19-year survival for cemented THAs was 84.4%, 83.6% for uncemented, and 84.03% for hybrid THAs. Cemented fixation continues to display a better long-term survivorship [46].

All these data have to be considered with caution as registries do have some limitations; most registries only document implant-related issues such as complications and survivorships and not all include patient reported outcome measures (PROM). Similarly, the registries only indicate the risk of revision and represent the regional data.

With data of these annual reports and from randomized studies we conclude that, overall cemented THAs displayed better good long-term survivorship than uncemented fixation in primary THA.

In the following section we have tried to summarize the data taking into considering the age of the patients and the diagnosis.

1.3.1 Results According to Age

There are many factors that influence the outcome of a THA, such as age, sex, diagnosis, ASA score, body mass index (BMI), or type of prosthesis employed. In the preceding text we have described the general data and now we are going to summarize the data stratified by age. Based on data from registries [6, 42–46], cemented THAs implanted in primary osteoarthritis tend to show a lower revision risk in patients over the age of 75 (Fig. 1.6). Based on the registries, uncemented fixation carries a lower revision risk or no significant difference when performed in any other age groups (Table 1.5).

- Norwegian registry: after stratifying the data into four age groups (<55, 55–65, 65–74, and >75 years), cemented fixation has the lowest revision risk when used in people over 75, though this difference was not significant (RR was 0.88, 1.01, 1.05 and 1). Cementless fixation showed no obvious difference when performed in any age group. However, for hybrid fixation, a much higher revision risk was found in patients between 55 and 64 years (RR = 1.61).
- NJR: at 10-year follow-up, the cementless fixation has higher cumulative revision probability than either cemented fixation or hybrid fixation (stratified by gender and age).
- Australian registry: revision rates stratified by age showed that hybrid fixation had the lowest revision rate across all age groups. Additionally, cementless fixation had a much higher revision rate than cemented ones in patients over 75 (3.8% vs 3.0%). In patients under 75, the long-term survivorship was higher with cementless fixation (Table 1.5).
- New Zealand: cementless implants had a significantly lower revision rate than cemented ones in patients under the age of 55 (yearly

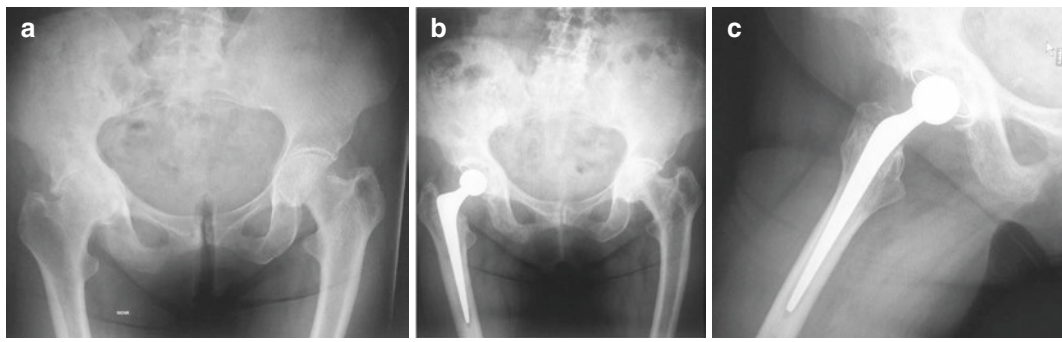

Fig. 1.6 (**a**) Anteroposterior preoperative radiograph of a 77-year-old man with osteoarthrosis secondary to acetabular protrusion. (**b**) Anteroposterior radiograph at 7-year follow-up after an all-cemented total hip arthroplasty (THA). (**c**) Lateral radiograph at 7-year follow-up after an all-cemented THA

Table 1.5 Kaplan–Meier estimates of cumulative revision at 10 years (95% CI) for primary THA by age and fixation considering only primary diagnosis of osteoarthrosis. Data from Norwegian register are expressed as relative risk (RR)

Registry	>75 years old Cemented vs uncemented	65–74 years old Cemented vs uncemented	55–64 years old Cemented vs uncemented	<55 years old Cemented vs uncemented
Norwegian registry (2019) (relative risk)	0.68 vs 1	0.86 vs 0.93	1.02 vs 0.97	1 vs 1
AOANJRR (2019)	3% vs 3.8%	5.4 vs 3.2%	7% vs 3.4%	7.6% vs 3.7%
NJR (2018)	Male: 2.9% vs 4.5% Female: 1.9% vs 3.9%	Male: 3.9% vs 5.4% Female: 2.9% vs 5.5%	Male: 4.6% vs 7.1% Female: 3.9% vs 6.9%	Male: 6.4% vs 8.5% Female: 6.0% vs 8.2%
New Zealand (2018) (yearly revision rate)	0.37 vs 0.74	0.69 vs 0.64	1.06 vs 0.90	1.81 vs 0.97

AOANJRR Australian Orthopaedic Association National Joint Replacement Registry, *NJR* National Joint Registry (England-Wales-Northern Ireland)

Table 1.6 Periprosthetic femoral fractures, comparing cemented and uncemented stems in primary total hip arthroplasty (THA). Date based on national hip registries

Registry	Cemented stems	Uncemented stems	
Nordic Arthroplasty Register Association (NARA) Report (2016)	0.07%	0.47%	Relative risk (RR), 8.72 (95% CI, 7.37–10.32); $p < 0.0005$
NJR (2018)[a]	0.48 (0.45–0.51)	0.72 (0.68–0.76)	
AOANJRR (2019)[b]	1 year: 0.1–0.3 3 years: 0.3–0.5 5 years: 0.6	1 year: 0.4–0.5 3 years: 0.5–0.6 5 years: 0.5–06	

AOANJRR Australian Orthopaedic Association National Joint Replacement Registry, *NJR* National Joint Registry (England-Wales-Northern Ireland)
[a]Number of failures per 1000 prosthesis-year
[b]Cumulative percent revision

revision rate: 0.97 vs 1.81) and in the 55–64 age range (1.06 vs 0.9). In the 65–74 and >74 age groups, hybrid and cemented fixation had a significantly lower revision rates (0.37 vs 0.74).

In a systematic review of all registries published in 2020 and, after stratifying by age, THAs have the lowest overall risk of revision compared with uncemented when performed in patients over the age of 75. This pattern was true in Denmark, Australia, New Zealand, Finland, England, and Wales. This pattern was not observed amongst Finnish males over the age of 75, where there was no difference in the risk of revision [47].

1.3.2 Periprosthetic Femoral Fractures

Aseptic loosening remains the main cause for revision of THA in most of the registries [41, 42, 45, 46, 48]. To date, other causes for revision are instability, periprosthetic femoral fractures (PFF), and infection. It is known that the design of the implant (cemented or uncemented) could influence the emergence of these problems.

Periprosthetic femoral fractures following primary THA are a devastating complication and are associated with functional limitations and an increased overall mortality. Multiple national joint registries show an increased prevalence and a lower risk with the use of a cemented femoral

component when compared with uncemented fixation, especially in patients older than 75 years and in women older than 65 years [8, 21] (Table 1.6). In a large case-series study published over a 40-year period, intraoperative fractures were more frequent with uncemented stems than with cemented stems (1.7% vs 0.23%). The authors also reported that the probability of a post-operative fracture within 30 days of surgery for an uncemented stem was ten times higher than for a cemented stem [49].

In a systematic review published in 2017, the authors analyzed the contribution of implant geometry and design of uncemented stems on the risk of both intraoperative and post-operative PFF. The incidence of PFFs was significantly higher for uncemented stems ($p < 0.001$) and, specifically, with the use of single-wedge and double-wedge, which have the highest PFF rates in the literature. Within cemented stems, loaded-taper stems were associated with more PFFs than composite-beam stems ($p = 0.004$) [50]. Considering this, specific attention should be given to the choice of fixation and stem design in high risk groups (women, osteoporotic bone).

1.4 Conclusion

The most appropriate choice of implant fixation in THA remains a matter of debate. Current cemented and uncemented THAs are generally associated with excellent long-term results. Selection of the implant should be determined based on its design, fixation, and geometry, but also on patient factors such as age, activity level, the bone quality, and deformities. Data based on arthroplasty registry studies have found that uncemented fixation is associated with higher revision rates, particularly in older patients and of female gender. In addition, uncemented fixation may be associated with an increased rate of periprosthetic fractures. Thus, we conclude that clinical outcomes support the use of cemented fixation in older patients and those with poor bone quality. In younger patients uncemented fixation is preferred. Periprosthetic fractures were common in uncemented fixation, and patients should be informed of this risk prior to surgery.

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2 Hip Resurfacing Arthroplasty or Total Hip Arthroplasty?

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2.1 Introduction

Hip resurfacing arthroplasty (HRA) is a bone conserving alternative to total hip arthroplasty (THA) for patients with end-stage hip arthrosis. The femoral HRA implant is a metal shell which caps the femoral head; the acetabular implant is typically a monobloc metal cup. Several defective metal-on-metal (MoM) HRA implant designs have been associated with metal debris and very high revision rates and have since been withdrawn from use. Safe designs have continued to deliver excellent clinical outcomes and longevity when performed by expert surgeons. After a dip in usage since 2010, HRA has seen a resurgence due to their recent use in high profile athletes returning to sporting activity—considered a key advantage of HRA over THA [1, 2]. Still, THA remains the mainstay of management for hip arthrosis, and HRA is controversial. This is primarily due to high patient satisfaction, low revision rate, and established long-term outcome data of THA. Despite some evidence that HRA can deliver more physiological movement and a higher level of function than THA, it is more commonly revised and there are persisting fears regarding metallosis, which has limited its re-uptake.

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2.2 History of Hip Resurfacing

Early HRA designs can be traced back to the 1920s [3]—Marius Smith-Petersen's 'mold arthroplasty' was a single, thin temporary hemispherical shell of glass, bakelite then finally vitallium (a cobalt-chromium alloy) interposed between the worn femoral head and acetabulum. Evolutions included a stemmed femoral resurfacing implant made initially of acrylic by Robert and Jean Judet; John Charnley's 'double cup' arthroplasty made of polytetrafluoroethylene (Teflon™); and later Edward Haboush's cemented metal-on-metal implant. These later designs showed significantly worse long-term performance in comparison to THA [4, 5], due to cement fragmentation, metal degradation, or third-body wear of the polyethylene [6]. Further attempts in the 1970s did not prove successful—large metal femoral heads articulating with first generation Ultra High Molecular-weight Polyethylene (UHMWPE) resulted in significant osteolysis and prosthetic loosening [7], with a failure rate of 66% at 5 years [5]. HRA was revived by Derek McMinn (Midland Medical Technologies, Birmingham, UK) in the 1990s who developed a metal-on-metal implant. Its success led to its acquisition by Smith and Nephew (Tennessee, USA) in its current guise—the Birmingham Hip Resurfacing (BHR) [8] (Fig. 2.1). Alongside the BHR, a slew of new HRAs were released including the Articular

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Fig. 2.1 Birmingham hip resurfacing (Smith and Nephew)

Surface Replacement (ASR, Depuy Synthes, Warsaw, USA). In comparison to the BHR, the ASR had a smaller radial clearance between the femoral and acetabular components [9], resulting in significant metal wear leading to implant failure and surrounding tissue damage [10]. When the ASR was recalled in 2010 with a 44% revision rate at 10 years, it had already been implanted in over 100,000 patients [11], and is thus widely considered the biggest disaster in orthopaedic history. Several other MoM HRA implants were withdrawn due to similar design problems and high revision rates. Currently, HRA represents less than 1% of hip arthroplasty, with the BHR and the Conserve Plus implants (Wright Medical, Middlesex, UK) being the most used [12, 13].

2.3 Indications for Hip Resurfacing

Younger patients with good femoral bone stock and high functional expectations are appropriate candidates for HRA. Registry data and observational studies suggest that the 25-year survivorship of THA may be as low as 58% [14] and functional outcomes from revision THA are modest. Hence HRA is appropriate for patients who are likely to live longer than the THA implants, with subsequent conversion to a 'primary' THA—a position supported by the UK's National Institute of Clinical Excellence (NICE) guidelines [15]. Registry analyses of revision have shown that smaller HRA sizes are associated with a higher risk of revision. With this in mind, female sex is a contraindication in some countries, while most manufacturers have ceased production of head sizes smaller than 48 mm. Older age is a relative contraindication but contentious—older patients have a lower risk of revision, but are likely to benefit less from HRA compared to THA [12, 13]. Therefore, current controversies surrounding performing HRA include age-, gender-, and disease-related contraindications, and limiting HRA to surgeons with proven expertise.

2.3.1 Gender

Developmental dysplasia of the hip and a smaller native femoral head size are more likely in, but not unique to women. They are predictors of HRA failure as smaller component size and unsafe cup orientation are more likely to result in HRA edge loading and wear [16–18]. The mechanical explanation for this clinical observation is simple, while the thickness of the metal is constant, as the size of the device reduces, the coverage angle reduces rapidly, making edge loading more likely [19]. A systematic review of ten studies of MoM HRA identified female sex as an independent risk factor for poor outcomes [20]. In particular, there is an increased chance of developing adverse local tissue reaction (ALTR) (Odds Ratio 5.7) and revision (OR 2.5) [20].

Registry data comparing implant survival of different sizes of MoM HRA with THA showed similar survivorship in men with large femoral heads [21]. In men with smaller femoral heads, resurfacing resulted in poor implant survival. The predicted 5-year revision rate in 55-year-old men was 4.1% with a 46 mm resurfacing head, 2.6% with a 54 mm resurfacing head, and 1.9% with a 28 mm cemented metal-on-polyethylene stemmed THA [21]. In contrast, the predicted 5-year revision rate in the same study for 55-year-old women was 8.3%. Women are also more likely to develop osteoporosis—resulting in femoral neck fracture or subsidence of the femoral

implant [22]. Therefore, there is a complex relationship between risk of HRA revision and age, sex, femoral head size, hip morphology, and age-dependent bone quality.

2.3.2 Surgical Expertise

HRA is considered a technically more challenging procedure than THA. Alongside appropriate patient selection, surgical expertise is linked to outcome. Accurate implantation—particularly in sizing and machining the femoral head and orienting the acetabular component—is linked to risk of femoral fracture and ALTR, respectively. MoM femoral components which are in varus alignment notch the neck or leave exposed cortical bone are associated with femoral fracture [23], and HRA cups which are positioned in greater than 50–55° inclination are associated with higher levels of serum metal ion release and pseudotumors [24].

For experienced THA surgeons learning HRA, Nunley et al. described a learning curve of 25 HRA cases before complications reduced and plateaued [25]. More experience may be required to reliably orientate the components (75–100 cases) [26], though computer navigation is likely to reduce outliers [27, 28]. Registry data from the Nordic Arthroplasty Register Association has shown that hospitals performing more than 100 HRA procedures annually had a lower risk of revision [29]. Acknowledging this long learning curve and the protective effect of high-volume centres, HRA in France can only be performed in designated hospitals and by fellowship-trained surgeons performing over 50 cases annually. Since this change in 2013, the 5-year revision rate in France is 1% [30].

2.3.3 Bone Stock

The minimum volume and quality of bone in the femoral head required to safely perform HRA is a topic of ongoing research. Case series have shown excellent survivorship of MoM HRA in patients with osteonecrosis/avascular necrosis of the femoral head [30, 31], with comparable results to THA in young patients [32]. However, outcomes of HRA on patients with femoral heads with advanced disease, defects with lateral extension, or a large Kerboul angle are less predictable [33]. Cementless HRA with bone grafting avoids the risk of thermal damage from cemented HRA, and may be a safer option [34]. Several studies have reported acceptable results when performing HRA on patients with rheumatoid arthritis (RA) [35, 36]. As kidney disease is common consequence of RA, and this may impair the patient's ability to clear metal ions from MoM HRA, caution is advised.

2.4 Hip Resurfacing Compared to Total Hip Arthroplasty

2.4.1 Safety

A large registry-based, propensity score matched study showed a surprising and substantial difference in safety between THA and HRA in favour of HRA [37], confirming an earlier study by the BHR's designer surgeon [38]. After correcting for age, gender, co-morbidity, deprivation, surgeon volume, and year of surgery, the hazard ratio for death at 10 years was 0.5 for HRA against cemented THA and 0.55 against cementless THA. Residual confounding is a major consideration, as this is observational data, but despite the well-publicised issues of metallosis, 'cobaltism', and higher revision rate, HRA appears to be safer than THA when death of the patient is the endpoint.

2.4.2 Revision

For all patients and including withdrawn implants, the 10-year cumulative revision rate of HRA is 8–11% compared to 4–7% for THA [12, 13]. The only resurfacing implants available today—the BHR, Conserve Plus and Adept (MatOrtho) implants—have 10-year revision rates between 5 and 8% [12, 13]. An Australian joint registry study of patients younger than 65

compared 4,790 BHRs with femoral head size ≥50 mm with 2,696 modern THAs [39]. It reports a higher rate of all-cause revision (Hazard Ratio 2.8), with HRA particularly prone to implant loosening and fracture, but no mention is made of the substantial difference in standardised mortality (5.5 for HRA vs 5.9 for THA) reported by the Australian Registry's own annual report [40]. Again, residual confounding bias in patient selection is difficult to account for—patients undergoing HRA tend to be more active and this may increase risk of fracture and rate of wear, thus reducing implant longevity and increasing the revision rate. There may also be a lower threshold for surgeons to convert HRA to THA in a dissatisfied patient, in comparison to revising a primary THA. Periprosthetic fractures are treated differently: femoral neck fractures beneath HRA are usually treated by revision, recorded by implant registries, while Vancouver B and C fractures below a THA are usually treated with implant retention, so do not appear on registry data. Patients undergoing revision of HRA can expect to achieve function and quality of life similar to their best after their primary surgery [41], though the same cannot be said of outcomes after revision THA in younger patients [42]. Historically, revision of HRA due to pseudotumors in women was associated with poorer outcomes due to the local soft tissue destruction [43].

2.4.3 Patient-Reported Outcome Measures

Randomised controlled trials comparing HRA to THA have failed to demonstrate any significant difference in the Oxford Hip Score or the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) in the short term [44–46]. Two systematic reviews comparing HRA with THA similarly concluded that HRA conferred no advantage in clinical outcome [47, 48]. The patient-reported outcome measures used in these studies have severe ceiling effects: single-arm studies for both replacement and resurfacing report modal scores of 100% for both procedures [49, 50].

After HRA, there are case series of patients returning to high-impact activities [2] including extreme triathlons [51], though the majority will take up low-impact sports [52]. For THA, there is a general consensus between British and American surgeons [53, 54]—the majority allow intermediate-impact sports such as cycling, but few recommend high-impact sports such as jogging. There are few direct comparisons of return to sport between patients with HRA and THA. Meta-analysis of studies using the UCLA hip score [55] shows that patients who have undergone hip resurfacing are more likely to return to a high level of activity compared to THA [56].

2.4.4 Biomechanics

HRA restores native hip biomechanics more effectively than HRA. By maintaining the shape and structure of the femoral head and neck, length and offset are thus more reliably restored, compared to THA [56], with a more anatomical pattern of femoral loading [57]. Proximal femoral stress shielding is reduced with maintenance of bone-mineral density [56, 58]. By more closely restoring the femoral head size, HRA restores capsular biomechanics and jump-distance [59], and in registries HRA is associated with a two to four times reduced risk of early dislocation when compared to THA [13]. Gait-analysis has shown that patients with HRA have a more normal gait [60] and a higher top walking speed [46, 61] than those with THA; in those with a HRA in one limb and THA in the other, HRA accepts more weight and pushes off with greater force [60]. In a randomised clinical trial, HRA reproduced a symmetric gait at higher speeds, while patients with THA were unable to walk as fast, and loaded their healthy hip excessively, sparing the leg with the replaced hip [62]. HRA does not confer an advantage over THA for standing balance [46, 63, 64] or gait symmetry at comfortable walking speeds [46, 65]—adding further credence to the argument that HRA particularly benefits more active patients. HRA may confer a more stable single-leg stance than THA,

perhaps due to the preservation of the proximal femur with its soft tissues, and the maintenance of a head diameter similar to the native joint [64]. However, a study measuring proprioception after HRA versus THA showed little difference [63].

Silva et al. compared pre-and post-operative radiographs of an unmatched series of THAs and HRAs [66]. THA may be more suitable in patients with a pre-operative leg length inequality of more than 10 mm or where a change in femoral offset is desired.

2.5 Monitoring Patients After Hip Resurfacing Arthroplasty

In the UK, the Medicines and Healthcare Products Regulatory Agency (MHRA) recommends that patients who have undergone metal-on-metal hip resurfacing with a prosthesis other than the Birmingham or the Conserve (both being rated by the Orthopaedic Data Evaluation Panel, ODEP, as 10A), or smaller than 50 mm in diameter be routinely monitored to identify implant loosening, wear or pseudotumor formation (Fig. 2.2). Abnormal metal ion concentrations, suspicious radiographic findings, or reduced clinical function will prompt further investigation by ultrasound or MRI [67]. Conversely, patients with an ODEP 10A HRA are followed up in the same way as a modern THA. For men with an HRA of 48 mm, a higher burden of surveillance exists, as it does for patients with any device that has been withdrawn.

2.6 The Future of Hip Resurfacing Arthroplasty

The current limitation of hip resurfacing arthroplasty is mainly related to material and design, rather than functional results. Novel HRA implants include metal on highly cross-linked polyethylene [68–70] and ceramic on ceramic [71, 72] which may obviate complications secondary to metal debris.

2.7 Conclusion

Hip resurfacing remains a safe and effective option for active people who want to return to sport, but its use is currently restricted to larger men owing to limitations of design and materials.

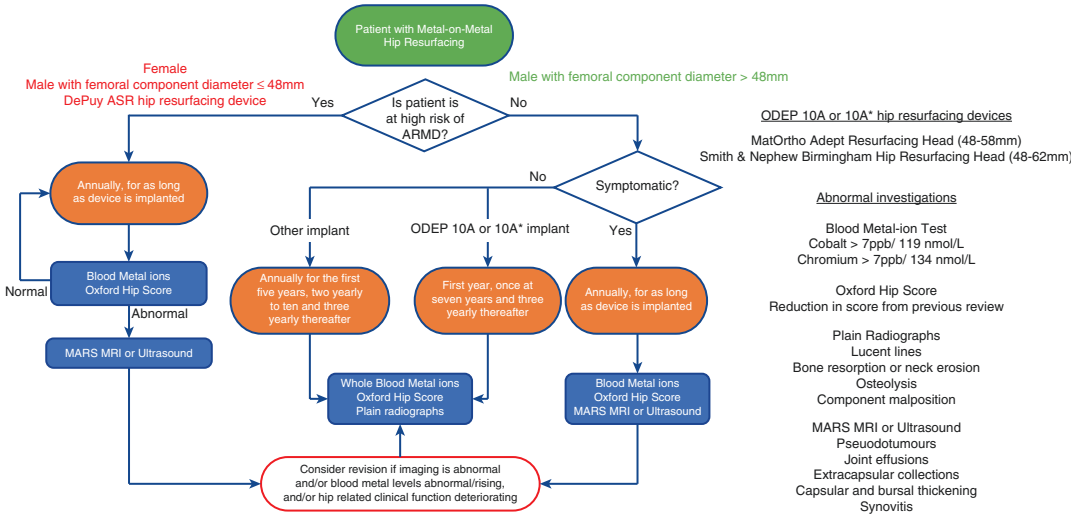

Fig. 2.2 Flowchart to appropriately investigate and manage patients who have undergone metal-on-metal hip resurfacing. *ARMD* adverse reaction to metal debris, *ODEP* orthopaedic device evaluation panel, *MARS MRI* metal artefact reduction sequence magnetic resonance imaging, *ppb* parts per billion

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3 Bilateral Total Hip Arthroplasty: One-Stage or Two-Stage

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3.1 Introduction

Jaffe and Charnley first described single stage bilateral total hip arthroplasty (THA) in a series of 50 consecutive bilateral procedures in 1971. The authors concluded that the complication risk was slightly higher but with the added advantage of a single anesthesia, and a shorter hospital stay and rehabilitation period. Several reports of bilateral procedures showed no increased risk of complications [1–5]. Bilateral procedures gained popularity in the late 90s and the turn of the century. At The Hospital for Special Surgery in New York, the number of bilateral surgeries increased from 20 to 70 procedures per year [1, 6]. However, concerns over the safety of bilateral procedures remained.

The introduction of spinal hypotensive anesthesia, preoperative clearance of patient medical conditions, improvements in surgical technique with reduced blood loss, and the development of thromboprophylaxis guidelines led to a reduction in the rate of adverse effects and complications following total hip replacement. This has rekindled an interest in performing simultaneous bilateral procedures to manage bilateral hip osteoarthritis.

Ritter reported a decrease in blood loss since the introduction of hypotensive anesthesia. In the year 1978, replacement requirements dropped from 3 units to 0.5 units following unilateral THA and from 6 units to 3 units in bilateral simultaneous replacements. Since the introduction of new prophylaxis strategies, a dramatic decrease in phlebitis and pulmonary embolisms was also reported [7, 8].

The advantage of simultaneous total hip replacement is an improved cost effectiveness without a higher complication risk. Rehabilitation time and time to return to work are significantly reduced in simultaneous procedures. In the presence of a severe bilateral hip osteoarthritis with high flexion contractures, the contralateral hip will impair postoperative rehabilitation. Another indication for a bilateral procedure would be when a considerable limb length discrepancy is generated following a unilateral hip arthroplasty.

Several studies have shown greater mortality risk or major complications in simultaneous vs staged THA [8–12]. Simultaneous THA is indicated in younger patients with fewer comorbidities. The complication risk of a total hip arthroplasty is related to the preoperative condition of the patient. The most common tool for stratifying patient risk is the American Society of Anesthesiologists (ASA) score. It is regarded as the only independent predictor of perioperative

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mortality following a simultaneous THA [9]. Thus, most studies include the ASA score to measure the preoperative difference between groups. Generally, surgeons consider bilateral simultaneous THA only in patients with a low ASA score. However, patients with low and high ASA scores do not always display a significant difference in their complication rate [10].

The optimum timing for staging a bilateral total hip arthroplasty is still under debate. Following a 1-week interval, recovery time is faster but with increased hospitalization because of concomitant complications [13–15]. However, there is lack of information regarding secondary complications due to said prolonged hospitalization in bilateral THA. Common practice delays the second arthroplasty until the patient's medical condition has returned to its baseline [12].

3.2 Clinical Results

Most of the studies have reported excellent results with both simultaneous and staged THA [11, 13–18]. Rehabilitation is hampered in cases having great deformities or flexion contractures of both hips. However, in our current practice the percentage of patients with bilateral severe deformities is low. In some cases with bilateral disease, the first arthroplasty generates a large limb length discrepancy that must be corrected to allow gait rehabilitation. Simultaneous THAs provide greater hip flexion than two-stage or unilateral THA, but with similar pain scores. Stiffer hips generally obtain a greater range of motion after surgery [3, 14, 15]. Some authors have reported a higher rate of ectopic ossification following bilateral THA than in the unilateral THA and therefore a better range of motion [2].

In some patients rehabilitation goals are affected in simultaneous procedures. Houdek did not report any difference in the proportion of patients discharged home following either type of surgery [16]. Lindberg and Larsen in a fast-track protocol discharged simultaneous patients 6 days after surgery [17]. However, other studies report a lower proportion of home-discharge after simultaneous THA through an anterior approach [12]. In spite of their younger age, only 53% of the patients were able to return home after a simultaneous procedure, whereas in the staged group, with a mean interval of 8 months between both surgeries, 80% of the patients were discharged home [13]. The proportion of patients discharged to a rehabilitation unit also differed in Parvizi et al. 96% in the bilateral THA vs 74% in the unilateral THA group [18].

Many historical series do not report patient outcome measures [19]. Most studies analyze Harris Hip Score or Merle d'Aubigné and Postel score following bilateral arthroplasties, with equivalent results in simultaneous replacements [13, 18, 20–23]. Only a few authors analyze quality of life parameters, but these have found higher EuroQol index and EQ-5D Vas scores following simultaneous THA [22]. However, most studies are unable to show significant differences in Patient Reported Outcomes between unilateral and bilateral surgeries [22, 24, 25].

3.3 Mortality

One of the concerns of performing a bilateral simultaneous total hip arthroplasty is the risk of increased mortality [25–28]. Most of the literature regarding bilateral procedures describes historical series with large differences when compared with current clinical guidelines. In a recent study, Houdek et al. compared 94 patients undergoing simultaneous surgery with a matched cohort of staged bilateral arthroplasty. They found no difference in mortality between groups. However, the mean age of this series is 52 years old and mortality of that age group is low in general [16].

Mortality rate following THA has been decreasing over time. Hunt reported a 90-day mortality of 0.56% in 2003, whereas in 2011 it was merely 0.29% [29]. Partridge et al. taking in over half a million total hip arthroplasties described a drop in 90-day mortality from 0.60% in 2005 to 0.15% in 2014, despite a more elevated Charlton comorbidity score in the second group [30]. Improved perioperatory clinical management, spinal hypotensive anesthesia,

mechanical and chemical thromboprophylaxis, and less invasive surgical techniques have helped to reduce mortality [29]. These data have widened the indication for a total hip replacement in more fragile patients. The number of patients over 80 years of age with more co-morbidities is increasing. This age group is at higher risk of medical complications [31]. Mortality in the >80 year-old age group is of 2.5%, compared to the 0.2 in the <70 year-old group [32].

After adjusting for age, sex, and other comorbidities, perioperative mortality in THA is increased by several medical conditions: ischemic heart disease (odds ratio (OR) 2.3 with a 95% confidence interval from 2.1 to 2.7 $p < 0.001$), insulin dependent diabetes mellitus (DM) (OR = 2.8, 95% CI = 2.2–2.8, $p < 0.001$), non-insulin dependent DM (OR = 1.4, 95% CI = 11.2–1.6, $p < 0.001$), and chronic obstructive pulmonary disease (OR = 2.8, 95% IC = 2.4–3.3, $p < 0.001$) [30].

The leading causes of death following a total hip arthroplasty in current practice are cardiovascular events (myocardial infarction or heart failure), followed by cerebrovascular and thromboembolic events [33, 34]. Lower respiratory tract infections and renal failure are associated with death following THA. However, renal failure is often associated with other complications and medical conditions and may not be an independent cause of death. This is more frequent in the presence of previous comorbidities, which should be addressed in the preoperative evaluation [30].

In older patient groups, the individual scheduled for a total joint replacement is likely to have less comorbidities than the whole population suffering from osteoarthritis [33]. This same selection bias can also be noted amongst patients who are considered for a simultaneous bilateral THA. These patients are younger, healthier, and with a better body mass index (BMI), and are thus appropriate for simultaneous procedures.

Several meta-analyses have shown that there is no significant difference in mortality between bilateral simultaneous or staged THA [27, 34]. However, mortality is dependent on study follow-up and on the age of the patient group. In a retrospective analysis of the Swedish Hip Registry (1992–2012), patients with simultaneous hip replacements were younger, more often male and with a lower ASA class [26].

Mortality after THA is low [29, 33]. Thus, many of the series comparing mortality between simultaneous and staged arthroplasty are underpowered and lack control groups [27, 34]. Registry studies are needed to detect relevant differences between both groups [26]. Most studies compare mortality of bilateral simultaneous arthroplasty to unilateral arthroplasty [10]. There are few studies reporting staged group mortality [20, 35]. So far, registry studies have not shown significant differences in mortality following simultaneous procedures [26]. However, a recent analysis from the National Registry from England, Wales, Northern Ireland and the Isle of Man reported a 0.4% mortality in the simultaneous procedures group vs 0.1% for the staged arthroplasties [36].

3.4 Complication Rate

THA is a safe procedure with a 3% complication rate [30]. Previous reports have demonstrated no significant differences in systemic complications between simultaneous bilateral THA and staged bilateral or unilateral THA [3, 5, 18, 20, 21, 35, 37, 38]. Theoretically, patients undergoing two-stage surgery are at higher risk for suffering any complication in one of the episodes [39]. Meta-analysis data reveal a reduction in the occurrence of thromboembolic events (deep venous thrombosis—DVT) and (pulmonary embolism—PE) in simultaneous bilateral THA. The number of hospitalizations is halved, thus reducing its incidence [27].

Thromboembolic events were the leading cause of death following total hip replacement before the introduction of mechanical and pharmacological thromboprophylaxis. Endothelial damage and the liberation of coagulating agents during femoral canal preparation activate the coagulation cascade. Surgical time, tissue damage, and venous stasis are doubled in simultaneous THA compared to a conventional THA. For

these reasons some authors have reported a higher risk of DVTs and pulmonary events following bilateral surgeries [5, 6].

Wroblewski et al. reported a rate of fatal embolism of 0.67% (122 deaths), following 18,104 cemented THAs performed between 1980 and 1986 [40]. The adherence to thromboprophylaxis guidelines, the use of spinal anesthesia, and early mobilization ~~has~~ have reduced the incidence of major thromboembolic events. Contemporary data show an incidence of 0.55% for PEs, accounting for only 0.018% of fatal events following THA [30].

Babis et al. in a meta-analysis studied the risk of thromboembolic events in simultaneous versus staged bilateral total hip arthroplasty. After comparing 5868 simultaneous procedures with staged bilateral or unilateral THA, no statistically significant differences were found for DVT or PE [41]. However, many studies select younger and healthier patients for bilateral simultaneous procedures and this could be a selection bias in order to show differences in the incidence of DVT and PE between groups.

Berend et al. in 2005 reported a higher risk of thromboembolic pulmonary events in simultaneous replacements. In a large series of 900 simultaneous versus 450 unilateral THAs, the authors found a higher rate of pulmonary embolism 1.6% vs 0.7%, $p < 0.001$. However, the series covers patients between 1970 and 1997, all surgeries were performed under general anesthesia and thromboprophylaxis treatment changed in 1986. This long recruitment period could introduce bias, making the groups less homogeneous. Thus, the authors recognize a higher mortality in the first years of the study, especially in the older patient group (69.8 vs 62.3 years) [42].

Two years later, Berend and Lombardi reported their results with a single uncemented design in 277 consecutive bilateral patients. Patients were younger, with a lower BMI and a higher percentage of male patients in the simultaneous group. Blood loss was higher in the simultaneous group with more transfusion requirements. Seventy percent of patients suffered adverse effects, compared to only 40% in the staged surgeries. The need for subsequent hip surgery for revision or complications was also higher in the simultaneous group [13]. Garland also reports a higher revision risk after simultaneous procedures in the Swedish Hip Registry. However, after adjustment for age, gender, diagnosis, and type of implant the difference was not statistically significant [26].

Simultaneous THAs generally present a higher transfusion rate [9, 10, 12, 18, 19, 21, 43]. Houdek et al. reported no difference between simultaneous and staged. However, almost 40% of patients in the staged group required allogenic blood transfusion, in spite of a mean age of 52 years in this series [16]. The same author and Alfaro-Adrian describe a higher rate of cardiovascular and digestive complications in simultaneous vs staged bilateral THA [18, 44]. Alfaro-Adrian also noted no difference in blood requirements between both groups. The introduction of blood saving strategies has reduced the transfusion requirements in bilateral THA. While autologous blood reinfusion strategies are not recommended in unilateral THA, its use is helpful in simultaneous bilateral procedures [37, 44].

Most of the series that analyze complications are retrospective. Parvizi et al. in a prospective series of 50 patients with simultaneous bilateral (100 hips) vs 50 patients with unilateral THA report a similar complication rate for both groups. The transfusion rate was higher in the bilateral group. However, in his institution patients with previous myocardial infarction, pulmonary embolism, cerebrovascular disease, or active cardiopulmonary disease are excluded from undergoing simultaneous surgery [18]. In another retrospective study of 400 simultaneous arthroplasties matched to 400 unilateral THA, complications were more frequent in the bilateral group with a higher dislocation risk (1.6% vs 0.5% during hospital stay) [9].

Swanson et al. described that ASA score was the only independent predictive factor for major and minor complications. They also recommended bilateral procedures only in patients with ASA score of 1 or 2 [9]. However, in a more recent study comparing bilateral simultaneous THA with unilateral THA with a variety of ASA

scores, Kim reports no significant difference in their complication risk between both groups [13].

The rate of medical complications following a total hip arthroplasty is low, thus requiring numerous patient cohorts to show differences in hazard risk between simultaneous and staged bilateral procedures. Partridge analyzes 2507 simultaneous versus 9915 staged procedures (between 3 and 6 months). Patients operated on the same day were significantly younger, male and with a similar Charlson comorbidity index. However, they presented an elevated risk for pulmonary embolism, chest infection, myocardial infarction, and renal failure. Patients undergoing simultaneous surgeries had a significantly shorter hospital stay. The elevated odds ratio for medical complication was of 3.4 for pulmonary embolism, 4.6 for myocardial infarction, 2.7 for chest infection, and 6.2 for inpatient death after adjusting for age, gender, and comorbidity [36].

Table 3.1 shows results between simultaneous bilateral total hip arthroplasty (SimBTHA) vs staged bilateral total hip arthroplasty (StgBTHA) or unilateral total hip arthroplasty (UTHA) (studies before 2005). Table 3.2 shows results between simultaneous bilateral total hip arthroplasty (SimBTHA) vs staged bilateral total hip arthroplasty (StgBTHA) or unilateral total hip arthroplasty (UTHA) (studies after 2005).

3.5 Surgical Technique

Most surgeons stick to their usual surgical technique. After general spinal anesthesia, the most symptomatic hip is operated first. After completing the fist arthroplasty, a sterile dressing is applied. The second hip is prepared and the surgeon is rescrubbed, before carrying out the second replacement. The most commonly used approaches are posterolateral and anterolateral with equivalent results [10, 42].

Cemented femoral implants present a more extensive activation of the coagulation cascade than uncemented stems. Thus, some surgeons prefer to use uncemented implants for bilateral procedures [9]. Kim, in a prospective randomized study could not find significant differences in thrombotic complications comparing both types of implants [45]. These have also been reported in other studies [20]. However, there is a consecutive series with a single uncemented design describing more complications following simultaneous procedures [13]. Meta-analysis data show no significant differences regarding blood loss for either cemented or uncemented in simultaneous procedures [19].

Several less invasive approaches with reduced soft tissue trauma have been described. They theoretically provide the advantages of a shorter surgical time and lower blood loss [46]. However, a mean drop of around 5 points in the hemoglobin (Hb) level has been described in minimally invasive bilateral surgery [46]. Better limb inadequacy has been described in simultaneous procedures [13, 22].

The direct anterior approach (DAA) has gained popularity in the last decade. DAA offers earlier functional recovery with lower rates of leg length discrepancy and lower postoperative dislocation risk [47]. For bilateral surgeries, patient position remains unchanged, which saves surgical time, as turnover time takes about 15 min [18]. There are few studies that analyze the superiority of minimally invasive surgery (MIS) approach in simultaneous THA, as most of them are retrospective studies with short term follow-up. All of them report excellent clinical results with a comparable complication rate [15, 22, 46, 48–52]. The anterior approach has gained popularity in recent years. Tamaki, in 325 patients undergoing simultaneous bilateral THA, describes major complications in only 0.9% of the cases with only one patient requiring blood transfusion [49].

Kim et al. in a retrospective series of patients with osteonecrosis described higher accuracy in cup placement in the second operated hip in the simultaneous group versus the staged group using a posterolateral approach [22]. Data from the Swedish hip arthroplasty registry identifies an elevated revision risk following bilateral single stage THA [26]. Amstultz also describes a higher revision rate in the one-stage group. Therefore, he recommends not performing single stage bilateral hip interventions [53].

Table 3.1 Type of study, follow-up, cost-effectiveness, clinical results with length of stay (LOS), mortality and relevant complications. Results between simultaneous bilateral total hip arthroplasty (SimBTHA) vs staged bilateral total hip arthroplasty (StgBTHA) or unilateral total hip arthroplasty (UTHA) are reported. One series with partial hip arthroplasty is also included. Studies before 2005

Author (Year)	Number of patients (years)	Type of study	Follow-up	Cost-effectiveness	Clinical result Length of stay (LOS)	Mortality	Complications
Ritter et Randolph (1976)	100 SimBTHA vs 50 UTHA	Prospective Control group	2–5 years	Not analyzed	Hospital for Special Surgery HIP Score Shorter LOS (21 vs 15 days)	No difference	Myositis ossificans Thrombophlebitis 12% Twice blood loss
Ritter et Stringer (1980)	392 SimBTHA vs 427 UTHA (1971–1978)	Retrospective Matched control		<30% total expenses	Hospital for Special Surgery HIP Score Better ROM UTHA (16.4 vs 13.9 days)	No difference Better ROM UTHA	HIgher incidence of ectopic Ossification (36 vs 25%)
Salvati et al. (1978)	122 Sim BTHA	Retrospective		Not analyzed	No difference	No difference 1 death	No difference 1/3 higher blood loss
Alfaro-Adrian et al. (1999)	95 SimBTHA vs 107 StgTBHA (1989–1995)	Retrospective	X	17% less medical cost (9300$ vs 11,200$)	No difference Charnley Hip Score Shorter LOS (35%)	No difference	No difference Greater transfusion rate
Egli et al. (1996)	128 SimBTHA 126 Stag BTHA < 6 weeks 256 StagBTHA 6 weeks–6 months	Retrospective	1.5 years	30% less hospital cost	Shorter LOS (5–6 days)	No difference Better walking SimBTHA	No difference
Shih et al. (1985)	20 SimBTHA 15 StgBTHA (1979–1982)	X	12 months	10% less hospital cost	Shorter LOS (18 vs 27)	No difference	No difference

Bracy et Wroblewski (1981)	400 SimBTHA	Retrospective			No difference	No difference	Higher incidence of pulmonary embolism
Cammisa et al. (1988)	35 SimBTHA	Prospective			No difference	No difference	No difference
Ilyas et Moreau (2002)	36 SimBPHA (1990–1998)		5.7 years (2-10)				Safe in Sickle cells disease
Egol et al. (1998)	60 SimBTHA		49 months				30% Heterotopic bone
Welters et al. (2002)	70 SimBTHA (1992–1998)	Retrospective			No difference Higher ROM in patients with Rheumatoid conditions	No difference	No difference

Table 3.2 Type of study, follow-up, cost-effectiveness, clinical results with length of stay (LOS), with mortality and relevant complications. Results between simultaneous bilateral total hip arthroplasty (SimBTHA) vs staged bilateral total hip arthroplasty (StgBTHA) or unilateral total hip arthroplasty (UTHA) are reported. Two series reporting bilateral hip resurfacing are also included. Clinical Score include Harris Hip Score (HHS), and Oxford Hip Score. Studies after 2005

Author (Year)	Number of patients (years)	Type of study	Follow-up	Cost-effectiveness	Clinical result Length of stay (LOS)	Mortality	Complications
Berend et al. (2005)	900 SimBTHA vs 450 StgBTHA (1970–1997)	Retrospective Matched-control	27 years	No difference	No difference HHS	3.1 vs 4% (1 years)	>Thromboembolic disease
Parvizzi et al. (2006)	100 SimBTHA vs 50 UTHA (1998–1999)	Prospective Matched study Exclusion criteria (comorbidities)	4.2 years (2–5.6)	Not analyzed	HHS SF-36 Shorter LOS 2.25 VS 4 days Better LLD	No difference	Greater transfusion rate 20% vs 10% rate More transfer to rehabilitation centers
Bhan et al. (2006)	83 SimBTHA vs 85 Stg BTHA (1996–2001)	Randomized Prospective Study	60 months	Not analyzed	No difference HHS Shorter LOS 7.25 vs 10 days	No deaths	No difference Greater transfusion rate
Swanson et al. (2006)	400 SimBTHA vs 400 UTHA (1987–2000)	Retrospective Matched control		Not analyzed	Not analyzed	No difference	Greater complication rate ASA Score predictor for complications Higher dislocation risk (1.6 vs 0.5%)
Parvizzi et al. (2006)	196 SimBTHA vs 196 Stg BTHA (1997–2004)	Retrospective study Control group	6 months	<30% total expenses	No difference HHS Shorter LOS 4.3 vs 8.1 days	No difference	Stg BTHA more complications and transfusions More transfer to rehabilitation centers
Berend et al. (2007)	334 SimBTHA vs 220 StgBTHA (1997–2005)	Retrospective	–	<28% Hospital reimbursement <15% Surgeon income	Shorter LOS 3.9 vs 5.6 days Similar clinical result (HHS)	Not analyzed	>Blood loss >Adverse effects Worse rehabilitation in SimTHA 71.3% vs 42% >Subsequent surgeries
McBryde et al. (2007)	37 Sim Resurfacing vs 55 Stg Resurfacing (1994–2006)	Retrospective	2.5 years	35% less hospital cost	Shorter LOS (5 days)	No difference Oxford Hip Score	No difference

Tsiridis et al. (2008)	2063 SimBTHA (1960–2003)	Meta-analysis		SimBTHA more efficacious economically	Shorter LOS in SimBTHA	No difference	No difference In DVT or PE Greater transfusion rate in SimBTHA
Kim et al. (2009)	1956SimTHA vs 1666 UTHA (1994–2002)	Consecutive Retrospective	10.5 years (5–14)	Not analyzed	HHS	No difference 0.31 vs 0.18%	No difference with High or Low risk ASA score Higher transfusion rate in SimBTHA
Aghayev et al. (2010)	247 SimBTHA vs 737 StgBTHA < 6 months 835 Stg BTHA 6 months–5 years (1965–2002)	Post hoc analysis of prospective data	Not analyzed	Not analyzed	Better HHS in SimBTHA than StagBTHA 6 months–5 years	No difference	More complications in StagBTHA 6 months–5 years
Amstutz et al. (2011)	75 Sim Resurfacing vs 87 Stag Resurfacing (1996–2006)	Retrospective	7 years	Not analyzed	Shorter LOS UCLA HHS SF-12	No difference	Higher revision rate in Sim group
Lindberg-Larsen (2013)	206 SimBTHA vs 740 StagBTHA < 6 months 414 StagBTHA 6–18 months (2010–2011)	Retrospective National Patient Registry		Not analyzed	Shorter LOS (4 vs 6 days)	No difference	No difference
Romagnoli et al. (2013)	126 simBTHA vs 97 UTHA (2001–2011)	Retrospective Matched control		Not analyzed	Shorter LOS Sim BTHA	No difference	No difference Greater blood loss Similar transfusion rate
Kim et al. (2017)	126 SimBTHA vs 120 StgBTHA (2007–2013)	Consecutive Retrospective	60.2 months	<16% Hospital charge	Sim BTHA >EurolQol5D >HHS Shorter LOS 10.5 vs 18.7 days Better LLD	No difference	Less complications in SimBTHA

(continued)

Table 3.2 (continued)

Author (Year)	Number of patients (years)	Type of study	Follow-up	Cost-effectiveness	Clinical result Length of stay (LOS)	Mortality	Complications
Houdek et al. (2017)	188 SimBTHA vs 188 StgBTHA (2000–2013)	Retrospective Matched-control	Mean 4 years (2–15 years)	28% less cost	Shorter LOS <23% 4.6 vs 5.9 days	No difference 6.4% vs 19% during f-u	No difference 13.8 vs 18.1% ASA had no effect 39% vs 34%blood transfusion
Huang et al. (2019)	33516 SimBTHA vs 84998 StgTHA	Meta-analysis	Not analyzed	Not analyzed	Not analyzed	No difference	Sim BTHA less DVT, Pulmonary Embolism and pulmonary complications No difference in dislocation or infection rate
Tan et al. (2019)	256 SimBTHA vs 256 StagBTHA (2013–2016)	Retrospective Multicenter (26 hospitals) Cohort study With ASA <2	90 days	No difference	Shorter LOS 8.7 vs 12.1 days	No difference	No difference Greater transfusion rate (49% vs 10%)
Taheriazam et al. (2019)	180 SimBTHA vs 180StagBTHA (2008–2011)	Prospective randomizaed study (ASA I or II)	1 year	Not analyzed	No difference HHS Shorter LOS (4.9 vs 9.8 days)	No deaths	No difference

Simultaneous MIS bilateral THA in the supine position minimizes surgical time. Contemporary Hb optimization strategies combined with less invasive hip approaches can improve the safety of simultaneous procedures. Petridis and Nolde combine preoperative iron supplementation and erythropoietin when Hb is <14 g/dL, the use of a cell saver for reinfusion of autologous blood and topic tranexamic acid before wound closure. In 130 patients, a mean preoperative Hb of 14.3 g/dL dropped to only 11.3 g/dL. Only 5.4 of patients required allogeneic blood transfusion, with a mean blood loss of 518 ± 144 mL [54].

There are concerns as to whether results of simultaneous THA are affected by the volume of patients. Data from the National Registry for England, Wales, Northern Ireland, and the Isle of Man, show that most of the simultaneous THA are carried out in low volume centers with less than five simultaneous procedures per year. "High volume units" are noted to select significantly younger patients with fewer comorbidities than "low volume units." "Low volume units" reported 0.7% mortality while no deaths occurred in "High volume units" and patient selection may reflect this [36]. This might advocate that simultaneous surgeries be restricted to high-volume hospitals which generally report superior outcomes with lower complication rate and mortality [26, 55–57]. Table 3.3 shows an overview of series of simultaneous bilateral minimally invasive total hip arthroplasty (SimBTHA).

Figure 3.1 shows a case of displaced femoral head epiphysiolysis sequela. Figure 3.2 shows a case of pseudoachondroplasia with bilateral degenerative changes in both hips. Figure 3.3 shows bilateral osteonecrosis of the femoral heads.

3.6 Cost Effectiveness

The growing number of patients requiring a total hip arthroplasty constitutes an increasing economic burden. Around 20% of patients suffer from bilateral involvement of their joints and will require both of them to be replaced [36]. Simultaneous bilateral THA is cost effective, allowing for a reduced anesthetic time, length of stay, and rehabilitation time.

Houdek et al. in a matched control study report a 27% reduction in total cost due to reduced surgical time and length of stay when comparing simultaneous with staged bilateral replacements [16]. Egli et al. also reported a 30% saving in single stage bilateral THA [3]. Many series associate bilateral surgeries with lower cost, and meta-analysis corroborate these data [13, 16, 17, 19, 22, 28, 48, 58]. In a more recent study by Tan there was no significant difference in cost between simultaneous or staged procedures, though the length of stay was shorter in the simultaneous group and their transfusion rate was five times higher. Increased age was a risk factor for higher cost hospitalization [43].

The first series performing single stage THA reported a reduced economic cost of less than 10% [20]. After 1992, Medicare reimbursement decreased by 50% in the second arthroplasty in a simultaneous bilateral procedure [59]. Some authors have questioned a reduction of potential hospital and surgeon revenues when simultaneous hip replacements are performed [13]. However, reduced hospitalization time and faster rehabilitation, would reduce cost for National Health systems. Bilateral surgeries with a single anesthesia would require 27% less operating time and 28% shorter total length of hospitalization [2, 3, 20, 60]. Some authors have advocated the use of fast-track protocols for simultaneous procedures in carefully selected patients [17].

3.7 Conclusions

If we analyze registry data and contemporary orthopedic practice, less than 1% of bilateral hip osteoarthritis is managed simultaneously. The reason for this is an alleged higher complication rate. Nevertheless, this is not supported by medical literature [3, 5, 8, 18, 20, 21, 35, 37, 44]. Recent data from the English National Health

Table 3.3 Overview of series of simultaneous bilateral minimally invasive total hip arthroplasty (SimBTHA). Several different approaches are included direct anterior approach (DAA), minimally invasive surgery (MIS) two incision technique, modified Watson Jones (anterolateral). Clinical scores include: Harris Hip Score (HHS), Visual Analogue Scale (VAS), Questions on Life Satisfaction (FLZ), High Activity Arthroplasty Score (HAAS), and Japanese Orthopaedic Association Hip Disease Evaluation Questionnaire (JHEQ)

Author (Year)	Number of patients (years)	Type of study	Follow-up	Cost-effectiveness	Clinical result Length of stay (LOS)	Mortality	Complications
Seol et al. (2005) MIS two-incision approach	147 SimBTHA vs 59 StgBTHA (2004–2009)	Retrospective Case control	34.4 months (12–112)	<18% total medical cost	HHS Womac Shorter LOS (14.6 vs 25.3 days)	No difference	No difference Greater transfusion rate
Divanji et al. (2009) MIS two-incision approach	124 SimBTHA (2003–2006)	Retrospective Without control group	41 months	Not analyzed	HHS Womac 12.9 days	No difference	No difference 2 Periprosthetic fractures
Parcells et al. (2015) DAA	22 SimBTHA vs 22 UTHA (2013–2014)	Retrospectice Consecutive matched	12.9 months	Not analyzed	No difference in HHS or LOS	No difference	Greater transfusion rate (23% vs 5%)
Tamaki et al. (2016) DAA	325 SimBTHA (2012–2014)	Retrospective Without control group	2 years	Not analyzed	Not analyzed	0 deaths	0.9% local complications No systemic complications
Yoshii et al. (2016) DAA	250 SimBTHA vs 304 UTHA (2013–2014)	Retrospectice Consecutive	12.5 months	Not analyzed	Greater improvement in SimBTHA JHEQ VAS	No difference	No difference
Martin et al. (2016) DAA	12 SimBTHA vs 12 UTHA (2013–2014)	Retrospectice		16% less hospital cost (mostly for Operating Room)	Not analyzed	No difference	No difference
Kutzner et al. (2017) MIS Watson Jones	54 SimBTHA	Prospective cohort	2 years	Not analyzed	HHS VAS	Not analyzed	1 Greater Trochanter fracture 1 DVT
Petridis-Nolde (2017) DAA	130 SimBTHA (2011–2014)	Retrospective 2 centers Without control group	2 years	Not analyzed	HHS HAAS FLZ 7.4 days	No deaths	No complications 7.4% blood transfusion

Table 3.3 (continued)

Author (Year)	Number of patients (years)	Type of study	Follow-up	Cost-effectiveness	Clinical result Length of stay (LOS)	Mortality	Complications
Villa et al. (2019) DAA	61 SimBTHA 143 Stg < 1 years BTHA 143 Stg > 1 years BTHA (2010–2016)	Retrospectice Consecutive <75 y few comorbidities		Not analyzed	Longer stay 2.61 days Sim 2.06 days Stg <1 years 1.63 days Stag > 1 years		Higher advese affects Greater transfusion rate (45.9% vs 7%) More transfer to rehabilitation centers

Service show that only 0.6% of bilateral procedures were carried out the same day between 2005 and 2014. It is the first study to compare the results of both types of procedures with a nationwide analysis and a significant number of patients [36].

Garland, in the Swedish Hip Registry from 1992 to 2012, found that only 1680 of 42,238 bilateral total hip arthroplasties were done the same day (450 of 15,226 with ASA data included in the Registry after 2008). Though no differences in 90-day mortality were found after adjusting for age, gender, diagnosis, and prosthesis fixation, 90-day mortality was reported to be higher in male patients over 75 years. The percentage of patients with simultaneous replacements was lower in the latter years [26].

In the Mayo Clinic, with over one thousand primary total hip arthroplasties per year, only 1.4% of the bilateral procedures were performed simultaneously [16]. This shows that in spite of supporting literature, staged procedures are generally preferred by the surgeons and their patients. It is generally reserved for healthier patients with disabling hip disease and continued rehabilitation needs after a unilateral replacement. When a surgeon decides to operate on a patient with bilateral involvement, they must consider their overall physical and medical condition to assess the potential risk of performing both surgeries simultaneously or staged.

Three published meta-analyses from 2008 and 2019 found no significant differences in thromboembolic complications and dislocation rate between simultaneous or staged surgeries. However, Tsiridis doubles the incidence of DVT and dislocations in the unilateral THA group to allow a comparable analysis [19, 27, 34]. A recent meta-analysis of simultaneous vs staged total hip replacements studies published between 1995 and 2015 was carried out. After more than 17,000 one-stage bilateral arthroplasties, the publication found a lower risk of major systemic complications, including thromboembolic events, with a shorter operative time and no significant differences in mortality, infection, or cardiopulmonary complications [39]. However, of the 13 studies analyzed there was only one prospective randomized study and another 11 reported retrospective data [61].

Simultaneous THA can be done safely in the younger and fitter patient with little comorbidity. Most studies show no difference in terms of patient outcomes with respect to perioperative mortality, complication rate, or revision or reoperation risk. For all other patients, the 90-days frame is the time when mortality drops back to the base line for the selected age group [33]. Most of the mortality and medical complications could be avoided if we exclude patients with a Charlson score over 0 for simultaneous bilateral THA [36]. Single anesthetic bilateral THA is cost effective and allows a lower overall operating room utilization and hospital length of stay. However, prospective studies with greater patient numbers and control groups are needed to draw definitive conclusions.

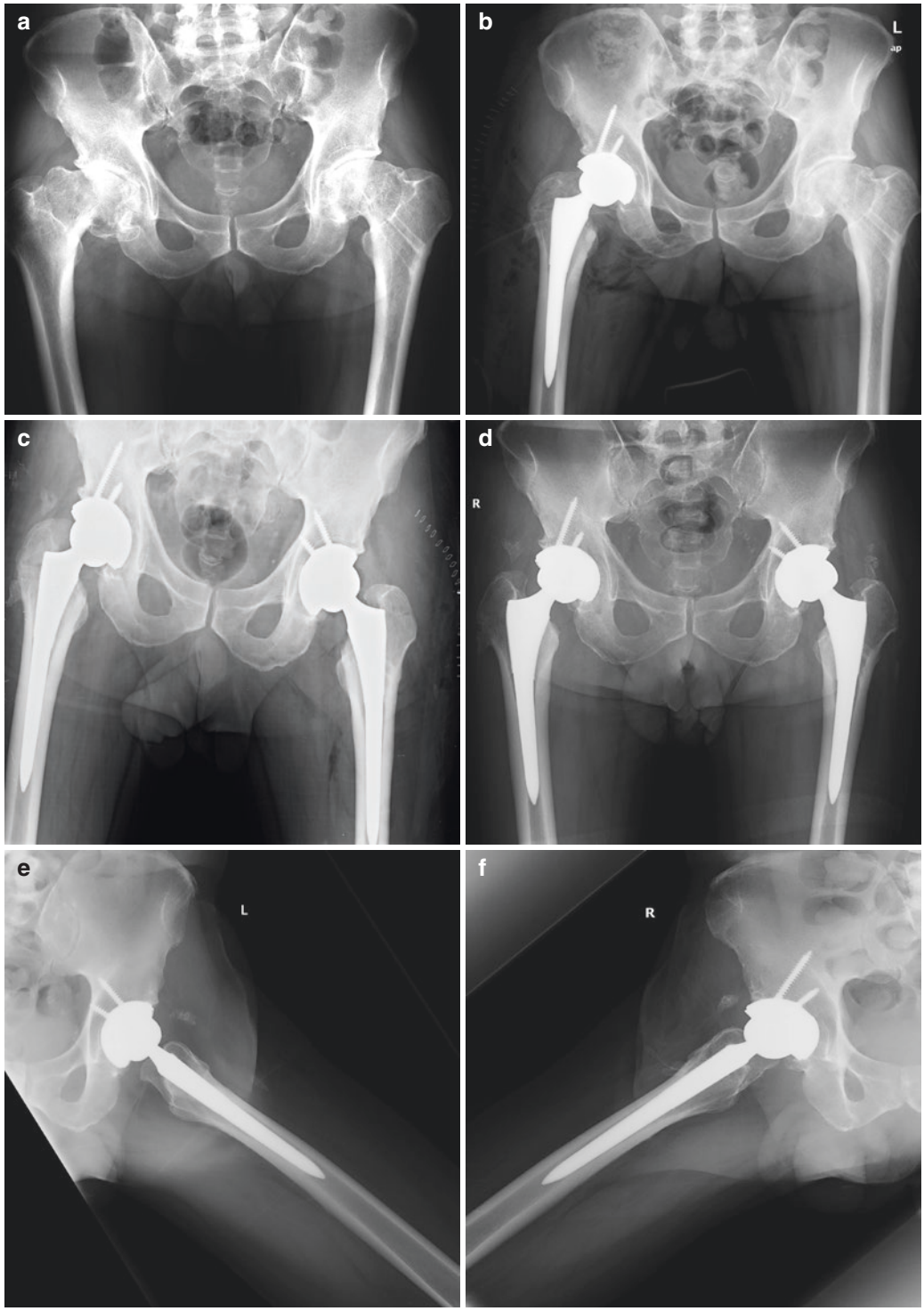

Fig. 3.1 53-year-old male patient with displaced femoral head epiphysiolysis sequela. Presented severe groin pain with a Harris Hip Score of 29 and a bilateral flexion contracture of both hips of 10° (**a**). He was implanted an uncemented THA in his right hip with ceramic on ceramic bearing (**b**). Three months after the first surgery, the left hip is operated with a similar THA also with ceramic on ceramic. The VAS and quality of life scores did not improve until the second surgery was performed (**c**). 10 year follow-up plain X-ray with good integration of the prosthesis (**d**–**f**)

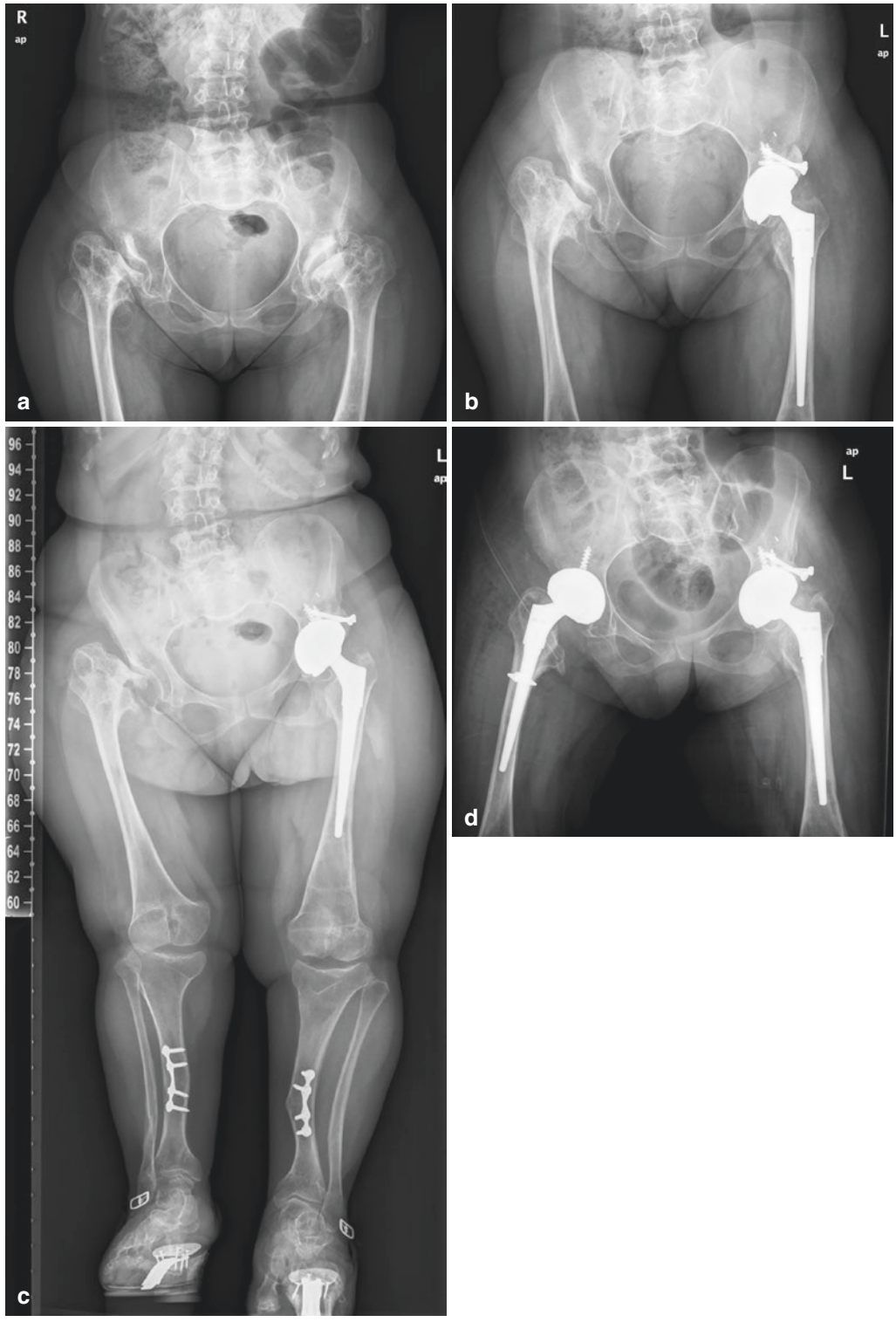

Fig. 3.2 57-year-old female patient revised with pseudoachondroplasia with bilateral degenerative changes in both hips (**a**). The left hip is operated first with a modular stem and a dual mobility cup (**b**). The patient complained about severe limb length discrepancy with difficult rehabilitation (**c**). The patient did not recover adequate gait function until the right hip was operated (**d**)

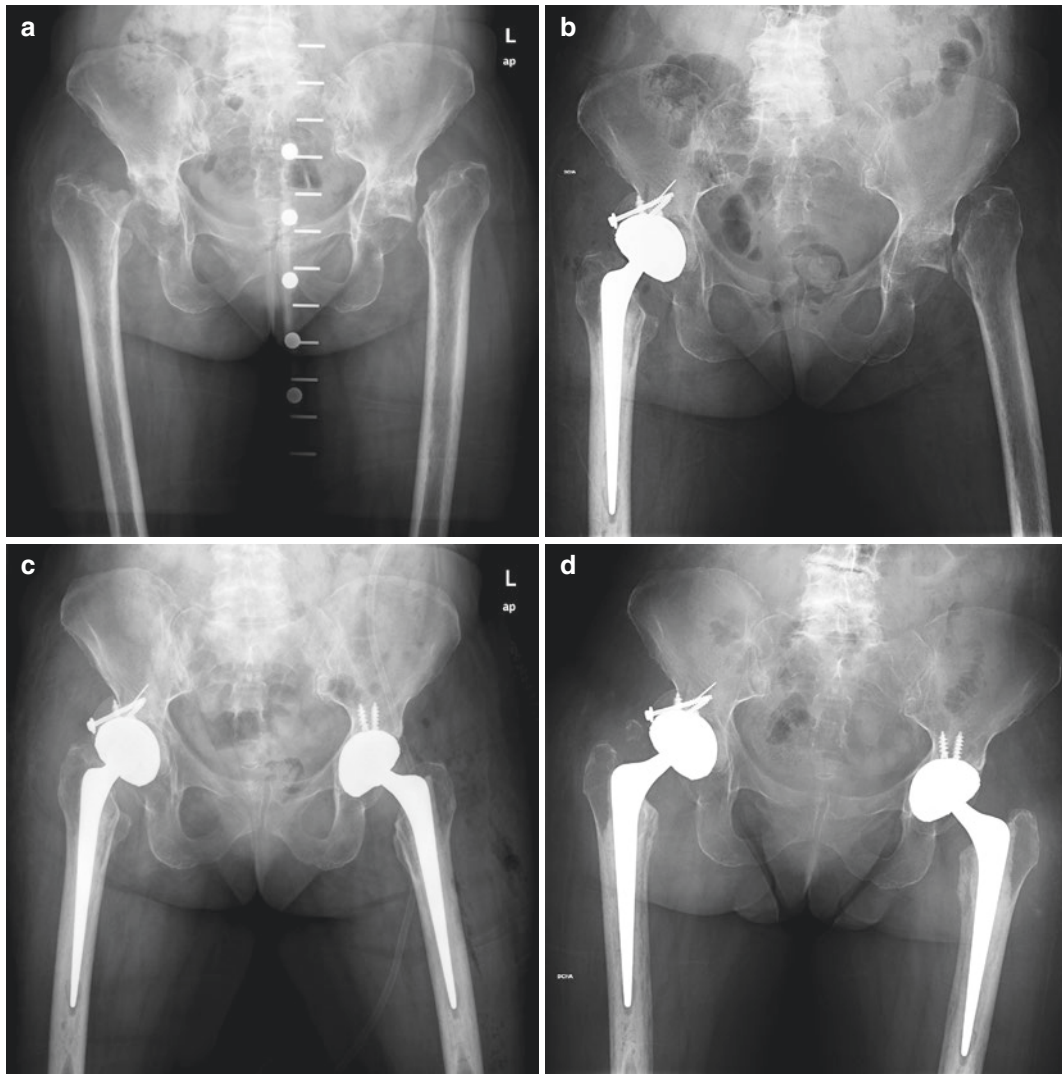

Fig. 3.3 Radiograph of 59 years old woman, showing bilateral osteonecrosis of the femoral heads (**a**). The patient presents Rheumatoid Arthritis with Chronic Steroid treatment and Tofacitinib. The patient also suffers anemia of chronic disease, congestive heart failure, and chronic obstructive pulmonary disease. The right hip is operated first with a cemented stem and a dual mobility uncemented cup (**b**). The patient suffered medical complications including nosocomial pneumonia that resolved following 2 weeks of intravenous antibiotics. One month later the second hip is operated (**c**). One-year follow-up X-ray with good orientation of both implants (**d**)

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4 Approaches for Total Hip Arthroplasty

Francis Connon and Kartik Logishetty

4.1 Background

There are three broad categories of surgical approach to the hip for the purpose of total hip arthroplasty: the posterior approach (PA), the anterior approach (AA), and the lateral approaches (LA) (Fig. 4.1). Within each, several variations have been described which most commonly identify an alternative intermuscular interval. Each has unique advantages, limitations, and complication profiles, but all can be safely used for total hip arthroplasty (THA). There is wide international variation in choice of approach (Tables 4.1 and 4.2). The body of evidence regarding the relative benefits and risks of each approach is sometimes conflicting; suggesting that the success of THA is multifactorial, and influenced by surgeon experience and training, surgical efficiency, implant choice, and perioperative patient optimisation.

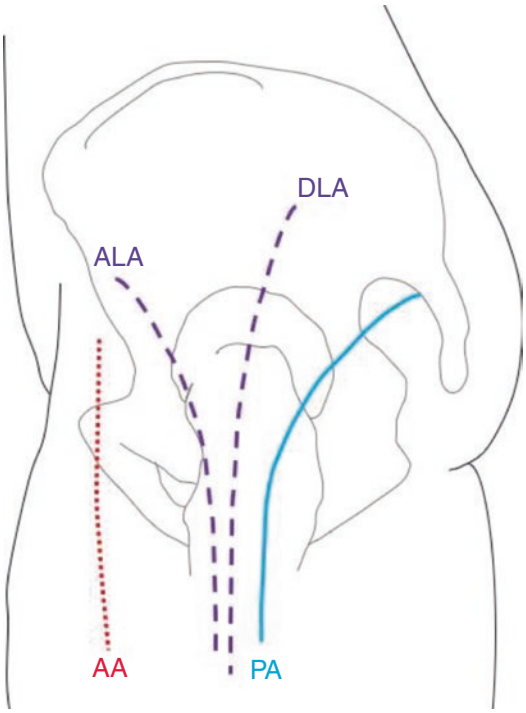

Fig. 4.1 Surgical approaches to the hip. Red, dotted line = *AA* Anterior approach, Purple, dashed lines = *ALA* Anterolateral approach and *DLA* Direct lateral approach, Blue, solid line = *PA* Posterior approach

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Table 4.1 Surgical approaches reported in international hip arthroplasty registries

Country	England and Wales	Sweden	Norway	Denmark	Switzerland	France	Australia
Registry	NJR [35]	SHAR [36]	NNR [37]	DHAR [38]	SIRIS [39]	SOFCOT [40]	ANJR [41]
Anterior	NR	<1	8	<1	46	21	26
Anterolateral or lateral	25	46	18	3	40	16	20
Posterior	72	54	71	96	14	53	54
Other	3	<1	1	<1	<1	10	<1
Unknown	NR	NR	3	NR	NR	NR	NR

UK NJR National Joint Registry of England and Wales, *SHAR* Swedish Hip Arthroplasty Registry, *NNR* Norwegian National Registry, *DHAR* Danish Hip Arthroplasty Register, *SIRIS* Schweizerisches Implantatregister, *SOFCOTL* Société Française de Chirurgie Orthopédique et Traumatologique, *ANJR* Australian National Joint Registry

Table 4.2 Surgical approaches reported in international hip arthroplasty registries, continued

Country	Italy	Canada	New Zealand	Slovakia	Portugal	Netherlands	Belgium
Registry	RIAP [42]	CJRR [43, 44]	NZOAJR [45]	SAR [46]	SPOT [47]	DAR [48]	Orthopride [49]
Anterior	2	10	4	<1	7	32	36
Anterolateral or lateral	44	70	26	80	42	12	23
Posterior	41	20	67	18	51	55	37
Other	5	<1	2	<1	<1	<1	3
Unknown	8	NR	NR	NR	NR	NR	NR

RIAP Registro Italiano Arthroprotesi, *CJRR* Canadian Joint Replacement Registry, *NZOAJR* New Zealand Orthopaedic Association Joint Registry, *SAR* Slovakian Arthroplasty Register, *SPOT* Sociedade Portuguesa de Orthopedia e Traumatologia, *DAR* Dutch Arthroplasty Register, Orthopride

4.2 The Posterior Approach

The posterior approach is synonymous with the Southern approach, the Moore approach, the dorsal approach, and the posterolateral approach. Although it was initially described by Theodor Kocher and Bernhard von Langenbeck in 1892 [1], the PA became more popular with the development of hemi- and total hip arthroplasty in the 1940s to avoid the problems with non-union encountered after trans-trochanteric approaches. The PA spares the abductor musculature while providing the opportunity for wide exposure of the acetabulum and femur, making it the most popular surgical approach currently worldwide for THA, including for complex primary or revision hip arthroplasty.

The fascia lata is split longitudinally and the gluteus maximus muscle is split in line with its fibres, posterior to the greater trochanter. The posterior aspect of the hip capsule is exposed by

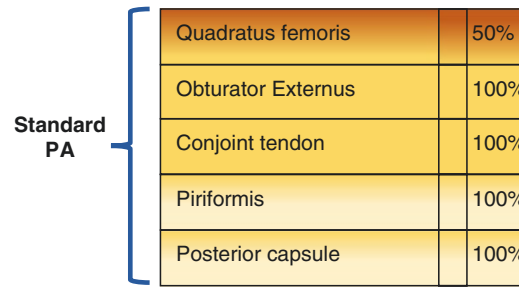

Fig. 4.2 Releases for the posterior approach

dividing the short external rotator muscles close to the femur, and typically the piriformis tendon (Fig. 4.2). Structures at risk during the PA are the medial femoral circumflex artery (MFCA) and the sciatic nerve. The MFCA is critical for the blood supply of the femoral head which is pertinent for operations where the femoral head most be preserved (fracture fixation and sepsis debridement) but less relevant for Total Hip Arthroplasty. The sciatic nerve has a variable course near the

piriformis tendon (most commonly emerging from the sciatic notch anterior to the tendon) [2].

4.3 The Direct Lateral Approach

The direct lateral approach (LA) was described by McFarland and Osborne in 1954 [3] and popularised by Hardinge from 1982 [4]. After the PA, it is the most commonly performed surgical approach for THA in some countries, and particularly for arthroplasty in the setting of hip fracture. The fascia lata and TFL are incised, and the 3–5 cm of the gluteus medius is bluntly split, starting at the greater trochanter. The gluteus minimus, the proximal end of the vastus lateralis, and the anterior third of the gluteus medius are elevated from the anterolateral femur. This exposes the anterior capsule which can be incised or resected. The abductors must be repaired back to a cuff of tissue on the greater trochanter after THA, prior to closure of the fascia lata and skin incision. The LA does not disrupt the posterior capsule which protects against dislocation in deep flexion and internal rotation [5]. Therefore, the incidence of dislocation after LA is very low, and not dependent on capsular repair [6].

Abductor weakness, due to damage to the abductors or the superior gluteal nerve, or failure of the tenotomy repair, is a particular concern after LA THA, with a reported incidence of 4–20% [7]. Electromyography suggests that superior gluteal nerve injury may occur as often as 25% of LA THA, but recovery at 1 year after surgery is almost universal [8].

4.4 The Anterior Approach to the Hip

The anterior approach (AA) to the hip may have first been described in 1838 by German surgeon, Carl Heuter [9]. Marius Smith-Petersen and Robert and Jean Judet published extensively on its use for hip arthroplasty in the mid-twentieth century [10–12]. Its global uptake has increased since the 1990s, popularised as an open approach to perform surgery for femoroacetabular impingement [13], femoral head [14], and acetabular fractures [15], and as a less-invasive technique for THA and hip resurfacing arthroplasty (HRA) by Kristaps Keggi [16, 17] and Joel Matta [18, 19].

The patient is positioned supine, either on a standard operating table or a traction table (Fig. 4.3) with the operative leg securely held in a boot, as per the surgeon's preference. The traction table, if used, is to aid hyperextension and external rotation of the femur to access the femoral canal which can be difficult in certain patients, particularly when the surgeon is learning the technique. The TFL and gluteus medius muscles are retracted laterally, and the sartorius and rectus muscles medially. The lateral femoral circumflex vessels cross the intermuscular interval just distal to the intertrochanteric line, and these are cauterised or ligated. Underneath the perivascular fat, the hip capsule is incised or resected to expose the anterior femoral neck (Fig. 4.4).

Capsular releases are important to avoid the risk of trochanteric fracture—the pubofemoral ligament and superior capsule are released so that the femur can be elevated. In some cases, release of part or all of the conjoint tendon and piriformis tendon may be required (Fig. 4.5).

Structures at risk in the AA are the LCFN superficially, the muscle fibres of the TFL which

Fig. 4.3 Example of a traction table used to perform a direct anterior approach total hip arthroplasty. The traction table is used by some surgeons to aid hyperextension and external rotation of the femur to access the femoral canal. It is particularly useful for more difficult cases, such as revision arthroplasty and for training surgeons

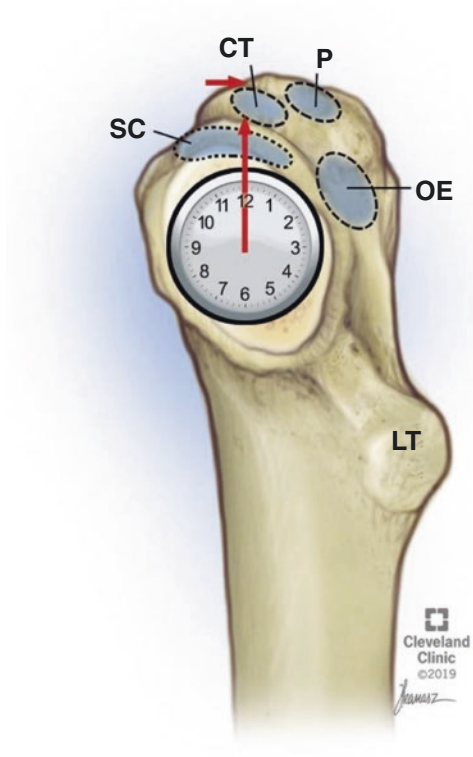

Fig. 4.4 Clockwise releases for the anterior approach, showing the right femur. *SC* superior capsule, *CT* conjoint tendon insertion, *P* piriformis tendon insertion, *OE* obturator externus tendon insertion, *LT* lesser trochanter. Permission: Chugtai et al. (2019)

lie laterally, and the femoral neurovascular bundle and external iliac vessels anteromedially. These neurovascular structures are particularly at risk from mispositioned or drifting retractors [20]. In osteoporotic patients, the anterior approach has been linked to an increased risk of femoral shaft fracture [21].

For better cosmesis, the AA can also be performed through an oblique "bikini" incision, centred in the inguinal fold [22]. This is used as a mobile window to sequentially view the femur and acetabulum. The bikini anterior approach is not extensile and more technically difficult, compared to its conventional counterpart, and may increase the risk of LCFN injury [23]. Therefore, it has been recommended only for experienced AA surgeons [22].

4.5 Less Common Approaches

The Watson-Jones approach is an anterolateral approach to the hip—initially described by Sayre in 1894 and modified by Watson-Jones in 1936 [24]. Failure of the abductor repair or denervation of the tensor fascia lata muscle from aggressive retraction can cause abductor weakness and Trendelenburg gait [25, 26]. Many surgeons approaching the hip through this interval now more commonly perform the less-invasive

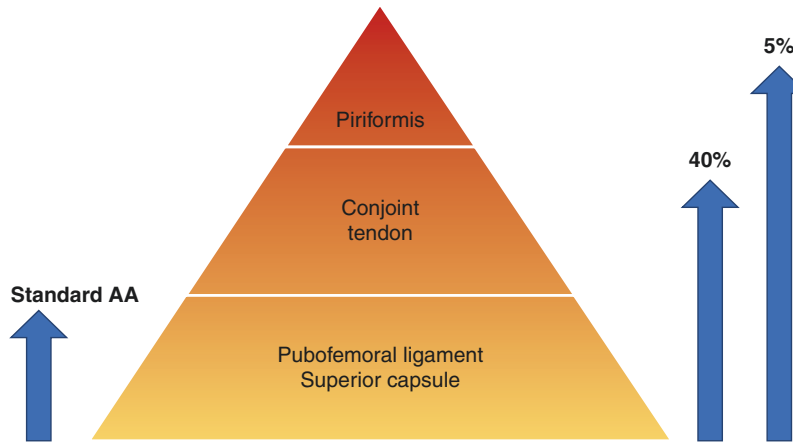

Fig. 4.5 Stepwise releases for the Anterior Approach (adaption of Chugtai et al., 2019)

Rottinger approach (also known as the Orthopaedic Clinic Munich technique) [27]. This spares the abductors but may offer inadequate exposure of the acetabulum and femoral canal with an associated risk of trochanteric fracture and femoral shaft fracture [28]. Compared to the direct lateral approach, the Rottinger approach results in significantly fewer defects and less atrophy of the gluteus medius, a lower incidence of Trendelenburg gait, and better clinical function [29]. A review of the literature encompassing over 20,000 patients who underwent THA through a variety of approaches showed that the Rottinger approach demonstrated no major differences in clinical outcome or complication rates at 6 months compared to any other approaches [30].

The Direct Superior Approach (DSA) is also a variation of the posterior approach to the hip, which avoids violating the iliotibial band or the quadratus femoris muscle and obturator externus tendon. Only the gluteus maximus fascia is incised, and the muscle fibres are split bluntly [31]. The piriformis and conjoined tendon are then released from the greater trochanter. While it is posited as a minimally invasive approach compared to the PA and AA [32], there are limited clinical data on its effectiveness [33].

The SuperPath approach is a direct superior portal-assisted approach for THA first described by Murphy in 2004. It utilises the interval between the gluteus minimus and piriformis muscles to access the hip capsule. Uniquely, the femoral canal is broached through a channel, while the head and neck remain intact. The acetabulum is prepared without release of the iliotibial band or remaining external rotators. Gofton et al. have reported on a multicentre study of nearly 500 SuperPath THAs, noting a 30-day all-cause readmission rate of 2.3%, a transfusion rate of 3.3%, and an average length of stay of 1.6 days [34].

4.6 Comparison of Different Approaches

THA was described as "the operation of the century" in 2007 [50] when the PA and LA were the primary means of performing the procedure. Since then, the use of the AA for THA has been rapidly increasing globally [51], whilst the relative rates of PA and LA usage are now in decline. However, there is conflicting evidence regarding the purported benefits and safety profile of the AA [44, 52, 53]. Here we shall discuss the specific considerations regarding the choice of hip approach, particularly with regard to THA but also for other indications.

4.6.1 Post-operative Pain and Function

The potential for reduced post-operative pain and better early post-operative function is one of the key drivers towards increased uptake of the AA in recent years. Miller [54] demonstrated in a meta-analysis of randomised controlled trials that compared to the PA approach, patients who had their elective THA via the AA were discharged earlier, used less opiate analgesia, reported less pain, and had better function as determined by Harris Hip scores for the first 3 months post-operatively. Whilst a multicentre randomised controlled trial has suggested that there could be some persistent advantage even beyond 1 year post-operatively with regard to lateral sided pain when employing the AA compared to PA [55], most other papers have demonstrated early benefit from the AA but no difference at 1 year [56–58]. Postulated causes for a persistently lower rate of lateral pain even after 1 year post-operatively include the fact that the PA transects the trochanteric bursa and ITB, whereas the AA does not, and possible increased stress on the ITB from increased offset utilised during some PA hip arthroplasties as a means to reduce dislocation risk.

The LA has been shown to result in gait abnormalities [59, 60] and associated trochanteric pain. Swedish registry data includes Patient Reported Outcome Measures with significantly better EQ-5D, higher satisfaction and lower pain scores with the PA than the LA at up to 6 years follow-up [61]. Compared to the AA, clinical function and health-related quality of life were lower after LA at 1 year after surgery, but equivalent after 2 years [62].

From a healthcare provider's perspective, earlier discharge is cost-effective [63] and is particularly incentivised by modern value-based payment strategies including episode-of-care payments [64, 65]. Performing AA hip arthroplasty as an outpatient procedure has been proven to be safe in selected patients [66, 67], so this is an increasingly attractive proposition.

4.6.2 Learning Curve

Surgeons using the AA for the first time have a higher revision rate [68] for their first 50–100 cases before their revision rate reaches the stable long-term average. The level of complications associated with the anterior approach is probably dependent on the availability of appropriate training: in countries with greater use of AA, adjusted analyses of large registry data sets suggest reduced incidence of infection and dislocation [41], periprosthetic fracture, and reduced risk of all-cause revision compared to the posterior approach [39, 51]. On the other hand, registry analyses and observational studies in countries with lower usage of the AA have observed the opposite [44, 69–71]. Training in a technically demanding newer technique such as the AA requires both access to mentoring and an initial and ongoing caseload to maintain competency that many existing surgeons do not have.

4.6.3 Revision Rate

Randomised controlled trial data has demonstrated no difference in implant longevity between posterior and anterior approaches [72]. Australian registry data has also demonstrated no difference in *overall* revision rates in the first 3 years post-operatively between the three major arthroplasty approaches to the hip [73]. However, the causation of revision was altered: posterior approaches were associated with higher revision for dislocation, the anterior approach was associated with higher rates of revision for fracture and aseptic loosening and the posterior and lateral approaches with higher rates of revision for infection when compared to the AA. Higher rates of aseptic loosening in AA are hypothesised to relate to undersizing of cementless implants via this approach as a result of the more difficult access to the femoral canal than when utilising the LA or PA. Many companies have in recent years attempted to address this issue through the manufacture of curved broaching instruments to and shorter or more curved femoral stems. This can also be addressed through fluoroscopic verification of trial broach position to prevent undersizing the femoral component.

The National Joint Registry of England and Wales (NJR) has reported higher overall revision rates and death rates with the LA than when utilising the PA [74]. Registry data is compromised by its lack of randomisation and the results can be skewed by relative numbers of both novice and large volume hip surgeons utilising the AA and experienced generalist orthopaedic surgeons using the PA and LA.

4.6.4 Periprosthetic Fracture

Periprosthetic fracture has been shown to occur more frequently in patients treated via the AA [73, 75] and registry results demonstrate that the AA is associated with higher rates of revision arthroplasty secondary to fracture [41]. Whilst this risk is related to the learning curve, it is not completely explained by this phenomenon and this elevated risk may remain even after a surgeon is adequately trained in the technique [21]. As more experience is gained with the AA, techniques to recognise this risk and avoid it have been developed, including improved techniques for performing capsular release, modification of instruments and implants to access the femoral canal with the greater trochanter in the way and increasing use of cement in appropriate cases such as osteoporotic elderly patients for the femoral component.

4.6.5 Infection

Data on infection are limited as rare complications require a large study population to provide

sufficient power for statistical and clinical significance. Randomised controlled trials have thus not demonstrated significant differences in rates of infection [54, 61, 76, 77].

Registries have the advantage of large numbers to detect differences in less common complications but are prone to bias, particularly selection bias. Australian registry data [41] shows the anterior approach has a lower reported revision rate for infection than the posterior or direct lateral approaches in the first 3 months ($p < 0.001$). However, some surgeons avoid the use of the direct anterior approach in morbidly obese patients, who are also significantly more likely to experience infections [78, 79]. Alternate theories to explain the lower reported revision rate include that the anterior approach is generally performed through a smaller incision with less associated soft tissue trauma, and the foot does not generally need to be held near the assistant's face—unlike with the posterior approach. Larger randomised controlled trials are required to properly answer this question.

4.6.6 Dislocation

The risk of dislocation after PA THA is reported to be higher than after other approaches [7, 80, 81], but can be mitigated somewhat with attention to capsular repair [6, 82–84]. Registry data [73] and other published series [18, 21, 85–87] have quoted lower dislocation rates for the AA than PA. Whilst the posterior soft tissue compromise using the PA is a contributing factor to its higher dislocation rate, we note that the technique for implanting a THA via the AA also permits intraoperative fluoroscopy, which could explain higher levels of compliance with Lewinnek's "safe zone" [88] in THA performed via the AA. Furthermore, when performing a PA THR, there is a tendency for the pelvis to drift anteriorly by approximately 15° [89] due to the anteriorly placed retractor. This can result in a distortion of the intraoperative planes of reference for the surgeon, resulting in the placement of the acetabular cup in a relatively retroverted position [90].

4.6.7 Nerve Palsy

Patients undergoing total hip arthroplasty via the AA have noticeably higher levels of neuropraxia [91] than other approaches, owing to frequent injury of the lateral femoral cutaneous nerve of the thigh, with a reported incidence ranging from 3.37 to 81.00% [92]. Symptoms may persist even after 5 years, though it is unlikely to result in a functional compromise [93, 94]. The reported incidence of injury to the far more clinically important femoral nerve is anywhere from 0.26 to 5.00% [92]. By contrast, patients receiving a THA via the posterior approach are exposed to a much lower incidence of neurological injury, but a sciatic nerve palsy is a substantially more clinically important complication due to its extensive motor function in contrast to the minor, purely sensory role of the lateral femoral cutaneous nerve. Sciatic nerve palsy after PA THA has a reported incidence between 0.1 and 0.6% [92].

4.7 Complex and Revision Total Hip Arthroplasty

There are currently a number of surgeons who employ a direct anterior approach for their primary hip arthroplasties but will not utilise it for complex or revision procedures. The AA permits adequate exposure of the acetabulum for primary and even some revision procedures but the femoral component can prove more technically demanding. Delivering the femur into the operative field, particularly to permit passage of a long femoral stem, is made more difficult by the natural anterior bow of the femur. Methods to permit this include the use of a traction table or utilising the extensions of the approach proximally or distally. Revision arthroplasty via the AA is thus currently the preserve of a smaller group of surgeons experienced in the anterior approach [95]. Patients who are muscular, obese, have varus femoral necks or protrusio acetabuli are considered by some surgeons to represent more difficult patients on whom to perform an AA THR and are commonly avoided by surgeons learning the AA.

4.8 Hip Approaches for Indications Other Than Arthroplasty

When performing hip washouts for septic arthritis the preservation of the blood supply of the femoral head is a key consideration that is not relevant when performing THA. For this reason, femoral head blood supply sparing approaches such as the AA or Watson-Jones (anterolateral) intervals are commonly utilised. The vascularity of the femoral head is predominantly via the medial femoral circumflex artery (MFCA), which is directly at risk when performing a PA. Furthermore, the sciatic nerve is at greater risk performing a septic hip drainage via a posterior approach than when performing THA as the external rotators are detached during arthroplasty and reflected, thus protecting the nerve. By contrast, the external rotator muscles and hence sciatic nerve are on tension when performing a septic hip washout in order to prevent damage to the trochanteric anastomosis.

Subcapital femoral fractures in young patients should ideally be anatomically reduced in order to preserve the femoral head blood supply, promote bony union, and prevent avascular necrosis and the need for hip arthroplasty. The Watson-Jones approach permits fracture reduction and internal fixation through a single long incision. The alternative option is to utilise the AA to obtain anatomical reduction and then perform internal fixation via a separate direct lateral approach. An anatomical dissection of cadavers [96] found that a larger area of the femoral neck was demonstrated via the AA than utilising the Watson-Jones approach. The PA is not appropriate as it provides an inadequate view and compromises the blood supply to the femoral head via the MFCA.

4.9 Conclusion

The recent growth in the utilisation of AA for THA described in international registries [40, 41, 49] is driven by patient, surgeon, and system factors. The AA offers the potential for less postoperative pain [54], faster functional recovery [56–58], and lower dislocation rates [7, 80, 81] with similar implant longevity [72, 73] to the PA or LA. However, the learning curve [68] required to reduce the risks of elevated rates of periprosthetic fracture [73, 75], aseptic loosening [73], and difficulty with exposure in more challenging cases requires a commitment to appropriate training that is not universally available and sometimes impractical for a surgeon already appropriately trained in an alternative approach. For many surgeons already trained in the PA or LA, their technique is the safest way for them to offer patients "the operation of the century" [50], a procedure that can reliably improve a patient's quality of life and mobility in most cases. The posterior approach offers such a degree of versatility and exposure that many surgeons who prefer the AA for certain indications including routine primary arthroplasty will still need to maintain the PA as part of their skillset for some complex cases. For training surgeons, it is worth developing competency in the AA for the potential benefits it offers in rapid recovery after routine primary arthroplasty, fracture management, and drainage of sepsis.

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5 Osteonecrosis of the Femoral Head: Core Decompression or Total Hip Arthroplasty?

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5.1 Introduction

Atraumatic osteonecrosis of the femoral head (ONFH) is a progressive and disabling condition that mainly affects male patients in the third to fifth decade of life. ONFH is characterized by bone cell death as a consequence of an impairment of the vascular supply to the subchondral bone. It usually leads to collapse of the load-bearing segment of the hip joint followed by degenerative osteoarthritis. Epidemiological data have reported that 300,000–600,000 people have ONFH in the USA, with an annual incidence between 10,000 and 20,000 cases [1, 2]. ONFH has been estimated to be the underlying diagnosis for 3–12% of total hip arthroplasties (THA) [2]. Compared with patients with osteoarthritis, those with ONFH showed increased risk of revision surgery [3, 4].

5.2 Basic Science

The mechanisms involved in the pathogenesis and progression of ONFH remain to be fully elucidated. ONFH is often diagnosed late and bone samples are not readily accessible to sampling. The sequence of events occurring in the pathophysiology of ONFH has been constructed by image observations, bone biopsies obtained from patients undergoing THA, and animal models. There is a general consensus on the potential mechanism of ONFH initiation that is local ischemia following an alteration of the blood supply to the subchondral bone. The timing as to when ischemia starts is difficult to know, as once the disease clinically appears it has usually been silent for a long period. There are three main mechanisms by which blood flow of femoral head could be impaired that are vascular interruption by trauma, intravascular occlusion by thrombi or emboli fat, and intraosseous extravascular compression [5].

It is well accepted that the main histologic signs indicative of osteonecrosis are empty osteocytic lacunae and bone marrow edema [6, 7]. Experimental studies suggest that marrow and osteocyte death appear approximately within 24–72 h after oxygen deprivation [8, 9]. Bone necrosis induces a reparative process characterized by reactive hyperemia and areas of revascularization. With the entry of blood vessels, a repair process begins consisting of coupled bone resorption and formation. In the subchondral bone, the repair process appears to be self-limited, and bone resorption tends to be uncompensated by bone formation thereby leading to loss of structural integrity of trabeculae [6]. The presumed mechanism of mechanical failure of the femoral head is accumulated stress fractures

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at the junction between the reparative zone and the necrotic bone [10]. There is evidence that weakening of bone structure with formation of microfractures is part of the osteonecrotic process (Fig. 5.1). Histological studies in femoral heads from patients with ONFH revealed that necrotic bone has lower mineral density than normal adjacent bone, together with disrupted trabeculae as well as microfractures and small regions of bone resorption [11]. In addition, biophysical and ultrastructural analysis of necrotic areas showed increased remodeling, loss of osteocytes, and calcified marrow [12].

Coagulation disorders have been associated with the development of non-traumatic ONFH. ONFH frequently occurs in sickle cell disease, in which loss of membrane deformability in red blood cells leads to intravascular obstruction, hypoxia, and inflammation [13]. ONFH associated with sickle cell disease has been reported in 11–37% of cases in prospective and cross-sectional studies [14]. Symptomatic ONFH in patients with sickle cell disease has a high probability of leading to femoral head collapse [15]. Thrombi formation related to other hemoglobinopathies and hemolytic disorders has also been associated with increased risk of ONFH. Epidemiological studies indicate that the two major risk factors of non-traumatic ONFH are massive corticosteroid administration and excessive alcohol intake. A multicenter case-control study reported that patients receiving corticosteroids have an approximately 20-fold increase in their probability of developing ONFH than patients who were not exposed to these drugs [16]. In addition, ONFH development has been associated with corticosteroid dosing and treatment duration [17, 18]. Similarly, there seems to be a dose-dependent relationship between alcohol intake and ONFH [19].

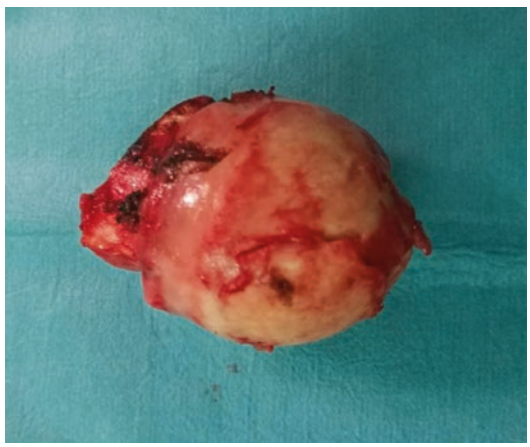

Fig. 5.1 Osteonecrosis of the femoral head during total hip arthroplasty. Subchondral fracture can be noted

Intraosseous extravascular compression has also been postulated as the ONFH pathogenic mechanism in other etiologies, including alcohol abuse, marrow packing disease (Gaucher disease), and dysbaric osteonecrosis [20, 21]. Further pathogenic mechanisms of corticosteroid-induced ONFH include alteration in the physiology of bone cells and progenitors [22]. In this regard, various studies in bone biopsies from patients with ONFH suggest that corticosteroids may have adverse effects on bone by decreasing the number of mesenchymal stem cells (MSCs) in the proximal femur [23] and the replicative capacity of osteoblasts in the intertrochanteric region [24]. In addition, MSCs isolated from patients with corticosteroid-induced ONFH showed lower ability to differentiate toward the osteoblastic lineage than MSC isolated from patients with no ONFH history [25]. The decreased MSCs osteogenic potential may be a reason why patients with corticosteroid-induced ONFH treated with autologous MSCs infusion often fail regenerative treatment strategies. Others authors have focused attention on the effects of corticosteroids on osteocyte viability and function. Abundant apoptotic osteocytes were found juxtaposed to the subchondral fracture crescent in femurs from patients with ONFH associated with corticosteroid therapy, whereas apoptotic bone cells were rarely found in bone specimens from patients with trauma, sickle cell disease, or alcohol abuse [26]. The adverse effects of glucocorticoids on osteocyte function were evident from a series of experiments in mice, which showed impaired perilacunar remodeling associated with subchondral bone degeneration [27]. It should be noticed that a large number of ONFH cases do not have any evident etiologic factor and are reported as idiopathic

[28, 29]. In the last years, several studies have investigated whether there is a genetic susceptibility to ONFH. Indeed, polymorphisms in genes related to coagulation, angiogenesis, hypoxia, bone remodeling, and inflammation have been related to ONFH development [30–34].

5.3 Diagnosis and Imaging

The etiology of ONFH is still largely unknown and appears to be multifactorial [35, 36]. Atraumatic ONFH is a pathology that produces osseus cells death because of the microvascular compromise by different causes as previously mentioned. A careful clinical questionnaire must be done in order to identify risk factors (glucocorticoid therapy, alcohol intake, hematologic conditions like sickle cell disease, myeloproliferative disorders, hemophilia, hypercoagulability states due to genetic disorders such as protein C/S deficiency or Factor V Leyden, HIV, or other autoimmune diseases such as Gaucher disease or Caisson diseases). Nevertheless, genetic susceptibility, particularly important in patients with corticosteroid therapies, and excessive alcohol intake, and the combination of different drugs associated with other co-morbidities can difficult clinical suspicion.

ONFH diagnosis must be established based on imaging tests after clinical suspicion. Typically, the patient reports groin pain irradiated to the buttock or knee. This pain can have an insidious or sudden onset. The physical examination usually shows a limited internal rotation of the affected hip creating pain.

Plain anteroposterior and lateral hip radiography is the first imaging test that must be performed once clinical suspicion is established. ONFH early stages may not be visible on plain radiographs, and can be reported as normal; in these patients Magnetic Resonance Imaging (MRI) should be prescribed in order to detect the disease. Computed tomography can be also useful to differentiate other lesion such as tumors.

Currently, there are many ONFH classification systems. The Ficat and Arlet classification is probably the most frequently used. Described in the early 60s, it has the advantage of being useful in daily clinical practice due to its simplicity. However, this classification does not include relevant factors determining the prediction of collapse such as the location and size of the necrotic lesion. In the 1980s, Steinberg classification added two more stages to Ficat's classification. This system subdivides each section according to the percentage of the femoral head affected in A, B, and C (<15%, 15–30%, >30%). At the end of this decade, another classification system was proposed, the Japanese Investigation Committee (JIC), considered the location of the necrotic lesion according to the degree of involvement of weight-bearing area. Other authors did also report other parameters in order to predict treatment as proposed by Kerboull et al. by measuring the combined necrotic angle area [37]; or Ha et al. describing two groups of collapse risk by measuring the combined necrotic angle over MRI images: <190° low collapse risk, >240° high collapse risk (5 years ahead) [38]. In the early 1990s, ARCO (Association Research Circulation Osseus) reported five stages considering the percentage of femoral head affected, the location of the lesion, and the extension of collapse (Table 5.1).

Nowadays, there is a lack of consensus about the ideal classification system in daily clinical practice (Fig. 5.2). In a comparative study between Steinberg, Kerboull and JIC classification systems, it was found that Japanese system has a higher inter- and intraobserver reliability and greater efficacy, especially in initial stages [39]. A relationship between the types of lesions and collapse risk has established according to JIC: Type A—0% collapse and Type C2—84.8% collapse. These outcomes are very important for making decisions about conservative or surgical treatment options. The greater weight-bearing surface involved, the higher risk of collapse. Moreover, ARCO developed in 2017 a task force group that used Delphi method (the data obtained from experts after participate in multiple round questionnaire) to generate a consensus for the glucocorticoid associated ONFH classification [40]. In the same way, another consensus was reported for the alcohol associated ONFH [41].

Table 5.1 Osteonecrosis of the femoral head: different classification systems

	Stage 0	Stage I	Stage II	Stage III	Stage IV	Stage V	Stage VI
Ficat and Arlet	Symptoms: NONE	Symptoms: GROIN PAIN	Symptoms: PAIN, STIFFNESS	Symptoms: PAIN, STIFFNESS, THIGH	Symptoms: PAIN, LIMP	–	–
	Rx: NORMAL	Rx: NORMAL/ OSTEOPENIA	Rx: SCLEROSIS, SUBCHONDRAL CYSTS	PAIN	Rx: SEVERE DEGENERATIVE JOINT DISEASE		
	MRI, CT: NORMAL	MRI, CT, histology: POSITIVE FINDINGS	MRI, CT, histology: POSITIVE FINDINGS	Rx: CRESCENT SIGN, COLLAPSE	MRI, CT, histology: POSITIVE FINDINGS		
	Histology: POSITIVE FINDINGS			MRI, CT, histology: POSITIVE FINDINGS			
Steinberg	Symptoms: NONE	Symptoms: GROIN PAIN	Symptoms: PAIN, STIFFNESS	Symptoms: PAIN, STIFFNESS, THIGH	Symptoms: PAIN, LIMP	Symptoms: PAIN, LIMP	Symptoms: PAIN, LIMP
Size	Rx: NORMAL	Rx: NORMAL	Rx: CYSTIC/ SCLEROTIC CHANGES	Rx: CRESCENT SIGN, COLLAPSE	Rx: ARTHRITIC CHANGES	Rx: JOINT SPACE NARROWING/ ACETABULAR CHANGES	Rx: SEVERE DEGENERATIVE CHANGES
–	MRI, CT: NORMAL	MRI, CT, histology:	MRI, CT, histology: POSITIVE FINDINGS A, B or C	MRI, CT, histology: POSITIVE FINDINGS A, B or C	MRI, CT, histology: POSITIVE FINDINGS. Millimeters depression.	MRI, CT, histology: POSTIVE FINDINGS Mild, Moderate, Severe	MRI, CT, histology: POSTIVE FINDINGS
–	Histology: POSITIVE FINDINGS	POSITIVE FINDINGS A, B or C					
–							

ARCO	Symptoms: NONE	Symptoms: GROIN PAIN	Symptoms: PAIN, STIFFNESS	Symptoms: PAIN, STIFNESS, THIGH	Symptoms: PAIN, LIMP		–
Size: % area involvement, Length of Crescent, % Surface collapse & Dome depression	Rx: NORMAL	Rx: NORMAL	Rx: SCLEROSIS, SUBCHONDRAL CYSTS	Rx: CRESCENTE SIGN, COLLAPSE	Rx: DEGENERATIVE CHANGES	–	
–	MRI, CT: NORMAL	MRI, CT, histology: POSITIVE FINDINGS	MRI, CT, histology: POSITIVE FINDINGS	MRI, CT, histology: POSITIVE FINDINGS	MRI, CT, histology: POSITIVE FINDINGS		
–	Histology: POSITIVE FINDINGS						
–							
Location							
–							
–							
–							
JIC	Type A	Type B	Type C1	Type C2	–	–	–
Location	Medial one-third or less weight-bearing area	Medial two-thirds or less weight-bearing area	More medial two-thirds weight-bearing area	More two-third weight-bearing area extend laterally acetabular edge			

Rx Conventional radiographs, *MRI* Magnetic resonance imaging, *CT* Computed tomography, *ARCO* Association Research Circulation Osseous, *JIC* Japanese Investigation Committee

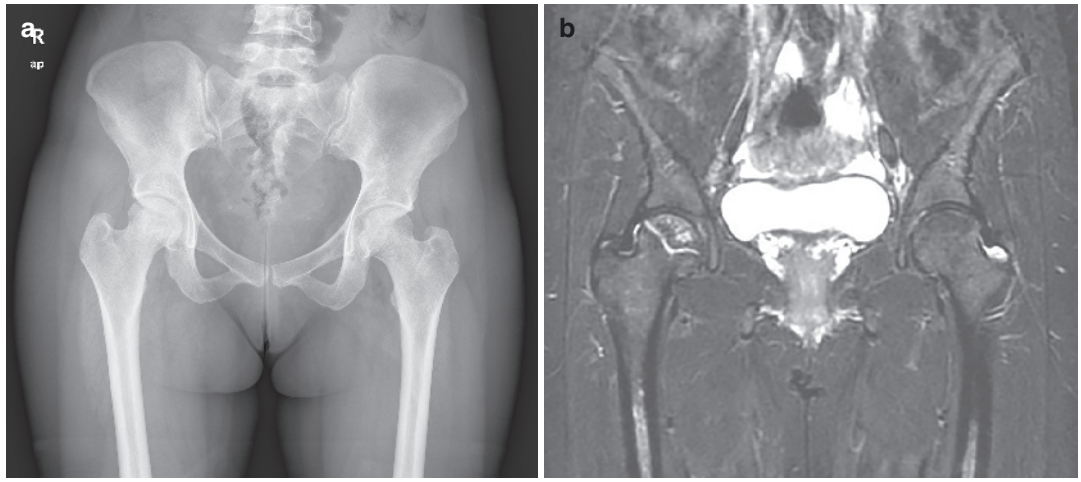

Fig. 5.2 (**a**) Radiograph and (**b**) MRI of a right hip showing osteonecrosis of the femoral head in a pre-collapsed stage

5.4 Core Decompression in Osteonecrosis of the Femoral Head

Despite weight-bearing restrictions having been recommended for early stages of femoral head ONFH, there are no real benefits when evaluating the progression of the disease [42]. In the same way, other non-surgical treatments including different pharmacological agents responding to the pathophysiology of the disease, like statins, enoxaparin, prostaglandin analogues, or bisphosphonates, have not shown substantial evidence [43–45]. Other studies with treatments like hyperbaric oxygen or extracorporeal therapy have also given inconclusive results [46, 47]. Since evidence does not support non-surgical treatment as a regular basis for ONFH management, it is critical to identify which patients are candidates for any so-called hip preserving surgery. In hips with a pre-collapse lesion core decompression (CD) is a reliable procedure, despite several important factors that may influence outcome.

Hungerford in 1979 and Ficat in 1985 reported good clinical results after CD for ONFH in early stages [48, 49]. This surgical procedure attempts to promote neovascularization by decreasing intraosseous pressure and, subsequently, increasing blood flow to the necrotic area. The original technique used a trephine introduced through the lateral cortex of the proximal femur into the subchondral bone of the femoral head. It also allowed the surgeon to obtain a biopsy to confirm the diagnosis. During those years, before MRI, the procedure was recommended for femoral head ON in stages I or II, but, after some years, other authors reported inferior results. Furthermore, there was an apparently poor correlation between intraosseous pressure and complications such as femoral proximal fractures associated with the procedure [50]. Thus, Learmonth et al. [51] found that 3 out 12 hips with ONFH staged I actually showed no histological evidence, and 26 of 29 staged II hips did not either. These authors also reported clinical and radiological progression in most cases, not only in stage II but in hips staged I, and a 44% THA conversion rate. They also emphasized that a single breach into the avascular segment would hardly promote neovascularization and confirmed, after sending femoral heads for histological analysis during THA, that the cores were filled with relatively fibrous avascular tissue; consequently concluding that once avascular necrosis is stabilized it is irreversible. In the same way, the results of early prospective randomized trials were also quite contradictory [52, 53]. Bozic et al. found in a long-term study with a mean follow-up of 10 years that patients with a Steinberg stage IIB showing cyst on the radiograph had symptoms for

less time and a worse result in corticosteroid-induced ONFH [54].

Further investigations and clinical studies assessing outcome in patients undergoing CD for early stage ONFH did not provide significant evidence to establish a general consensus. The introduction of MRI allowed a better understanding of the disease. Both femoral head lesion size and its location around the weight-bearing area were considered the most important prognostic factors [55]. Moreover, ONFH diagnosis, continued steroids intake, and other factors were also considered to be more frequently associated with a worse outcome. Level 1 evidence studies were already undertaken. The National Osteonecrosis Trial in Sickle Cell Anemia was designed as a prospective multicenter study and included 32 different institutions [56]. The trial compared 17 patients who underwent CD and physical therapy to 21 with physical therapy only during 6 weeks. After 3 years, the probability of not having complications or a re-operation was similar in both groups.

Steinberg et al. evaluated CD with a supplemental cancellous bone graft [57]. Bone was removed from the periphery of the lesion and patients were allowed to walk with partial weight bearing for 3 weeks. In a series of 406 hips in 285 patients, they found satisfactory results particularly in ONFH at early stages with small lesions. Other options such as impaction bone grafting or a composite bone graft substitute made of calcium sulfate-calcium phosphate after removal of the necrotic area of the femoral head provided good results, particularly in young patients [58].

Hernigou et al. pioneered the use of CD and percutaneous MSCs injection obtained from bone marrow concentration [59]. Ganji et al. also reported a slow collapse progression in 24 hips in a pilot study [60]. Patients with greater numbers of progenitor cells transplanted into their hips had better outcomes. In another comparative study, Yamasaki et al. evaluated 30 hips with CD and a porous hydroxyapatite cylinder with a MSC concentrate compared to control group of 9 hips without MSCs [61]. They found a reduction in the osteonecrotic lesion in the group with cells, in which only three progressed to collapse, in contrast to most of the patients in the control group showing collapse.

Basic research reported important factors associated with the success of the procedure [62]. The viability of the femoral head supplied with MSCs aspirated from the iliac crest depends on harvesting, processing, and injecting (Fig. 5.3). There is a high variability in terms of MSCs growth rates, no correlation between age or gender, or bone-specific gene induction [63]. It is important to know that each aspiration will be different from others obtaining different MSCs volumes and it is possible to aspirate from small peripheral vessels that will have lower cell concentrations (CFUs = colony forming units) [64]. Furthermore, the cell count, progenitor cell con-

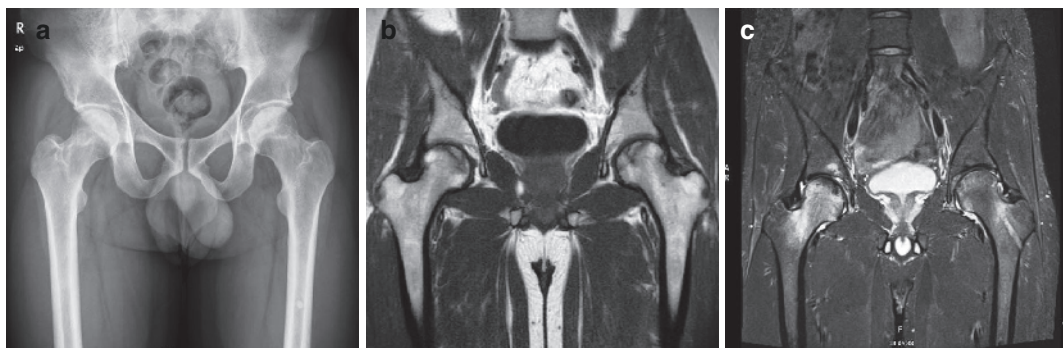

Fig. 5.3 (**a**) Radiographs showing a hip in a 34-year-old male patient after core decompression with injection of autologous bone-marrow cells, (**b**) Pre-operative MRI, (**c**) post-operative MRI 6 months after surgery

centration (colonies/mL marrow), and progenitor cell frequency (per million nucleated cells) obtained from bone marrow aspirates are also associated with syringe type [65].

Despite promising results for CD and an MSCs injection obtained from iliac crest being a standard procedure, there is a lack of well conducted randomized controlled trials: Hazeur et al. reported poor results in stage III ONFH in 19 patients for CD with or without implantation of autologous bone marrow aspirate concentrate [66]; the same group has recently reported no benefits after CD with osteoblastic cells over bone marrow aspirate in 56 patients with stage I or II, however, the overall results were better than in stage III [67]. An interesting matched pair case-control study including 100 patients with similar ONFH etiologies and stages I, II, and III showed better results for CD with bone marrow concentrate than CD alone. ONFH progression was similar in both groups although the 10-year survival for THA conversion, particularly after 3 years, and at stages I or II [68]. CD with bone marrow aspirate concentration may be beneficial in stage I or II ONFH of the femoral head, nevertheless, the technique must be carefully addressed and the patients should be informed that this procedure may not change disease progression. Based on patients treated in our institution, we have not been able to identify any benefit in preventing femoral head collapse resulting from the use of a standard bone marrow concentration injection combined with CD [69]. Our results confirm that the number of progenitor cells injected should be monitored in order to improve outcome. Long-term results are lacking, although Tomaru et al. have recently reported a 34% higher overall THA conversion rate that was higher in patients with higher bone mass index and ONFH stage III or IV (49% vs 14% in ONFH stages I or II) [70].

Recently advances in cell therapies are worth mentioning. New cell based technologies to promote bone healing such as aspirated bone marrow using concentrates are beneficial, however, the quantity of injected mononuclear cells, MSCs, purity, and lack of knowledge regarding the effect of different blood factors makes this procedure technique-dependent [71]. Although culture expansion of cells ex vivo is more complex than centrifugation, this method can generate millions of cells in contrast to the thousands obtained from a conventional aspirate [72]. Expanded MSCs properties in bone regeneration are promising: however, basic research, proper regulation, preclinical studies, and randomized trials are all necessary before these techniques can be generally introduced [73]. After two decades of many studies reporting well design research, there are still important issues to clarify such as the number of cells per injection, a sample quality, or ONFH etiology [74].

5.5 Total Hip Arthroplasty in Osteonecrosis of the Femoral Head

ONFH is the most frequent etiology in young patients undergoing THA [75]. Although the number of conservative and surgical treatments trying to preserve the native joints is very high, a post-collapse stage II or IV usually determines the success of these procedures and THA is usually inevitable [76]. Early reports showed poor results for THA in patients with femoral head ONFH compared to primary degenerative osteoarthritis [77]. Different factors were associated with THA failure such as ONFH etiology, a young age, weight, physical activity, bone quality, implant fixation, and bearing surface. Cemented fixation has been widely used providing very good long-term results, but, polyethylene wear and the possibility of late aseptic loosening in this young population leaded to use cementless fixation and alternative bearing surfaces [78].

During last decade, most surgeons would probably implant a cementless THA. The first studies reporting good results in terms of bone fixation in this population were confirmed by

others using different implants [76]. On the acetabular side hemispherical with different radii and coated surfaces can provide satisfactory fixation [79, 80]. On the femoral side similar findings are being reported with different designs [81, 82].

Overall, once cemented and cementless fixation have been shown to provide excellent long-term results, the most important cause for THA failure remains wear. The older polyethylenes are no longer used. Highly cross linked polyethylenes and ceramic bearings have dramatically changed this controversial issue regarding THA in young patients. Recently, a study from the Mayo Clinic reported excellent results in patients undergoing cementless THA with contemporary highly-cross linked polyethylene at a median follow-up of 10 years [4]. They matched 413 patients with ONFH to 427 patients with primary osteoarthritis and were able to identify still better results in the osteoarthritis group. They could detect that 15-year re-operation survival was related to ONFH etiology, but, they did not find consistent radiographic indications of loosening or osteolysis.

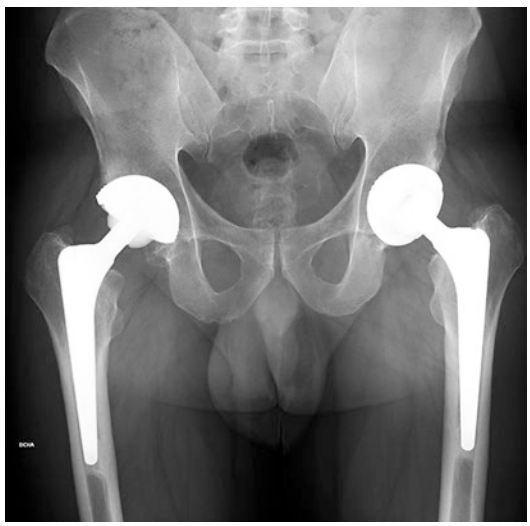

Fig. 5.4 Radiographs of a bilateral alumina-on-alumina uncemented total hip arthroplasty in a 39-year-old male patient 14 years after surgery

Ceramics have also confirmed their theoretical advantages in terms of preventing osteolysis (Fig. 5.4). A study from Lariboisiere also reported excellent results in young ONFH patients [83]. In a series of 41 patients they reported excellent results in terms of osteolysis with the use of different acetabular components and a cemented stem. The most important problem here was cup fixation. Our institution has confirmed these results in terms of wear-related complications also with cementless stems [75]. In that study we could not identify any failure in patients diagnosed with ONFH. Like the Nich et al. original report, newer acetabular components can improve results in these patients [84].

5.6 Osteonecrosis of the Femoral Head: Core Decompression or Total Hip Arthroplasty?

After reviewing the evolution of CD through last decades, there are still many controversies. First, the orthopedic surgeon has to clearly diagnose and stage of ONFH. This is probably the most difficult issue since clinical diagnosis must be suspected. Hip pain is sometimes difficult to evaluate, so a complete clinical record with a physical examination is mandatory. Conventional radiographs need a careful assessment in order to correlate symptoms; this step may misdiagnosed ONFH. If a collapsed hip can be found in conventional radiographs, it is better to perform THA. If not, MRI can differentiate, i.e., transient osteoporosis, and define ONFH, so CD combined with implantation of autologous bone marrow cells can be considered when available and surgically predictable. For small asymptomatic lesions without associated risk factors, clinical observation can be recommended; moreover, clinical deterioration can be detected and CD performed (Fig. 5.5). Nevertheless, current THA can offer excellent long-term outcomes in young in most cases, so unless a small-moderate lesion can be defined on imaging THA should be performed.

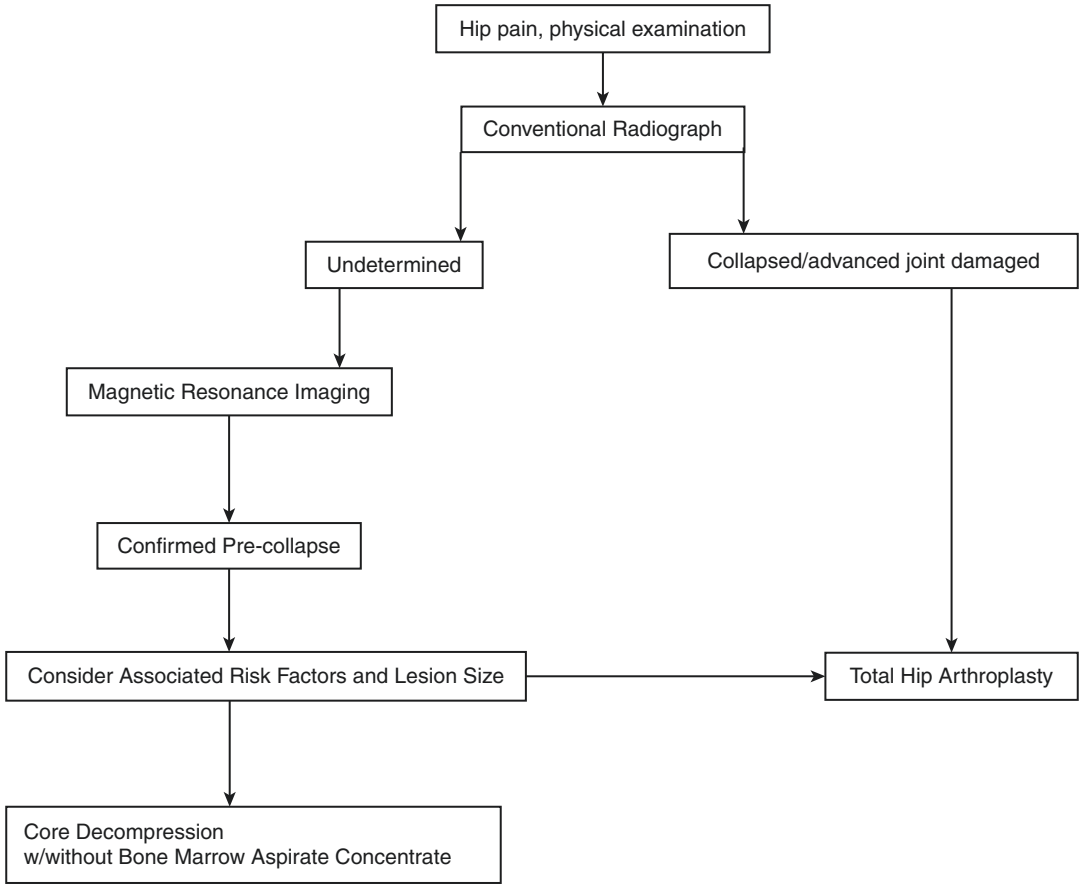

Fig. 5.5 Algorithm decision for osteonecrosis of the femoral head management

5.7 Conclusion

Most frequent diagnosis in patients undergoing THA under the age of 55 years is ONFH. Despite basic research has attempted to clarify many issues related to this condition, there are still many questions to answer. Annual incidence in many countries is to rise and there are factors associated that are difficult to evaluate. Although some co-morbidities and drugs are strongly correlated such as corticosteroids and some particular conditions as sickle cell disease, there is a great number of patients suffering from this pathology without a known cause. After a clinical suspicion of ONFH, a clear description of the stage of the disease is critical in order to recommend the best management. Recent investigations have reported advances in imaging and classifications. Furthermore, basic and clinical research on MSCs are reporting promising results for hips in a pre-collapsed stage undergoing core decompression. Nevertheless, many patients would require a THA. After introducing newer bearing surfaces such as highly cross linked polyethylene and ceramics during last years, many clinical reports have confirmed excellent results at a long-term.

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6 Controversies on the Surgical Treatment of Cartilage Defects of the Knee

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6.1 Introduction

Defects in the knee cartilage are common and can cause significant pain and morbidity. Cartilage injuries commonly being found in approximately 60% of knee arthroscopies [1–3]. In addition to symptoms they produce directly, chondral defects produce increased contact stresses on the intact cartilage adjacent to the injury [4–6]. If left untreated, cartilage defects can lead to progressive cartilage degeneration and ultimately early osteoarthritis [7].

The current management of chondral defects is controversial and various surgical techniques have been used. In this chapter we review the current therapeutic options for the treatment of osteochondral knee defects.

6.2 Arthroscopic Debridement

Weissenberger et al. studied whether or not debridement was beneficial in isolated focal chondral defects, and whether or not performing a partial meniscectomy influenced the results [8]. They analyzed 126 patients, with a follow-up of 12 months, from the German Cartilage Registry. They created four subgroups according to the size of the cartilage defect and the presence of meniscal pathology: "debridement-only <2 cm^2," "debridement-only >2 cm^2," "debridement and partial meniscus resection <2 cm^2," and "debridement and partial meniscus resection >2 cm^2." They concluded that arthroscopic debridement for focal lesions of knee cartilage could, in general, be beneficial (regardless of size), in terms of functional outcome (WOMAC—Western Ontario and McMaster Universities Osteoarthritis Index). However, in patients with large cartilage defects (>2 cm^2) and associated meniscal pathology, the improvement was small. While WOMAC scores improved, there was no significant improvement in the numerical rating scale for pain [8].

6.3 Microfracture (MFX) (Fig. 6.1)

Orth et al. conducted a systematic review of MFX treatment of articular cartilage defects of the knee (level IV evidence) [9]. They found that MFX treatment of full-thickness (3.4 cm^2) articular cartilage defects was generally performed late (43.4 months after onset of symptoms). Postoperative evaluation at 79.5 months revealed

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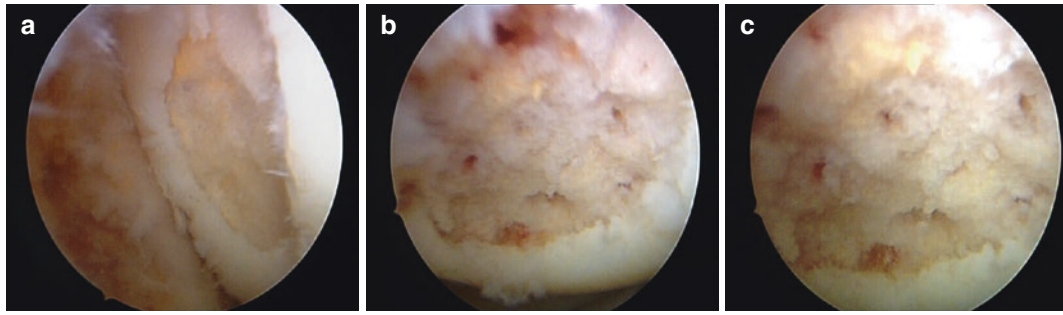


Fig. 6.1 (**a**–**c**) 42-year-old male with a degenerative chondral lesion in the lateral femoral condyle treated by arthroscopic microfractures: (**a**) Intraoperative image of the articular cartilage lesion; (**b**) appearance of the lesion after microfractures; (**c**) another image of the chondral lesion area after surgery

failure rates of 11–27% at 5 years and 6–32% at 10 years. Protocols, demographics, and defect size varied between studies; in many cases, the defect size was greater than 3 cm^2—which is where in modern practice other techniques such as autologous chondrocyte implantation (ACI) may be considered to be the gold standard. As such, they concluded that comparing the effectiveness of MFX to other techniques was not possible on the basis of the data included in the study [9].

Da Cunha et al. systematically analyzed the postoperative results of "enhanced MFX"—where the microfracture is augmented using an acellular collagen scaffold [10]. They examined single group studies, concluding that enhanced MFX techniques produce significant improvement in patient-reported outcomes, although imaging results were inconsistent. Their conclusion was that current clinical evidence does not allow unequivocal advice for enhanced MFX for the treatment of symptomatic Outerbridge grade III/IV focal lesions of the knee cartilage.

6.4 Mosaicplasty (Osteochondral Autograft Transplantation) (Figs. 6.2 and 6.3)

Kizaki et al. compared open versus arthroscopic mosaicplasty in a systematic review of the literature [11]. They compared clinical outcomes, postoperative complications, defect location, and defect size. The size of defects in open mosaicplasty was three times larger than arthroscopic mosaicplasty (2.96 versus 0.97 cm^2). Regarding the location of the defects, the medial femoral condyle (MFC) was the most commonly affected (75.4%), followed by the lateral femoral condyle (LFC; 12.1%), the patella (6.7%), and the femoral trochlea (5.7%). Open mosaicplasty was performed at any location of the defect, while arthroscopic mosaicplasty was performed only on MFC and LFC lesions. There were 53 postoperative complications (39/279 in open mosaicplasty vs. 14/594 in arthroscopic mosaicplasty). The most frequent complication was hemarthrosis (13/39 in open mosaicplasty vs. 1/14 in arthroscopic mosaicplasty) [11].

According to Inderhaug et al., mosaicplasty is often used in large (>3 cm^2) articular cartilage lesions of the knee [12]. Patient selection is a key to a successful outcome; mosaicplasty should not be performed in patients with established osteoarthritis or systemic disorders such as rheumatoid arthritis. A 3-month rehabilitation program involving neuromuscular training should be attempted before mosaicplasty. The procedure can, in many cases, be performed arthroscopically. After an initial phase of non-weight bearing focused on regaining range of motion, a gradual increase in neuromuscular exercises is advisable. Patients are usually advised not to return to sports for at least 6 months after surgery. According to this study, the results of mosaicplasty showed that the pro-

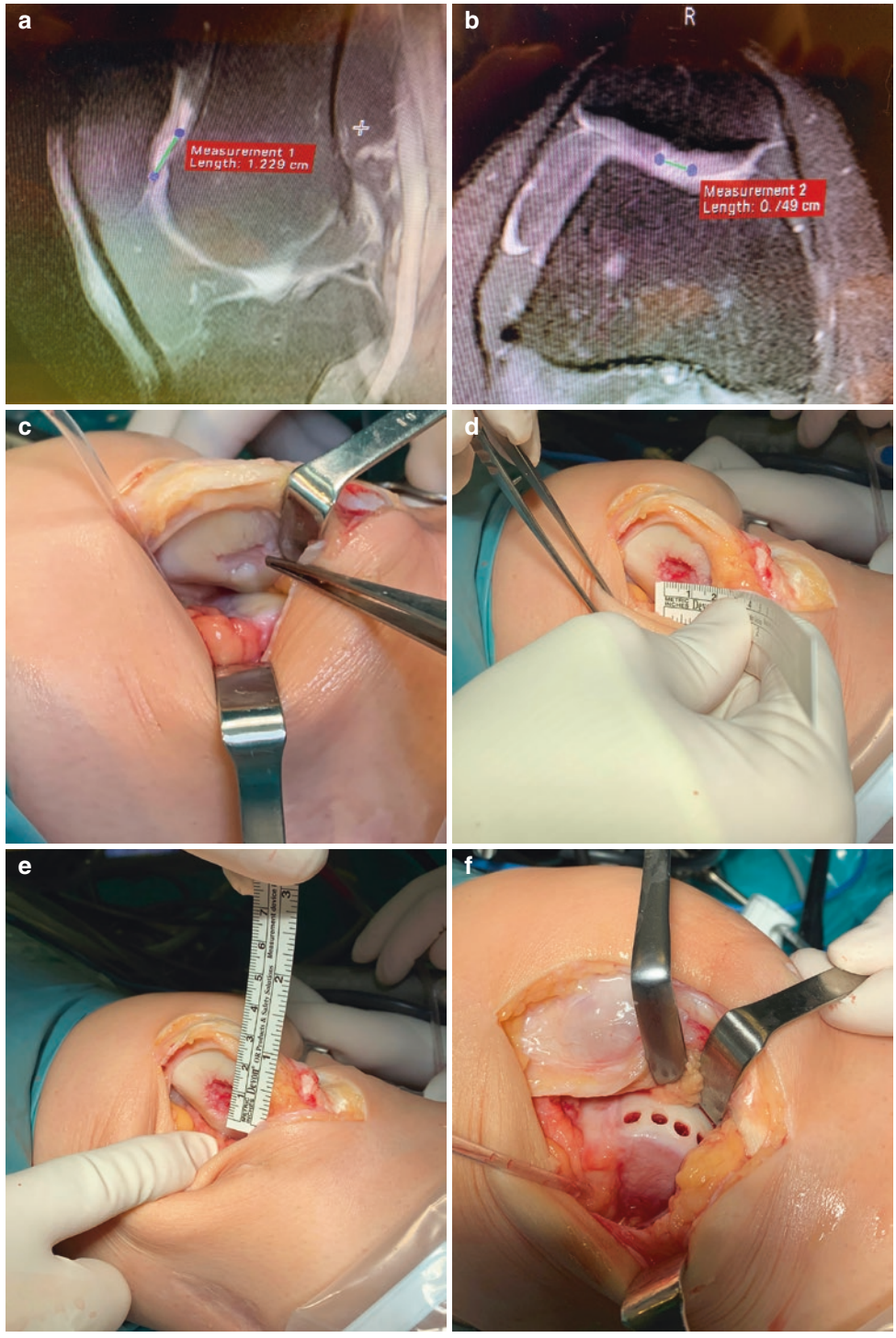
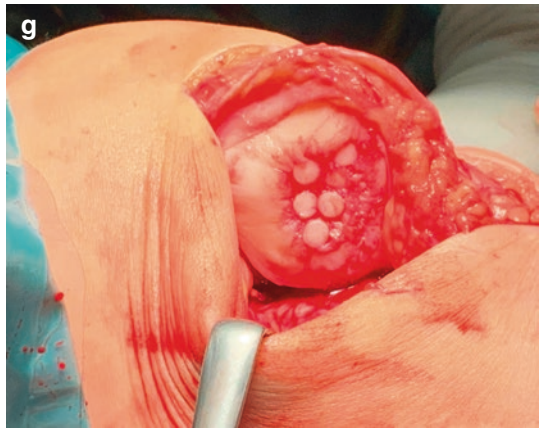


Fig. 6.2 (**a**–**h**) 37-year-old woman with anterior knee pain associated with patellofemoral instability. She did not improve with dextrorotatory upper tibial osteotomy. One year later a chondral lesion was detected in the patella. Then, open mosaicplasty (6 cylinders of 4.5 mm) was performed: (**a**) lateral MRI image showing the patellar lesion; (**b**) skyline MRI view of the affected area; (**c**) intraoperative image of the lesion; (**d**) measurement of the size of the affected area; (**e**) another image measuring the cartilage lesion; (**f**) image of the donor area (osteochondral autograft cylinders); (**g**) aspect of the affected area at the end of mosaicplasty; (**h**) another image showing the final result of the procedure



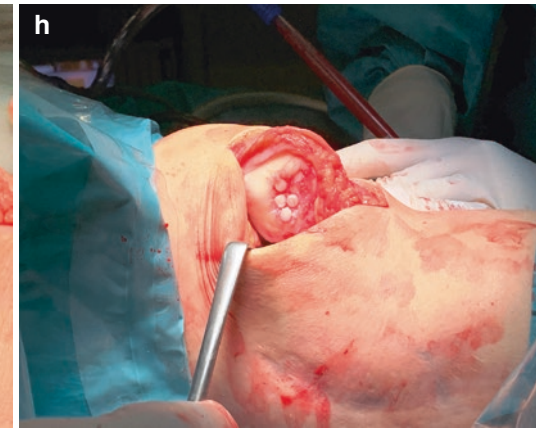


Fig. 6.2 (continued)

cedure improved subjective outcomes compared to baseline function, up to 10 years after surgery [12].

6.5 Osteochondral Allograft Cartilage Transplantation

Osteochondral allograft cartilage transplantation is a good option in large osteochondral defects or after the failure of other therapeutic options [13]. Fresh allografts are usually transplanted into the involved femoral condyle although they can also be used in the patella, tibial plateau, or femoral trochlea.

Melugin et al. analyzed the results of cryopreserved osteochondral allograft treatment of full-thickness cartilage defects of the patellofemoral compartment of the knee [14]. Nineteen patients were treated, with a mean age of 31 years (range 15–45 years), including 12 women and 7 men. The reoperation rate was 21.1% and two patients (12.5%) presented progressive patellofemoral osteoarthritis requiring conversion to patellofemoral arthroplasty. The conclusion was that at 2 years of follow-up, patients with unipolar cartilage defects of the patellofemoral compartment of the knee had good results after surgical treatment with cryopreserved osteochondral allograft. However, the rate of reoperation was high and bipolar cartilage lesions increased the failure rate [14].

6.6 Autologous Chondrocyte Implantation (ACI) (Fig. 6.4)

ACI has been in use for many years for chondral defects within the knee and has a large amount of evidence supporting its use. Its use is discouraged by cost, difficulties in culturing the cells necessary for ACI, and the need for two-stage procedures. This has led to the development of new variants of ACI which may overcome some of these hurdles.

6.6.1 Arthroscopic Gel-Type ACI

Yoon et al. investigated the clinical, radiological, and histological results of arthroscopic gel-type ACI in the treatment of chondral knee defects (level IV evidence study) [15]. This small, prospective study examined clinical, radiological, and histological outcome at 10 years in ten patients (male:female, 5:5) with a mean age of 40.3 years. The gel was composed of a mixture of 1 mL of fibrinogen plus 0.1–0.2 mL of thrombin. The mean size of the chondral defect was 2.9 cm^2 (range 1.2–5.4 cm^2). Small but in some cases statistically significant improvements were seen in WOMAC subscales, and complete filling of the defect was seen in all patients by 2 years. 8/10 patients had a second look arthroscopy and biopsy at 18 months, which demonstrated filling of the defect with hyaline-like cartilage. Therefore, arthroscopic gel-

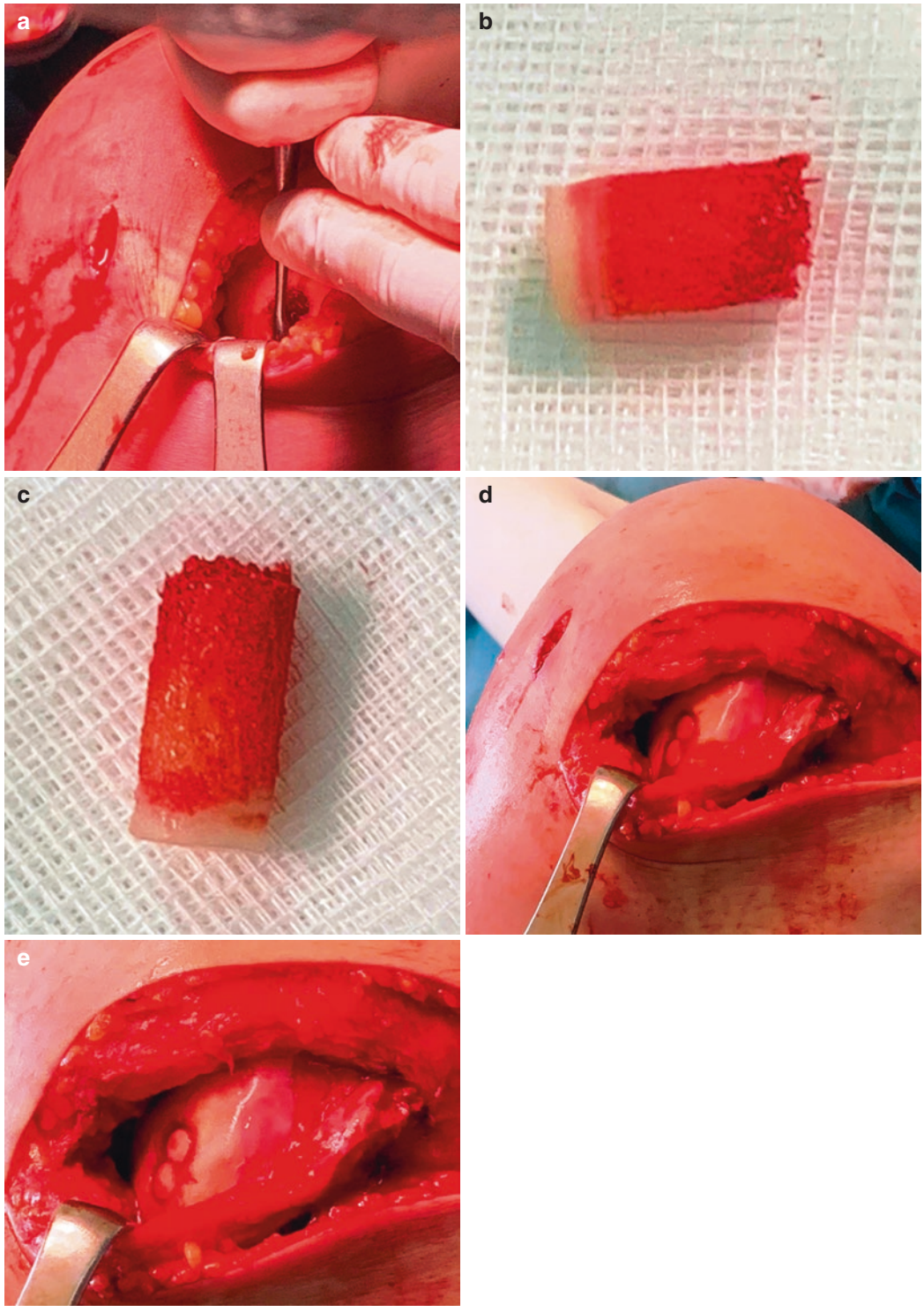


Fig. 6.3 (**a**–**e**) 38-year-old male with lateral femoral condyle lesion associated with posterior cruciate ligament (PCL) insufficiency and knee valgus deformity. A correcting osteotomy and a mosaicplasty with two 6 mm cylinders were performed: (**a**) Intraoperative image of the lesion; (**b**) first cylinder of osteochondral autograft obtained; (**c**) image of the second cylinder extracted; (**d**) aspect of the lesion at the end of mosaicplasty; (**e**) another image showing the final result of the procedure

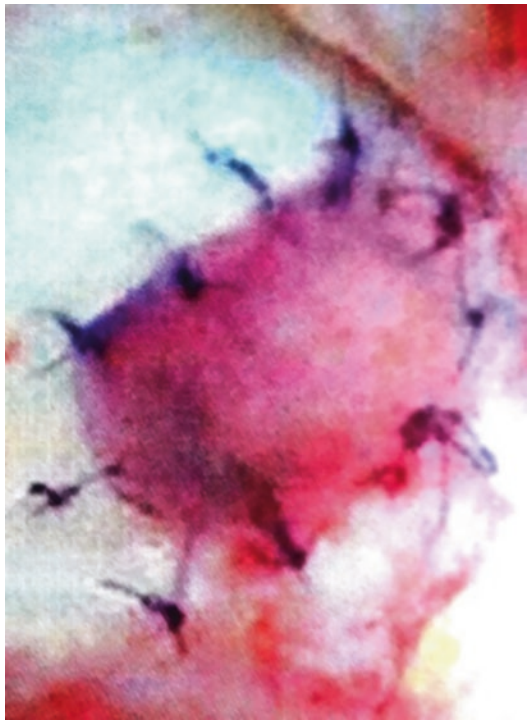


Fig. 6.4 First generation ACI (autologous chondrocyte implantation). Chondrocytes had to be covered by a periosteal patch

type ACI was considered an acceptable, minimally invasive and technically simple option for the restoration of knee cartilage defects [15].

6.6.2 Third-Generation ACI (Novocart) After Failed Bone Marrow Stimulation (BMS)

Müller et al. investigated the effect of prior bone marrow stimulation (BMS) on subsequent ACI therapy (level III evidence-based study) in 40 patients, with a follow-up of 3 years [16]. Twenty patients (group I) with knee cartilage defects were treated with third-generation ACI (Novocart® 3D) as first-line therapy. The mean size of the defect was 5.4 cm^2. The results of group I were compared with those of 20 patients paired with ACI as second line therapy (group II). Both groups showed significant improvements in IKDC (*International Knee Documentation Committee*) score but with greater improvements in the first-line group. No revisions were required in the primary group while 30% of the grafts failed in the patients who had previous bone marrow stimulation [16].

6.6.3 Costal Chondrocyte-Derived Pellet-Type ACI

Yoon et al., in a series of cases with level IV evidence, evaluated whether implantation of a chondrocyte-derived pellet-type (CCP) ACI (CCP-ACI) allowed safe, functional, and structural restoration of full-thickness cartilage defects of the knee [17]. The intention of this technique is to provide an easily accessible, more expandable source of chondrocytes than is available from the knee, with less potential for donor site morbidity. Seven patients with symptomatic full-thickness cartilage lesions were analyzed. Chondrocytes isolated from the patients' costal cartilage were expanded, and then a three-dimensional pellet culture was performed to prepare the CCP-ACI. Pellet implantation was performed by minimal arthrotomy, secured with a fibrin sealant. Both clinical scores (IKDC and Lysholm) and MRI (magnetic resonance imaging) appearances [MOCART (Magnetic Resonance Observation of Cartilage Repair Tissue) score] improved significantly to 5 years. The results of this first in human clinical study suggested that in the medium-term CCP-ACI was a promising therapeutic option for articular cartilage repair with good clinical results and good structural regeneration [17].

6.7 Matrix-Associated Chondrocyte Implantation (MACI) (Fig. 6.5)

6.7.1 MACI with Spheroid Technology

Chondrosphere (Spherox) MACI is a form of ACI where the cultured cells are enclosed within spheroids before implantation. Hoburg et al. compared chondrosphere ACI vs MFX in a prospective phase III clinical trial with patients ran-

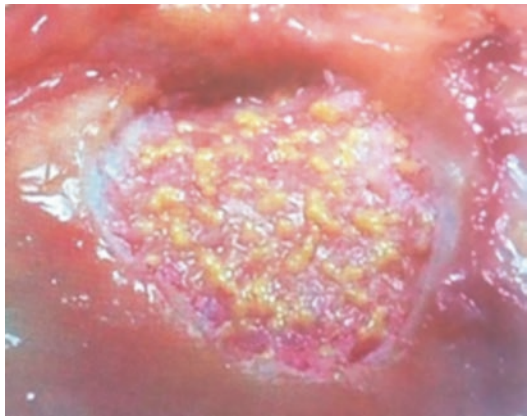


Fig. 6.5 MACI (matrix-associated chondrocyte implantation) with spheroid technology. Note the cartilage defect with the chondrospheres in place

domized to either the ACI ($N = 52$) or to MFX ($N = 50$) [18]. The trial was powered as a noninferiority study and achieved the aim of demonstrating that the chondrosphere ACI was not inferior to MFX; in fact, there were statistically significant differences favoring ACI in two of the KOOS (Knee Injury and Osteoarthritis Outcome Score) domains at 1 year. Four patients in the MFX group required reoperation, which was considered a treatment failure. There was no failure in the ACI group. Similar results were found in different age groups and chondral defect sizes [18]. The use of chondrosphere ACI was supported by this study compared to MFX; however, the question of whether it is superior or inferior to conventional ACI remains unanswered.

The same group investigated the effect of product dosing in MACI with spheroid technology for the treatment of full-thickness knee cartilage defects and evaluated its influence on clinical and morphological outcome in the medium term (grade I evidence study) [19]. Seventy-five patients were studied in a single-blind, randomized, prospective, controlled clinical trial. Patients were randomized to three different dose groups [low (3–7 spheroids/cm^2), medium (10–30 spheroids/cm^2), or high (40–70 spheroids/cm^2)]. All doses applied in this study led to significant long-term clinical improvement and were therefore considered to be effective doses. Thus, the recommended dose range was 10–70 spheroids/cm^2 [19].

6.8 Acellular Scaffolds

6.8.1 Potential Indications

Acellular scaffolds, which were developed for use as an alternative to periosteal patches in ACI, have the potential to serve as a mediator of cartilage repair when used without chondrocytes. Filardo et al. attempted to develop agreed guidelines for the use of scaffolds in chondral and osteochondral femoral condyle lesions [20]. The RAND/UCLA (RAM) method of fitting was used to develop patient-specific recommendations, combining the best available scientific evidence with the collective judgment of a group of experts guided by a central panel and multidisciplinary discussants. In common with other cartilage regeneration techniques, the use of scaffold-based procedures was considered appropriate in all cases of chondral or osteochondral injuries as long as the knee is not affected by osteoarthritis [20].

6.8.2 Cell-Free Scaffolds: Monotherapy

Kwan et al. published that cell-free scaffolds can aid in the regeneration of articular cartilage, thus having the potential to treat chondral defects [21]. They also stated there were very few studies on the subject and, despite the many biomaterials tested in cell-based scaffolds, most cell-free studies focused on a specific type I collagen scaffold. Therefore, according to Kwan et al., future clinical studies on cell-free scaffolds should adopt the modifications made to cell-based scaffolds. In addition, they stated that further studies would be needed to help us understand the underlying mechanism of cell-free scaffolds.

6.8.3 Synthetic Scaffold Plug

Shivji et al. have advised against the use of the TruFit™ plug (a synthetic biphasic polymer scaffold that is designed for implantation at the site of a focal chondral defect) [22]. They ana-

lyzed the long-term clinical and radiological results of six patients treated with TruFit™ plug in chondral knee defects, with a mean follow-up of 121 months. In all patients the incorporation of the plug was incomplete or absent, and persistent chondral loss was observed.

6.9 Mesenchymal Stem Cells (MSCs)

6.9.1 MSCs Implant

Kyriakidis et al. investigated the medium-term outcomes of a single-stage cell-based procedure in 25 patients with symptomatic focal knee cartilage defects using matrix-induced culture-expanded autologous adipose-derived (AD)-MSCs (level IV evidence study) [23]. Follow-up was 3 years and the mean age of patients was 30.5. The mean body mass index (BMI) was 23.6 kg/m^2, and the mean lesion size was 3.5 cm^2. Postoperative biopsies were performed in two patients, which demonstrated the presence of hyaline tissue. This study demonstrated that AD-MSCs are an efficient and safe procedure for symptomatic full-thickness chondral knee injuries. In the medium term all patients improved significantly from a clinical, functional, and radiological point of view [23].

Gobbi et al. published that one-stage cartilage repair with a hyaluronic acid-based scaffold embedded with MSCs sourced from bone marrow aspirate concentrate has a prominent role in the treatment of chondral defects as it is a simple technique that could improve the problem and be cost-effective in the near future [24].

According to Arshi et al., preliminary clinical trials of MSCs therapy were promising (as a non-surgical treatment option or as an adjunct to existing surgical techniques for restoring cartilage) [25]. While quality evidence supporting MSCs therapy has emerged in recent years, the methodology for advising its routine clinical use will need to be further refined.

6.9.2 MSCs Plus MFX and Hyaluronic Acid (HA)

The study published by Qiao et al. (ClinicalTrials.gov Identifier: NCT02855073) preliminarily evaluated the safety and efficacy of human adipose-derived mesenchymal progenitor cells (haMPCs) in combination with MFX and hyaluronic acid (HA) for the treatment of knee cartilage defects [26]. A total of 30 patients with medial femorotibial condylar cartilage defects were randomly assigned to three groups: arthroscopic MFX and normal saline injection, arthroscopic MFX and intraarticular HA injection, or arthroscopic MFX in combination with intraarticular HA and haMPCs injection. The results showed that intraarticular injection of haMPCs plus MFX and HA was safe and improved knee function in cartilage defects [26].

6.10 Autologous Collagen-Induced Chondrogenesis (ACIC)

Kim et al. have described a technique called autologous collagen-induced chondrogenesis (ACIC) and presented their results in a clinical study (level IV of evidence) of 30 patients, with a follow-up of 6 years [27]. All patients had grade III/IVa symptomatic chondral defects of the knee according to the International Cartilage Repair Society (ICRS) and were treated with enhanced microdrilling using atelocollagen (which is an improvement of the traditional MFX method using an off-the-shelf product). In moderate to severe chondral lesions, this enhancement produced hyaline-like cartilage and improved symptoms.

6.11 Novel Autologous-Made Matrix

Cugat et al. have published the clinical, functional, and MRI-based results of a novel autologous-made matrix consisting of hyaline cartilage chips combined with mixed plasma poor

rich in platelets clot and plasma rich in growth factors (PRGF) for the treatment of 15 patients with full-thickness osteochondral defects (level of evidence IV—therapeutic case series) [28]. In young, active individuals with full-thickness cartilage or osteochondral defects, this novel surgical technique of cartilage restoration provided excellent clinical, functional, and MRI-based results.

6.12 Comparative Studies

6.12.1 MFX vs Mosaicplasty

Solhemin et al. investigated the survival of knee cartilage repair by MFX ($n = 119$) or mosaicplasty ($n = 84$) in a level III therapeutic study [29]. For the survival analysis, "failure" was defined as a Lysholm score <65 or the patient needing an ipsilateral total knee arthroplasty. The long-term failure rate (62% overall) was significantly higher in the MFX group (66%) than in the mosaicplasty group (51%). In addition, the mean time to failure was significantly shorter in the MFX group (4 years) than in the mosaicplasty group (8.4 years). In the mosaicplasty group, the survival rate was greater than 80% at 7 years, and greater than 60% at 15 years, while in the MFX group the survival rate was reduced to less than 80% at 12 months, and less than 60% at 3 years. The same pattern was found in a subgroup of patients ($n = 134$) of the same age (<51 years) and size of the treated lesion (<500 mm^2). Non-failures (48%) were followed for an average of 15 years (1–18 years). The conclusion was that MFX failed more often than mosaicplasty, both in the whole group and in the subgroup of patients matched for age and size of the treated lesion, indicating that mosaicplasty was more durable [29].

6.12.2 ACI vs MFX

MFX is often considered a first-line treatment option because of its ease and low cost, as well as its good short-term results [30]. However, multiple studies have recently shown that MFX results in the knee worsen after 5 years, especially in larger chondral injuries. Because of this, and the fact that the results of ACI are worse in patients with previous MFX, ACI has been proposed as a first-line rather than a salvage procedure for focal chondral knee defects. However, its long-term results need to be better analyzed.

6.12.3 ACI vs Osteochondral Allograft Cartilage Transplantation

When a bone marrow stimulation (MFX or subchondral drilling) technique fails, many cartilage restoration techniques are employed, such as ACI and osteochondral allograft cartilage transplantation. Riff et al. concluded that both ACI and osteochondral allograft cartilage transplantation were viable therapeutic options for chondral knee defects, even after failure of a BMS technique [31]. The functional outcomes, subjective satisfaction, and reoperation and failure rates of secondary ACI were comparable to those of primary ACI and secondary osteochondral cartilage allograft transplantation [31].

6.12.4 Synthetic Biphasic Scaffolds vs MFX

In a series of 132 patients, Wang et al. compared the results of a biphasic synthetic scaffold (TruFit, Smith and Nephew) ($N = 66$) with those of MFX ($N = 66$) in the treatment of isolated chondral or osteochondral femoral defects of the knee [32]. The mean age of patients in the series was 42.8 years (69% men). They found that in the long term, the activity level and appearance of MRI were better in the biphasic synthetic scaffold group (TruFit, Smith and Nephew) than in the MFX group.

6.12.5 Mosaicplasty: Patellofemoral vs Tibiofemoral Joints

Solheim et al. investigated the survival of mosaicplasty in relation to the location of the chondral

lesion: patellofemoral joint (N = 26) versus medial or lateral femoral condyle (N = 58) [33]. Survival was not significantly different between groups. This study (therapeutic, with level III of evidence) suggested that in the long term, mosaicplasty provides similar results in the patellofemoral joint and the tibiofemoral joint.

6.12.6 Mosaicplasty vs MFX vs ACI vs MACI

Zamborsky et al. published a large systematic review and network meta-analysis of randomized controlled trials [34]. A total of 891 patients were included from 21 studies; trauma was the most common etiology. At 10 years of follow-up there were significantly higher rates of failure (defined by a number of criteria which vary by study) in the MFX group than in the ACI group. At 3 years follow-up, there were more good or very good clinical results in the mosaicplasty group than the MFX group; there were more poor results in the MFX group than were the case in ACI and MACI. Patients who underwent mosaicplasty had higher rates of return to activity than those who underwent MFX. Finally, there were no significant differences between the various techniques in terms of reoperation or complications. The conclusion was that ACI and MACI provided better quality tissue repair and had fewer failures and higher return to activity rates than MFX. The authors recommended the conduct of further studies with longer follow-up periods and larger numbers of patients to confirm the efficacy and safety of these interventions [34].

According to Chimutengwende-Gordon et al., MFX often gives poor results [35]. In addition, MFX is often not suitable for the treatment of defects larger than 2–4 cm^2. Mosaicplasty has been shown to produce better clinical results than MFX although it is technically more difficult and may cause morbidity at the donor site. However, mosaicplasty is limited by the availability of grafts. In addition, failure to incorporate them can be a problem. ACI has been shown to result in hyaline-like cartilage, but it involves a two-stage procedure that is relatively expensive. Rehabilitation after ACI takes about 12 months, which is uncomfortable (especially in patients practicing sports). A recent method that attempts to regenerate cartilage is autologous stem cell transplantation, which can be performed in a single stage, usually has a shorter rehabilitation period, and is less expensive than ACI. However, long-term studies of this method (autologous stem cell transplantation) are needed [35].

6.13 Cost-Efficacy of Cartilage Therapies

Everhart et al. analyzed the cost-effectiveness of cartilage therapies (MFX, mosaicplasty, osteochondral allograft cartilage transplantation, ACI, and MACI) in the USA, taking medium- and long-term results as a reference [36]. The conclusion was that the treatments used for knee cartilage defects in the USA were cost-effective in most clinically acceptable applications. However, MFX was not a cost-effective initial treatment for defects >3 cm^2. In addition, mosaicplasty of patella or bipolar lesions was potentially cost-ineffective, so they should be used judiciously.

6.14 Conclusions

Current methods of treatment of chondral knee defects lead to the formation of fibrocartilage, and are therefore only suitable for small defects of less than 2–4 cm^2 in diameter. Cell-based methods, especially ACI and MACI, have produced excellent functional results for periods of up to 20 years, being able to form hyaline-like cartilage in larger defects. That is why ACI and MACI are now accepted for these types of lesion, and are also being used to treat early osteoarthritis. Stem cell transplantation has provided promising results, although more high level, larger and longer term studies are needed to definitively demonstrate its efficacy. Before recommending augmentation of cartilage regeneration procedures with the use of growth factors and improved scaffold materials for widespread clinical use, especially for osteoarthritis, long-term randomized studies evaluating its efficacy are required.

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7 Acute Anterior Cruciate Ligament Injuries: Repair or Reconstruction?

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7.1 Introduction

The current gold standard for the surgical management of an acute rupture of the anterior cruciate ligament (ACL) is surgical reconstruction (ACLR) (Fig. 7.1) [1, 2]. This is because poor results have been reported historically following open primary repair of ACL injuries [3]. ACLR has a high rate of success as measured by return to sport [4–6]. There is a large body of evidence supporting ACLR [7]. In a therapeutic study (level 2 of evidence) it was demonstrated that patients undergoing ACLR were able to perform sports-related functions and maintain a relatively high knee-related quality of life 10 years after ACLR although activity levels significantly declined over time [7]. Multivariable analysis identified several key modifiable risk factors that significantly influence the outcome. The patient-specific risk factors for inferior 10-year outcomes were lower baseline scores; higher body mass index (BMI); being a smoker at baseline; having a medial or lateral meniscus procedure performed before index ACLR; undergoing revision ACLR; undergoing lateral meniscectomy; grade 3 to 4 articular cartilage lesions in the medial, lateral, or patellofemoral compartments; and undergoing any subsequent ipsilateral knee surgery after index ACLR [7].

However, it has recently been reported that favorable results are possible after primary ACL repair when the technique is selectively performed early, on patients with proximal tears and good tissue quality. Preservation of the ACL has the advantage of maintaining proprioceptive function and native ligament biology while eliminating donor site morbidity. In addition, the technique is minimally invasive and reduces the inflammatory reaction often seen after ACLR [2, 3, 8].

Various methods of protecting the primary repair of the ACL have been suggested in recent years. Suture ligament augmentation (SLA) of the primary repair technique may be beneficial in protecting the healing of the ACL during early knee motion [3]; however, high rates of early failure of ACL repair with SLA have been reported in adolescents [9]. Dynamic intraligamentary stabilization (DIS) [10, 11] and InternalBrace ligament augmentation are alternative methods of protecting or augmenting primary repair techniques [12]. Although contemporary ACL repair techniques have shown good short-term results in several studies, there is a lack of high quality evidence on the effectiveness of such treatment compared to ACLR [6].

Thus, there is currently some controversy over which of the two techniques is better in acute ACL ruptures: repair or reconstruction.

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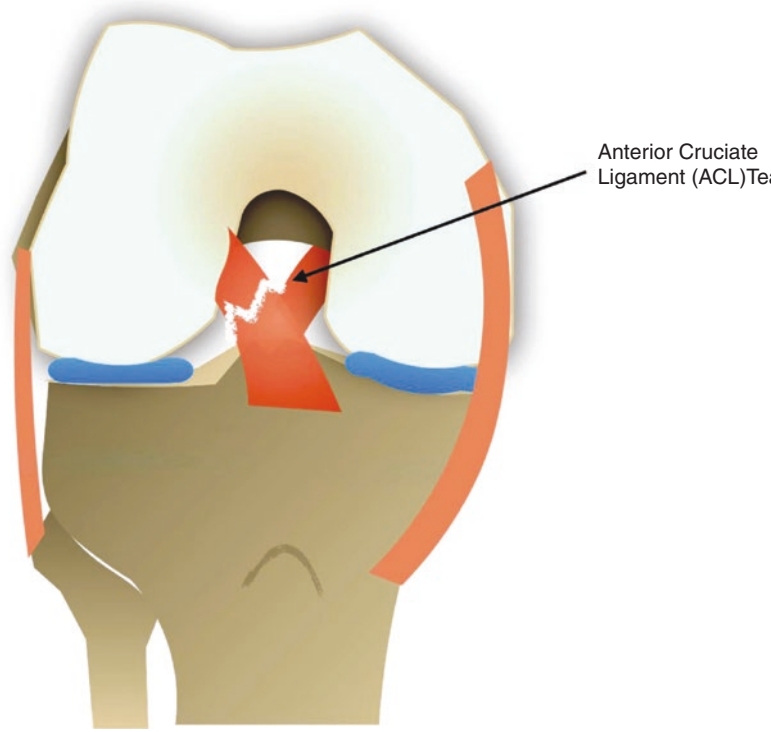

Fig. 7.1 Anterior cruciate ligament (ACL) rupture

In this chapter we will analyze the latest literature data on both techniques, with special emphasis on comparative studies, with the intention of clarifying the aforementioned controversy.

7.2 ACL Repair

7.2.1 Patient Factors Associated with Eligibility for ACL Repair

In a study published in 2019 by van der List et al. [8], 371 patients undergoing ACL surgery during a 10-year period were analyzed, of which primary repair was deemed possible (the ligament being of sufficient quality and the tear being proximal) in 158 patients (44%). They reviewed the characteristics of the patients to determine what patient characteristics were associated with eligibility for repair. Their multivariate analysis showed that older patients (age > 35 years), surgery in the first 4 weeks and BMI < 26 were more likely to be eligible for repair while those who had sustained a lateral meniscal tear were less likely to be eligible.

7.2.2 DIS (Dynamic Intraligamentary Stabilization)

In 2020, Ahmad et al. [11] published a level 4 study of evidence on the long-term survival of ACL repaired with DIS (Fig. 7.2). Fifty-seven patients with proximal acute ACL ruptures underwent DIS repair within 3 weeks after the injury and were available for final follow-up at least 5 years after the operation. Failure (defined as need for ACL reconstruction, persistent laxity >5 mm or rerupture) was assessed using survival analysis. Survival was 70% at 6 years and 2 months. Premorbid activity level was the only factor significantly associated with survival: patients who played competitive sports before the injury fared worse (ACL survival 56.4%) while patients who performed only recreational sports fared better at 79.2%.

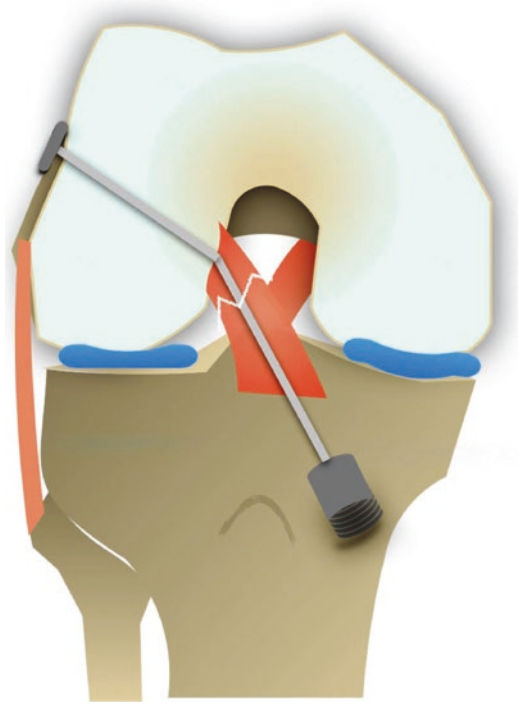

Fig. 7.2 DIS (dynamic intraligamentary stabilization) used in ACL repair

In 2019, Heusdens et al. [13] reported the results of the first 15 patients treated with DIS for ACL repair in their unit. They focused on technical problems, which were encountered in 11/15 cases. Of these, six were surgeon-related and 9 were implant-related, and all were resolved intraoperatively. Four patients had to be operated again for arthrofibrosis and another for a cyclops lesion and the DIS implant was eventually removed in 5/15 patients. According to Tegner score, 7 out of 10 (70%) patients returned to the level of sports activity before the injury within 6 months and patients returned to work at a mean of 5.4 weeks. On MRI, ten patients showed what appeared to be a normal ACL; three showed high intensity within the repaired ligament, and two showed no signs of healing (but had no instability clinically). None required ACLR.

The case-control study of Häberli et al. [10] examined the effect of hardware removal on knee laxity and functional scores at 2 years following DIS repair of the ACL in 173 patients. They compared 47 patients with hardware extraction to 126 without it. Groups were well matched with a mean age of 34 years in both groups; 47% were female in the hardware removal group and 50% were in the control group. There was no difference between the groups in terms of knee laxity at 2 years, or by any other outcome measure.

7.2.3 SLA (Suture Ligament Augmentation)

Less literature is available on SLA compared to DIS. A recent cohort study by Gagliardi et al. [9] compared surgical failures, functional outcomes, return to sport, and joint laxity in adolescents (7–18 years of age) undergoing ACL repair with suture ligament augmentation (SLA) with those of patients undergoing reconstruction of the ACL with quadriceps autograft (QPA). The study included 22 consecutive patients in the SLA group and 157 in the QPA group. The average duration of follow-up was similar for the two groups (2.7 years in the QPA group and 3.2 years in the SLA group). Outcomes were compared using a multivariable regression analysis (with covariates including gender, age, BMI, and time from injury to surgery). Outcomes were significantly worse in the SLA group, with a risk of graft failure 10.66 times higher than in the reconstructed group with no difference in function (as measured by rate of return to sport). The cumulative incidence of graft failure in the first 3 years after surgery was 48.8% in the SLA group, compared with 4.7% (2.1–10.3%) in the QPA group. The authors suggested that there was a high risk of short-term failure following SLA and that this should be taken into account when deciding to offer the procedure to adolescents.

7.2.4 Outcomes of ACL Repair

In 2019, Nwachukwu et al. [14] performed a systematic review of outcomes of primary surgical repair of the ACL. The authors' 28 studies, dating as far back as 2005; half (n = 14) of the studies examined direct suture repair and the other half examined repair with DIS. All but three included

only arthroscopic techniques, two included only open repair, and the final study compared open and arthroscopic techniques. The frequencies of rupture, revision surgery, and reoperations were 23.1%, 33.3%, and 51.5%, respectively. The overall ACL repair survival was between 60 and 100%. In the subgroup analysis for proximal ruptures treated with repair, the revision rate and the reoperation rate were 12.9% and 18.2%, respectively. Mean patient reported outcomes were reported infrequently (with reporting of preoperative PROMS particularly rare), and PROM results were often disappointing when they were reported. The authors conclude that, in light of the poor PROM outcomes and high revision rate when compared to existing literature for ACLR, reconstruction of the ACL remains the correct treatment in the majority of patients.

In a systematic review and meta-analysis of recent literature published in 2019, van der List et al. [15] evaluated the results of the various ACL primary repair techniques, the majority being DIS (level of evidence 4). The degree of recommendation for primary repair was weak. There were 9 failures of 74 primary repairs (10%), 6 of 69 after repair with static augmentation (7%), and 106 of 958 after dynamic augmentation (11%). Repair with dynamic augmentation had more reoperations (99; 10%) and more hardware removal (255; 29%) than the other procedures. All functional scores were >85% of the maximum scores. Overall, this meta-analysis, which included only more recent studies, had better outcomes than the review of Nwachukwu et al., with failure rates of 7–11%, and with functional results in general greater than 85% of the maximum scores. However, the studies included carried a high risk of bias and the follow-up was short (2.1 years).

In a systematic review (level 4, systematic review of level 3 and 4 studies) published in 2019, Houck et al. [16] described the clinical results after primary ACL repair. Six studies (2 levels III, 4 levels IV) were included. The six studies included exclusively proximal avulsion tears. Overall, 0–25% of patients suffered repair failures, and 0–20% of patients needed further reoperation.

7.3 Acute ACL Ruptures: Repair or Reconstruction?

There are three comparative studies comparing ACL repair to the gold standard, ACLR.

In 2019, Hoogeslag et al. [6] published a randomized controlled trial of 48 patients (level of evidence 1), comparing ACL repair with dynamic augmentation to ACLR with a single-bundle, all-inside, semitendinosus technique, with the primary endpoint being PROMs at 2 years. No statistical differences were found between groups for the mean subjective score of the IKDC (repair, 95.4; reconstruction, 94.3). There were two ruptures (8.7%) in the dynamic repair group and four ruptures (19.0%) in the reconstruction group. The conclusion was that at 2 years after surgery, the increased dynamic ACL suture repair was not inferior to the ACLR with a single-bundle, all-inside, semitendinosus technique in terms of subjective outcomes reported by patients, measured with the subjective IKDC score, suggesting that ACL repair with dynamic augmentation was a viable option in the treatment of acute ACL ruptures.

In 2019, Sporsheim et al. [17] reported the results at 30 years of an RCT comparing bone-patellar tendon-bone (BPTB) ACLR (Fig. 7.3) to two repair procedures; direct repair and synthetic ligament augmentation (ligament augmentation device—LAD) (Fig. 7.4). When BPTB reconstruction was performed, remnants of the ruptured ACL were retained alongside the reconstruction. A total of 150 patients were initially randomized, of whom 113 patients were available at 30 years. There was a significantly higher rate of failure with ACL repair (12/39 primary repairs and 9/39 augmented repairs had undergone revision to ACLR within the time period, compared to 1/35 in the reconstruction group). After excluding failures, no significant differences were found between the three groups with respect to range of motion, laxity, or Tegner and Lysholm scores. A total of 42% of all patients demonstrated radiographic evidence of OA. The authors concluded that BPTB reconstruction provided the most reliable strategy for treatment of the ruptured ACL.

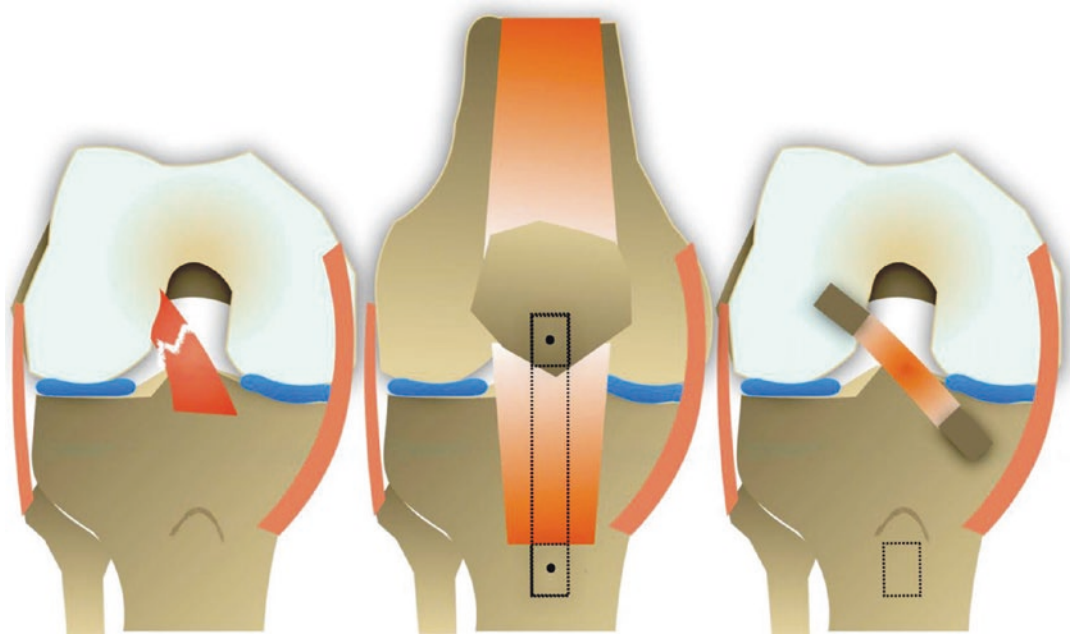

Fig. 7.3 Bone-patellar tendon-bone (BPTB) autograft utilized in ACL reconstruction (ACLR)

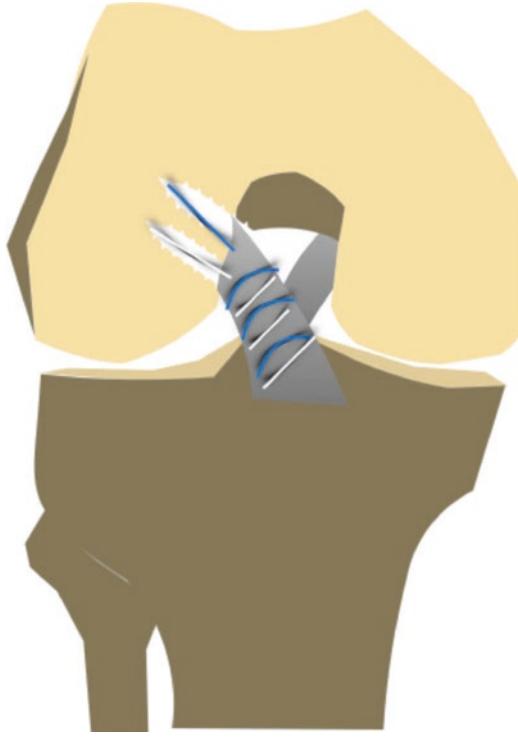

Fig. 7.4 LAD (ligament augmentation device) used in ACL repair

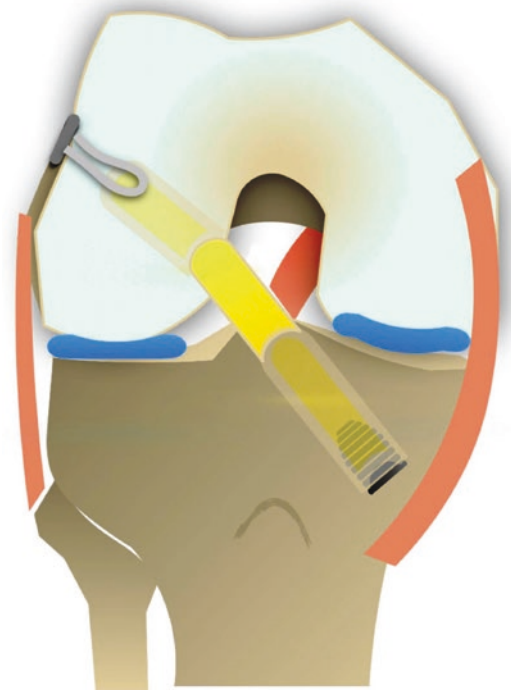

Fig. 7.5 Hamstring autograft utilized in ACL reconstruction (ACLR)

In a retrospective matched-pair study published in 2020, Ortmaier et al. [18] compared 24 patients who had undergone ACL repair with InternalBrace to 45 patients undergoing ACLR using hamstrings (n = 25) (Fig. 7.5) or quadriceps tendon (n = 20) autograft. The mean age was 33.4 years and the minimum follow-up was 12 months. The level of return to sport was 91.3% with no significant difference between the groups ($p \geq 0.05$); the level of post-operative sport participation was similar to pre-operative in both groups and overall. The conclusion was that, in the short term and in a selected patient population, ACL repair using internal reinforcement allows sports activity and patient satisfaction similar to the classic ACLR using hamstring or quadriceps autografts.

7.4 Conclusions

Primary repair of the ACL has several theoretical advantages over reconstruction but remains controversial. The single contemporary randomized trial comparing the two techniques suggests that repair with DIS may be a viable alternative to reconstruction in acute ruptures of the ACL. However, there is a large body of evidence from cohort studies that the rate of rerupture may be significantly higher overall than observed in ACLR. The understanding of the outcomes of ACL repair procedures is hampered by the relative lack of good quality studies and the diversity of techniques used. Although repair procedures have promise, ACLR would still be considered to be the gold standard for treatment of acute ACL rupture.

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8 Anterior Cruciate Ligament Reconstruction: Isolated or Combined with an Extra-Articular Procedure?

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8.1 Introduction

Some patients who undergo intra-articular anterior cruciate ligament reconstruction (ACLR) do not fully recover in terms of patient-reported outcomes (PROMs), knee kinematics, and return to sport. Technical factors only explain some of these failures. Residual anterolateral rotational instability (ALRI) associated with a positive pivot shift after surgery is a factor associated with poor functional outcomes.

Regardless of the technique used for ACLR, some retrospective reviews claim that up to 34% of patients continue to have excessive residual ALRI after surgery, as measured by the pivot shift test. Young patients (<25 years) have more flexible soft tissues and therefore a higher risk of residual instability. This can lead to worse long-term results and can influence the return to sports activities. It has been mentioned that this laxity could be improved by the addition of an extra-articular lateral procedure (LEAP) [1].

Another major concern is graft rupture after ACLR, which occurs in up to 28% of high-risk patients. To avoid this problem, combined procedures have been proposed to reduce stress on the anterior cruciate ligament (ACL) graft and protect it during ligamentization, with the expectation that this will result in less graft rupture and less need for revision surgery [2].

Current evidence shows that the anterolateral complex, composed of the iliotibial band (ITB) and its Kaplan fiber system, the anterolateral ligament (ALL), and the capsule, is an important stabilizing structure in the anterolateral part of the knee. Therefore, LEAPs are increasingly being added as concomitant procedures to primary intra-articular reconstruction and revision of the ACL [3].

LEAPs can be divided into the traditional lateral extra-articular tenodesis (LET) and the more modern technique of anatomic anterolateral ligament reconstruction (AALLR). Because of their important differences, the results between the LET and AALLR procedures should be considered separately.

8.2 Lateral Extra-Articular Tenodesis (LET)

LET is a non-anatomical procedure to restore anterolateral rotational stability and correct pivot shift. Lemaire described the use of a strip of ITB to make a lateral reinforcement. Since then, many variations of these procedures have been described. A better understanding of the anatomy and biomechanics of the anterolateral structures of the knee has led to the reappearance of LET as a combined procedure with ACLR.

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LET is performed using a strip of the ITB obtained from its central or distal part, without disinserting it from Gerdy's tubercle. The strip of ITB is passed under the lateral collateral ligament (LCL) and the posterior and proximal part is fixed to the lateral epicondyle with a clip, a suture anchor, or an interference screw [4] (Fig. 8.1). Postoperative overconstruction and stiffness are the most important historical concerns regarding the results of LET techniques.

8.3 Anatomic Anterolateral Ligament Reconstruction (AALLR)

The AALLR technique differs from ITB-based procedures in that it seeks to recreate the normal anatomy and biomechanics of the ALL. AALLR is most often performed with autografts, most often of gracilis tendons, which can be single or double braided, although allografts have also been used. There are three variants: single-bundle anatomic reconstruction, double-bundle anatomic reconstruction, and the combined intra- and extra-articular ACLR techniques.

8.3.1 Single-Bundle Anatomic Reconstruction

The femoral tunnel for the graft should be slightly posterior and proximal, or more precisely, 4 mm posterior and 8 mm proximal to the lateral femoral epicondyle; the tibial tunnel should be approximately 5–10 mm distal to the joint line, midway between the fibular head and Gerdy's tubercle [5] (Fig. 8.2).

8.3.2 Double-Bundle Anatomic Reconstruction

Tibial fixation can also be done with two tibial tunnels, in which an extra hole is made in the superolateral area of Gerdy's tubercle. In this method, the ALL grafts are positioned in the two tunnels as a "delta" or "inverted Y." An interference screw or a staple can be used to fix the graft in the tibial tunnel. The grafts will follow an anterior and inferior oblique orientation towards the tibia, below the ITB and superficial to the LCL.

8.3.3 ACLR Combined Intra- and Extra-Articular Technique

AALLR in combination with ACLR can also be performed by passing the graft over the top of the lateral femoral condyle or using a single femoral tunnel (Fig. 8.3); this is called the combined intra- and extra-articular technique of ACLR. In this technique, the ALL and ACL grafts share the same femoral tunnel, which extends from the lateral wall of the lateral femo-

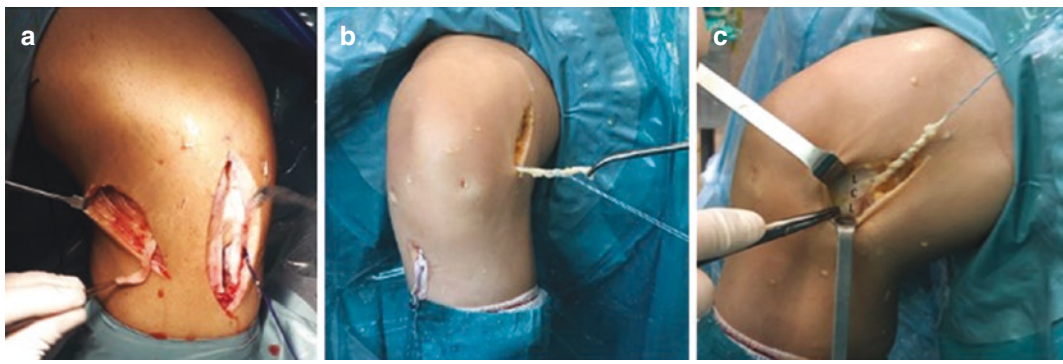

Fig. 8.1 (**a**) Combined anterior cruciate ligament reconstruction (ACLR) using bone to bone-patellar tendon-graft (BPTB) + lateral extra-articular tenodesis (LET). (**b**) Combined ACLR using hamstring tendon (HT) + lateral extra-articular tenodesis (LET). (**c**) Passage of the iliotibial band (ITB) under the lateral collateral ligament (LCL)

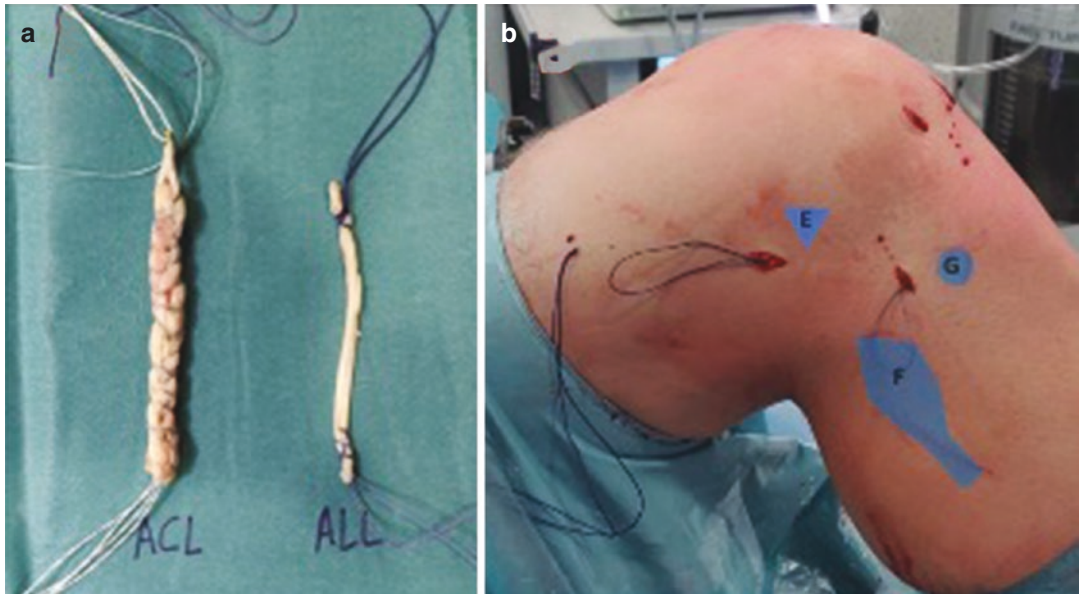

Fig. 8.2 (**a**) Graft preparation for combined ACL plus anatomical single-bundle anterolateral ligament (ALL) reconstruction with hamstring tendon (HT). (**b**) Anatomical references: lateral femoral epicondyle (E), fibula (F), and Gerdy's tubercle (G)

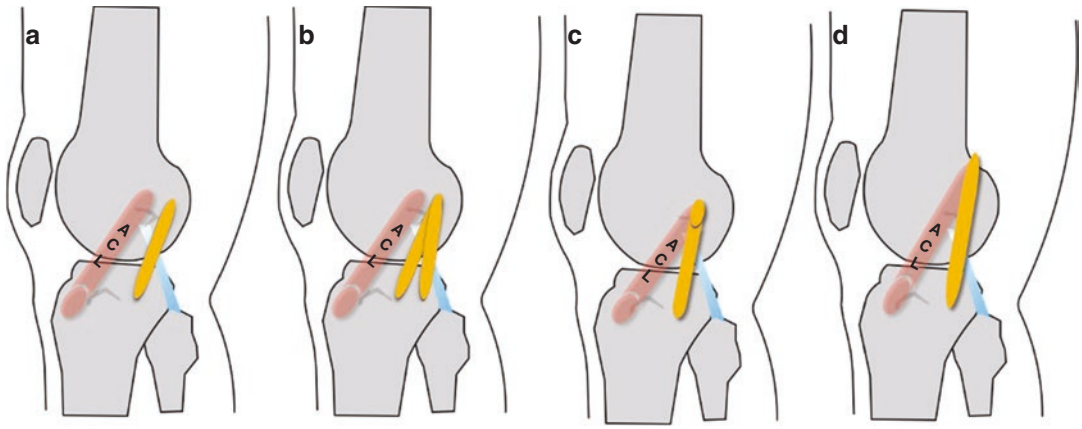

Fig. 8.3 (**a**–**d**) Types of anatomical reconstruction of anterolateral ligament: (**a**) single-bundle technique; (**b**) double-bundle technique; (**c**) combined intra- and extra-articular technique passing the graft using a single femoral tunnel; (**d**) combined intra- and extra-articular technique "over the top" of the lateral femoral condyle

ral condyle (ALL femoral insertion), slightly proximal and posterior to the lateral epicondyle, to the medial wall of the lateral femoral condyle (ACL imprint). The ACL portion of the graft is a combination of the semitendinosus and gracilis tendons and is passed intra-articularly from the tibia to the femur. The longest remnant of the gracilis tendon is pulled through the femoral tunnel or behind the femoral condyle and goes to the AALLR.

These procedures avoid a large lateral incision and do not require obtaining an ITB graft, which in itself may compromise the anterolateral stability of the knee or cause persistent lateral pain. The main disadvantage of this anatomical type of AALLR is that there are no published long-term series.

On the other hand, to date, no studies have compared clinical outcomes between LET and AALLR, when combined with ACLR. Delaloye et al. conducted a biomechanical study on six cadaver knees and found that in ACL-deficient and anterolateral knees, the combined ACL and anterolateral reconstruction restored native knee stability in the anterior socket and internal rotation as opposed to the isolated ACLR [6, 7]. In addition, both types of extra-articular reconstruction, AALLR or modified Lemaire LET, were similar in terms of restoration of knee kinematics. However, another study conducted on cadavers (20 knees) demonstrated superior biomechanical properties for LET than for AALLR [8]. In a recent systematic review the rotational stability and patient-reported outcomes (PROMs) were similar for ACLR combined with LET or with AALLR [8]. There is a significant cost difference between the two techniques: a LET only requires the addition of an implant for fixation compared to the use of ≥2 for most AALLRs.

8.4 ACL Reconstruction: Isolated vs Combined

Almost all recent clinical studies show benefits of combined ACLR versus isolated ACLR. The advantages that have been attributed to the combined reconstruction are the shared load with the ACL graft and the improved kinematics of the knee.

8.4.1 Studies to Determine If the Combination ACLR + LEAP Can Improve Graft Survival

In a comparative study (cohort study; level of evidence, 2) on the results of combined ACLR + AALLR (using gracilis tendon with one femoral tunnel and two V-shaped tibial tunnels) versus isolated ACLR in high-risk patients (young athletes, participating in contact sports), Sonnery-Cottet et al. analyzed 512 patients aged 16–30 years, showing that after an average follow-up of 38.4 months the graft failure rate for patients undergoing combined ACLR + AALLR was 3.1 times less than in isolated ACLR with a four strand autologous hamstring tendon (HT) graft and 2.5 times less than in isolated ACLR with bone-patellar tendon-bone (BPTB) [9]. Graft rupture rates were 10.77% for the isolated hamstring ACLR group, 16.77% for BPTB, and 4.13% for HT graft combined with AALLR. In addition, Sonnery-Cottet et al. found a lower failure rate of medial meniscus repair in patients undergoing combined ALL reconstruction [10].

Castoldi et al. conducted a randomized controlled trial (level of evidence, 2.) with a minimum follow-up of 19 years. In 121 knees they compared isolated BPTB ACLR versus BPTB ACLR combined with AALLR with gracilis tendon using a delta tunnel arrangement in the tibia [11]. The study showed a trend toward decreased risk of graft rupture in the combined group (13%) versus the isolated group (29%; $P = 0.1$). However, the study was not powerful enough to confirm these results.

In a recent study (randomized controlled trial; level of evidence, 2) immediately following ACLR surgery, the authors repeated the pivot shift test. If the pivot shift was ≥1 greater than that recorded in the uninjured contralateral knee, patients were randomly assigned to have no further surgery or the addition of LET. ACLR combined with residual pivot shift knee LET after ACLR was found to reduce the risk of recurrence [14.8% vs 0.0% ($P < 0.001$)] and improve clinical outcomes, after 2 years of follow-up. The persistence of a residual pivot shift immediately after the ACLR may be considered a practical indication for combining a LET [12].

In the first multi-center, prospective, randomized clinical trial comparing an ACLR (with single-bundle HT) with or without LET (performed with an ITB strip), a total of 618 patients aged 14–25 years were randomized. At 2 years after surgery, 11% of patients in the ACLR group suffered graft rupture, compared to 4% in the ACL + LET group (RRR, 0.67; 95% CI, 0.36–0.83; $P < 0.001$). In the isolated ACLR group, 40% of patients had persistent rotational laxity (clinical failure) compared to 25% of ACLR + LET patients (RRR, 0.38; 95% CI, 0.21–0.52;

$P < 0.0001$). The addition of LET to an ACLR in young patients at high risk of failure resulted in a reduction of the relative risk (RRR) of graft rupture by 66% and an RRR of clinical failure (considered as graft rupture or persistent rotational laxity) of almost 40%. The authors of this study believe that this difference is clinically important and should probably change current practice [13].

8.4.2 Studies Trying to Determine If the Combination ACLR + LEAP Can Improve Residual Rotational Instability

Helito et al. retrospectively reviewed (level 3 evidence, case-control study) an AALLR using combined intra- and extra-articular ACLR versus isolated ACLR in chronic ACL ruptures (defined as ruptures more than 12 months old) [14]. Patients in whom the combined technique was used had better results in the KT-1000 with less residual pivot shift, presenting only 9.1% of positives versus 35.3% in the isolated ACLR group. The subjective International Knee Documentation Committee (IKDC) and Lysholm functional outcome scores were also significantly better. There was no re-rupture in the combined group versus 7.3% in the isolated ACLR group.

In another study, Lee et al. evaluated the effect of AALLR (single-bundle anatomic reconstruction with gracilis tendon allograft) on revision ACLR (with tibialis anterior tendon allograft) [15]. ACLR review in combination with AALLR significantly reduced rotational laxity. In fact, 90.5% of patients in the combined group and 53.5% of patients in the isolated group had a negative pivot shift ($P < 0.001$) and showed a higher rate of return to the same level of sports activity than the isolated revision ACLR (57.1% vs 25.6%, respectively; $P = 0.008$). Graft rupture requiring revision surgery was found in two patients (4.4%) in the isolated group, while no patients in the combined group suffered rupture.

Helito et al. compared (in a Level 3 study) functional outcomes, residual instability, and rupture rates in patients with ligament hyperlaxity (Beighton minimum of 5) undergoing ACLR alone or in combination with AALLR (the femoral tunnel used for ALL was the same one used for ACLR, using the remaining portion of gracilis for reconstruction, and fixation of the ALL in the femur and tibia was performed with an interference screw) [16]. At final evaluation, patients in the combined group showed better anteroposterior stability as assessed by KT-1000 ($P = 0.02$), better rotational stability as assessed by the pivot shift test ($P = 0.03$), and a lower rate of failure (21.7% in the single group vs 3.3% in the combined group; $P = 0.03$). The combined ACL and ALL reconstruction in patients with ligament hyperlaxity resulted in a lower re-rupture rate and better knee stability parameters than when the isolated ACLR was performed.

Getgood et al. compared in a randomized controlled trial the functional outcomes of isolated ACLR with the combination ACLR + LET at 6, 12, and 24 months post-operatively. Patients undergoing ACLR + LET did not have a lower functional outcome compared to those treated with ACLR alone. There were no clinically significant differences in PROMs between groups, nor in strength or function at 12 months. There was also no difference in the return to sport or in the percentage of reoperations [17].

Comparative studies have shown that combined reconstruction is associated with a significantly lower risk of ACL graft rupture and of need for subsequent meniscectomy; also, that it is associated with significantly better knee stability and better rates of return to pre-injury level of sporting activity compared to isolated ACLR. In addition, significant advantages were reported in some specific populations, including young patients participating in pivoting sports, patients with hyperlaxity, patients with chronic ACL injury, and patients undergoing revision ACLR.

There are no studies evaluating the cost-effectiveness of lateral extra-articular procedures in ACLR. These procedures result in an increase in cost: they require a little more surgical time and also increase the cost for the use of fixation materials such as sutures, screws, staples, or anchors; furthermore, depending on the technique, they may require additional grafts. LEAPs

result in a lower degree of residual laxity and a lower risk of failure, which could contribute to reducing overall costs in the long term. In addition, the potential improvement in patient outcomes and reduction of the risk of failure could also allow for an earlier return to work and a reduction in lost productivity, which would also decrease indirect costs, and thus compensate for the higher initial resource use related to these procedures [18].

8.5 Indications for AALLR and LET

The indications for AALLR or LET remain controversial. The indications for combined ACL and ALL reconstruction are being expanded. Recent consensus papers published by the international Anterolateral Ligament Expert Group [19] and the International ACL Consensus Group Meeting [20] have reviewed their indications. Young patients (14–25 years) with ACL deficiency who have two or more of the factors shown in Table 8.1 are at greatest risk of re-injury. A combined ACL and ALL reconstruction would be indicated.

Table 8.1 Indications for combined anterior cruciate ligament reconstruction (ACLR) and lateral extra-articular procedure (LEAP)

Patients aged 14–25 years with ACL deficiency who have two or more of the following characteristics:
1. Participation in pivoting sports
2. Elite athletes
3. Presence of a grade 2 or higher pivot shift
4. Generalized ligament laxity (Beighton score of 4 or greater)
5. Genu recurvatum greater than 10°
6. Preoperative side to side laxity >7 mm
7. Associated Segond Fracture
8. Chronic ACL rupture
9. Lateral femoral notch signal on plain radiographs
10. Patients undergoing revision ACLR
11. Contralateral ACL reconstruction failure
12. Biologically compromised patients, e.g., ACLR with allograft or patients with increased tibial slope in the sagittal plane because it may protect the ACL graft

ACL Anterior cruciate ligament

8.6 Complications of LEAPs

Despite the promising results and the fact that very few complications have been published following LEAPs, other authors have reported concerns about the addition of LEAPs. An ongoing randomized controlled trial is studying whether combined ACLR + AALLR reconstruction is associated with a higher rate of adverse outcomes compared to isolated ACL reconstruction. This study has shown no evidence of increased risk of complications or reoperations with the combined ACL + AALLR procedure (with HT graft) compared with the isolated ACLR (with BPTB graft) [21]. In a systematic review, the published rate of complications in patients treated with revision ACLR associated with LET is 8% [22].

8.6.1 Difficulties with Grafting

It is advisable to prepare the ends of the graft with a No. 2 non-absorbable suture in a running-locked pattern to avoid tearing when the graft is fixed.

8.6.2 Injury to LCL

The proximity between the femoral insertion of the ALL and the LCL predisposes to iatrogenic LCL lesions during femoral tunnel reconstructions. Helito et al. observed in 8.3% of fresh cadaver knees an injury of at least 50% of the LCL fibers when the femoral tunnel was perforated for ALL grafts. The percentage of LCL injury rose to 41.6% when 8 mm diameter drills were used [23].

8.6.3 Wound Hematoma

It is the most frequently reported complication following LET procedures. Superior geniculate vessels are at risk during surgical approach Therefore, it is important to identify them and coagulate them to avoid post-surgical hematomas. Drains may also be placed in the area to prevent hematomas.

8.6.4 Persistent Lateral Pain

Getgood et al. observed that, both in patients operated for isolated ACLR and those operated for ACLR + LET, pain was minimal in the early postoperative phase (3 months): overall, pain was approximately 8/40 in the four-item pain intensity measure (P4: pain in the morning, afternoon, night and with activity during the last 2 days), although it was lower in the isolated ACLR group than in the ACLR + LET group (adjusted mean difference, −1. 6; 95% CI, −2.7 to −0.6; $P = 0.003$) [17]. This difference was not observed 3 months after the operation.

8.6.5 Discomfort Caused by Fixation Devices

This can happen especially if staples are used to fix the graft and may require removal of the fixing material (hardware).

8.6.6 Over-Constraint of the Lateral Compartment

This is due to the fixation of the graft with the tibia in external rotation and the over-tensioning of the graft.

8.6.7 Loss of Knee Mobility or Stiffness

No patient in the recently published series required manipulation under anesthesia or arthroscopic debridement for loss of knee mobility or stiffness.

8.6.8 Patellofemoral Crepitus

Distally, in the anterior aspect of the superficial layer of the ITB, curved fibers are identified that are anchored to the lateral aspect of the patella and patellar tendon, which are called the iliopatellar band. The distal edge of this portion of the iliopatellar band constitutes the lateral patellotibial ligament [24]. Tensioning the window at the ITB during a LET can lead to patellofemoral problems. We recommend not to close the ITB under tension or even to leave the distal part of the window unclosed.

8.6.9 Osteoarthritis of the Lateral Compartment

O'Brien et al. (in a small, non-randomized retrospective review) compared ACLR with BPTB autograft with or without LET in 80 patients. They found no clinical differences in KT-1000 and concluded that the addition of LET did not provide any benefit; in addition, 40% of patients had chronic pain and/or inflammation in the lateral area [25].

Marcacci et al. found no increase in degenerative changes in the lateral compartment after more than 10 years of follow-up in patients without lateral meniscal tears undergoing combined intra- and extra-articular ACL reconstruction [26]. Two other European studies with more than 20 years of follow-up have not shown a higher rate of development of osteoarthritis with the addition of LET [27, 28].

In addition, a recent meta-analysis also found no correlation between LET and osteoarthritis. The incidence of osteoarthritis was low up to 11 years post-surgery, but increased thereafter. The presence of meniscal injury at surgery was reported to be a major predictor of the development of osteoarthritis [29]. Previously reported osteoarthritis could probably have been the result of a combination of imperfectly anatomical ACLR and non-anatomic LET, fixed in flexion, and often with the tibia in external rotation and delayed rehabilitation due to immobilization in a cast for up to 2 months after the operation. Based on this study, it can be stated that the addition of extra-articular reconstruction to anatomic intra-articular ACLR followed by a modern rehabilitation protocol does not increase the risk of osteoarthritis [30]. Although there has been concern about the possible increased risk of osteoarthritis, there is no clinical evidence that lateral reinforcing procedures lead to it.

8.6.10 Malposition of the Fixation Devices

The fixing screws can migrate out of the tunnel and be located in the supracondylar area. Fixation devices can also migrate intra-articularly in tibial fixation and can damage the articular cartilage of the tibial plateau [31].

8.6.11 Convergence of Tunnels

On the femoral side, tunnel convergence represents a potential problem during a combined reconstruction. The tunnel orientations in the combined ACL-ALL reconstructions need careful intraoperative care to avoid convergence between the tunnels. This could compromise the fixation and integration of the graft, leading to the failure of the combined reconstruction or even causing lateral femoral condyle fractures. The most commonly used techniques require femoral fixation independent of the ACL. Among the many suggested femoral fixation methods, some require a bone tunnel.

In a study of ten cadaver knees, Jaecker et al. observed that tunnel convergence occurred in seven of ten cases (risk, 70%) using the Lemaire technique and in no case using the MacIntosh technique [32]. They concluded that tunnel convergence was most frequently observed in combined ACL and LET reconstruction using the Lemaire technique, regardless of knee size. The positioning of the LET femoral tunnel according to the MacIntosh reconstruction was not associated with the tunnel convergence.

In another study on ten cadaver knees, Jette et al. showed that tunnels with a 0° angle in the axial plane had a high risk of contact and disruption of the posterior femoral cortex; therefore, these angles should be avoided [33]. They recommended that when simultaneous ACL and AALLR reconstruction is performed, the femoral tunnel should be drilled at an angle of 30° anterior in the axial plane and 30° proximal in the coronal plane.

In an in vivo study, Smeets et al. have shown that the risk of tunnel convergence increases significantly when the AALLR tunnel is drilled at 0° in the axial plane [34]. The convergence of the tunnels can be avoided by pointing the AALLR tunnel 40° anteriorly and perpendicularly to the anatomical axis of the femur. A more horizontal orientation of the ACL, as in the anteromedial portal technique, is an additional risk factor for the tunnel coalition with respect to the use of the transtibial technique.

In an in vivo study Perelli et al. demonstrated 100% risk of tunnel convergence when the axial inclination of the LET tunnel was less than 15°, and a 92% chance of an unsafe bone bridge (<5 mm) between the tunnels for an axial inclination of 15°–20° [35]. The inclination in the axial plane seems to influence the possibility of convergence, while the inclination in the coronal plane does not seem to have the same effect. They recommended that to avoid any interference between an anatomical ACL femoral tunnel and a modified LEAP Lemaire femoral tunnel, the femoral tunnel should be drilled at an angle of at least 20° anteriorly.

The use of an inside-out ACL femoral tunnel drilling technique instead of an outside-out or the use of anchors for lateral brace fixation instead of bone tunnel can avoid this complication. In general, the number of complications or adverse events in LEAPs is low. Based on the current studies there is no evidence to support the concerns of high rates of adverse events reported following historical extra-articular lateral procedures. Table 8.2

Table 8.2 Complications/adverse effects of lateral extra-articular procedures (LEAPs)

INTRAOPERATIVE
Difficulties with the graft
Injury to LCL
POSTOPERATIVE
Wound hematoma
Cosmetic problems
Persistent lateral pain
ITB snapping
Muscular hernia in the lateral approach
Discomfort caused by fixing devices
Over-constraint of lateral compartment
Stiffness
Patellofemoral crepitus
Lateral compartment osteoarthritis
Malposition of fixing devices
Convergence of tunnels

LCL Lateral collateral ligament, *ITB* Iliotibial band

summarizes the complications/adverse effects of lateral extra-articular procedures (LEAPs).

8.7 Conclusions

The rate of graft failure after isolated ACLR remains a concern for knee surgeons despite the development of reconstructive techniques (transtibial, anatomic, or double-bundle techniques). This situation has led researchers to take a renewed interest in the role of anterolateral augmentation procedures. There is currently a great deal of interest in the role of the anterolateral structures of the knee in controlling rotational laxity and their ability to share loads with the ACL graft. Clinical results show that combined ACL and LEAP reconstruction is a safe procedure, reducing the rate of graft failure and increasing the rate of return to pre-injury sports levels. Research has shown that these procedures do not overconstrain the knee, nor do they increase lateral tibiofemoral contact pressure or cause loss of internal rotation.

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9 Optimal Technique in Knee Osteotomy

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9.1 Introduction

Aims of modern osteotomy can be divided into two categories. Firstly a morphological objective aiming to correct lower leg malalignment and provide an adequate bone morphology in both the coronal and sagittal planes [1–3]. Secondly, a biomechanical objective aiming to correct the weight-bearing axis and transferring it from a painful osteoarthritic compartment to a healthy compartment to allow restoration of function [4–6].

9.2 Is High Tibial Osteotomy (HTO) the Best Option in All of My Varus Knees?

An ideal range of postoperative mechanical axis of 2°–7° valgus is historically advocated to provide favourable clinical outcomes after medial open-wedge HTO (OWHTO) [2, 3, 7, 8].

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Correction errors and malalignment are well documented in previous studies [9–11] and it is well known that under or overcorrection following OWHTO can lead to complications and patient dissatisfaction [12, 13]. Thus, excessive overcorrection of the tibia is associated with lower functional outcomes [14] and may lead to an excessive joint line obliquity (JLO) that could lead to detrimental stresses to the articular cartilage [15]. It is still not clear as to what extent of an overcorrection of the medial proximal tibial angle (MPTA) after OWHTO is acceptable [16]. To avoid abnormal tibial or femoral anatomy and an oblique joint line, osteotomies should be performed at the location of the deformity which reinforces the importance of having knowledge of normal tibial and femoral angular values. Previous studies have shown a mean alignment of 3°–4° varus for the tibia and 3°–4° valgus for the femur in the non-osteoarthritic population [17–21].

One recent study defined the ideal osteotomy level to avoid an oblique joint line and found that in case of desired anatomic correction (MPTA <90°), only 12% could be corrected with an isolated HTO [22] but this study only analysed patients with an overall varus alignment >3°.

In our daily practice, we estimate the amount of correction to be performed and routinely evaluate the bony morphology of both the femur and tibia (Fig. 9.1). The ideal correction is then decided upon this bone morphology and a double-

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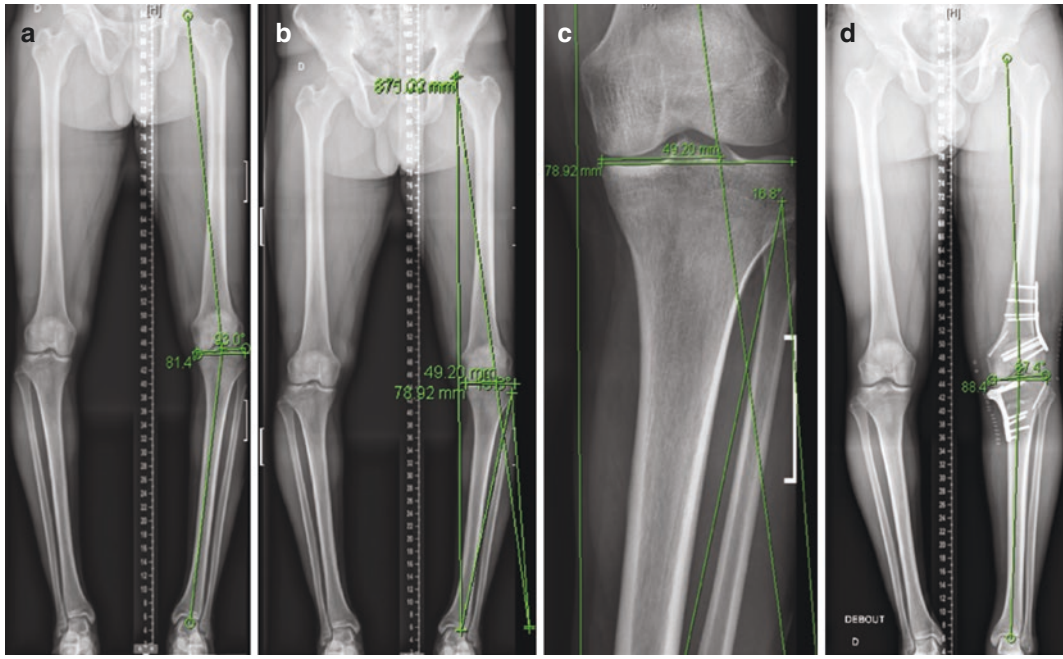

Fig. 9.1 (**a**–**d**) Double-level osteotomy performed with both tibial and femoral deformities: (**a**) Preoperative double varus: femoral (6°; "anatomical" = 87°) and tibial (5.6°; "anatomical") MPTA (medial proximal tibial angle = 87°) the HKA (hip-knee-ankle) angle was at 166.7°; (**b**) Planning of medial proximal tibial osteotomy, using Miniaci's method; (**c**) Obtaining a slight valgus mechanical axis will result to correct the tibia to 16.8° (postoperative planned MPTA = 98.2°) which will lead to an abnormal postoperative tibial morphology of an additional 11.2° (98.2°–87°); (**d**) To avoid this mistake, a double-level osteotomy has been performed allowing to restore a neutral mechanical axis in achieving "normal" femoral and tibial anatomy

level osteotomy with a threshold of 4° correction for each bone is planned. We think that below this 4° correction, the benefits of a second osteotomy site and plating are not sufficient to justify the inherent complication rate.

9.3 Should I Always Have a Vascular Surgeon Nearby When Starting My Osteotomy Cuts?

Despite good outcomes, complication rates following OWHTO have been consistently reported to be around 30%. Whilst rare (1.7%) neurovascular injury following OWHTO is a devastating consequence if it occurs [23]. To prevent neurovascular injury, several techniques have been previously described including utilization of a protective cutting system [24], patient-specific cutting guides [25], and computer-assisted navigation [26]. There has been considerable discussion about the management of the medial collateral ligament (MCL) following OWHTO [27, 28]. In a standard approach for OWHTO, the MCL is raised subperiosteally to the posteromedial part of the tibia prior to a large posterior tibial retractor (PTR) being placed behind the tibia to protect the neurovascular structures (NVS). However, the surgical assistant often has to fight against the resistance of the intact MCL and moreover, the instrument poses as an obstruction in the operative field.

According to the literature, there are anatomical variants in the division of the popliteal artery. An aberrant high branch of the anterior tibial artery running posterior to the popliteus muscle has previously been reported [29, 30]. Therefore, placement of the PTR after releasing the popliteus off the posterior aspect of the proximal tibia

will offer excellent protection of the NVS while the surgeon saw the posterior tibial cortex. Feedback of contact between the saw tip and the PTR confirms that the posterior cortex has been osteotomized.

We recently changed our practice and currently use a second surgical window through the same skin incision. This secondary window is created behind the posterior-oblique ligament anterior to the medial gastrocnemius, tangential to the hamstrings.

A soft instrument such as a blunt Hohmann retractor is inserted touching the posterior cortex of the tibia and then progressed to be placed anterior to the popliteus muscle to the posterior aspect of the fibular head.

This posterior window allows complete protection of the NVS by pushing away the popliteus muscle from the tibial cortex (and thus the oscillating saw) (Fig. 9.2). Besides offering complete protection of the NVS, positioning the posterior retractor through a second surgical window along the posterior border of the MCL allows us to perform a controlled and patient-specific release following opening of the osteotomy. We therefore have the potential to prevent both excessive pressure (from under release) on the medial compartment and medial instability (from over release).

9.4 Why Intra-Articular Wear and Soft Tissue Management Are the Most Complex Issues in Knee Osteotomies?

Preoperative planning for correcting lower limb alignment is essential to define tibial, femoral, and intra-articular morphologies in osteotomy surgery. Various methods have been advocated to plan and perform osteotomy with optimized accuracy [31–35]. However, in certain cases, surgeons often fail to achieve the desired level of correction due to the unpredictable influence of intra-articular deformity correction [9, 11, 36–38]. The soft tissue tension and intra-articular deformity are approximated by the joint line convergence angle (JLCA) which is rarely taken into consideration or measured intraoperatively [11].

There are two main considerations of the JLCA when performing osteotomy surgery:

Firstly, patients with preoperative JLCA greater than 3° on standing radiographs are more

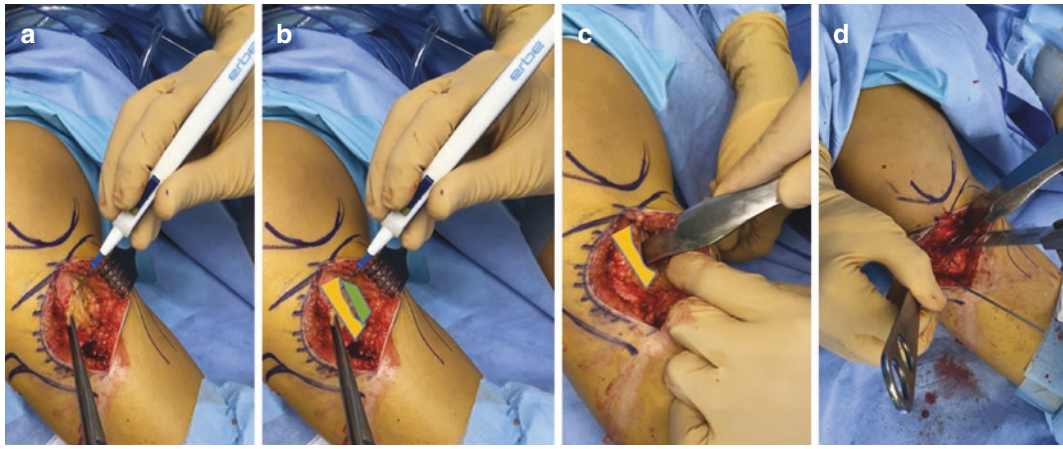

Fig. 9.2 (**a**–**d**) Double-level osteotomy performed with both tibial and femoral deformities: (**a**) The pes anserinus is detached from the tibia to expose the superficial medial collateral ligament; (**b**) The secondary posterior window is created behind the Posterior-Oblique Ligament anterior to the medial gastrocnemius, tangential to the Hamstring; (**c**) The "blunt" Hohmann retractor is inserted which touches the posterior cortex of the tibia and is slowly progressed until it is anterior to the popliteus muscle to the posterior aspect of the fibular head; (**d**) The neurovascular structures are protected by this posterior window thus allowing the oscillating saw to perform the osteotomy safely

likely to have a discrepancy in mechanical axis between supine and standing positions [39].

Secondly, JLCA is often enveloped in lower limb deformity analysis and thus "transformed" into the bony correction during osteotomy planning.

Noyes et al. described anatomic abnormalities of the varus knees into three categories:

Primary varus refers to tibiofemoral osseous alignment and geometry, whereas double varus refers to added varus due to separation of the lateral tibiofemoral compartment by deficiency of the lateral soft tissues [40]. Finally, triple varus has similar features than double varus but includes recurvatum in extension with severe deficiency of the posterolateral ligamentous structures.

In this way the preoperative planning should not only involve the mechanical axis but also differentiate bony and intra-articular deformities due to osteoarthritis (OA) and soft tissue laxity.

In preoperative planning, this can be measured between the lines connecting the distal femur and the proximal tibial articular surfaces on anteroposterior weightbearing long-leg radiographs [41–43].

Then, the hip-knee-ankle (HKA) angle results from the sum of tibial, femoral, and intra-articular morphologies, as represented by the medial proximal tibial angle (MPTA), the lateral distal femoral angle (LDFA), and the JLCA [42].

Many studies have reported differences in preoperative digital planning and postoperative achieved corrections due to the influence of soft tissue laxity which has not been accounted for prior to the osteotomy [11, 36–38]. The aim of planning is to obtain a predictable mechanical correction, and by not considering the JLCA in these calculations, there is an increased risk of overcorrection. Once the tibial and/or femoral correction has been performed, the previously elevated JLCA may be reduced to 0, resulting in an overcorrection.

In our daily practice we have used a simple equation to account for the influence of soft tissue laxity for preventing an overcorrection. A preoperative JLCA $\leq 2°$ can be considered as normal and in this case, no soft tissue correction should be considered. In this case, any intra-articular deformity might be totally or partially corrected during lower limb deformity correction.

For a JLCA greater than this, we estimate the value to be subtracted from the planned correction to be = (JLCA − 2)/2, to avoid overcorrection.

For example, if a patient had 6° of varus in the proximal tibia and a JLCA of 6° this corresponds to an intra-articular varus deformity of 4° (considering normal JLCA lower than 2°), the femur is neutral thus giving a global mechanical axis of 12° varus (global HKA 168°), we would consider a valgus overcorrection of 3° with a 13° of corrective osteotomy (6° tibia + 3° overcorrection + 4° intra-articular).

Firstly, this is likely to lead to an abnormal MPTA with a high risk of joint line obliquity unless a double-level osteotomy was performed (Fig. 9.3) but secondly the risk would be to have an overcorrection due to the intra-articular deformity (JLCA = 6°) which could only be partially corrected by the osteotomy. In this case, a correction based towards a "kinematic osteotomy" concept would be favourable, and we usually aim to only partially correct the intra-articular deformity. Following our formula above we would obtain a corrective value by subtracting from the planned correction of 13°, our planned intra-articular correction would be 2°: (JLCA − 2)/2 = (6 − 2)/2.

9.5 How to Improve Accuracy: CAO (Computer-Assisted Osteotomy)/PSI (Patient-Specific Instrumentation)/Robots

OWHTO is now a successful operation requiring an individualised approach to choose the intended correction. Preoperative planning and perioperative achievement of the target correction is a critical step when performing knee osteotomy. Using conventional techniques, the target correction may be difficult to obtain with substantial under- or overcorrection in HTO [4].

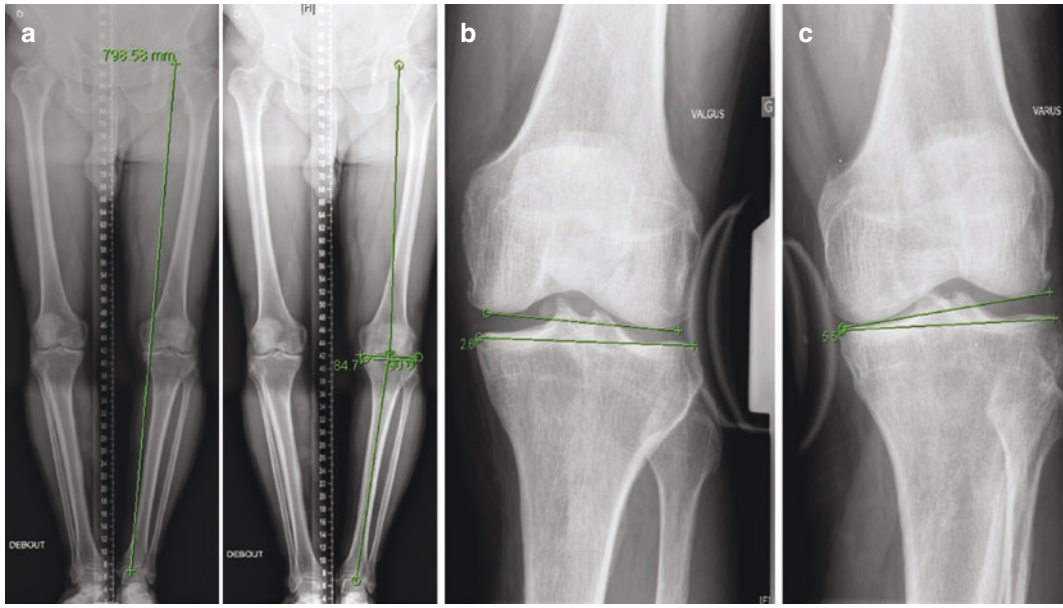

Fig. 9.3 (**a**–**c**) Double-level osteotomy performed with both tibial and femoral deformities: (**a**) Tibiofemoral varus associated with intra-articular deformity, the joint line convergence angle can be better assessed by stress radiographs because varus/valgus laxity appears to be important to predict influence of soft tissue laxity; (**b**) Valgus stress radiographs; (**c**) Varus stress radiographs

Newer technologies such as navigation have shown a more accurate and reproducible correction of the deformity with navigation both in frontal and sagittal plane [44]. More recently, patient-specific instrumentation (PSI) has developed allowing intraoperative precision [45].

Computer-assisted osteotomy (CAO) is a real-time aid that uses a navigation system to register anatomical landmarks intraoperatively allowing image acquisition but also dynamic references of the femur and the tibia. Navigation has been shown by some studies to be more accurate than conventional methods [44, 46, 47]. Bae et al. demonstrated a success rate of 86% in patients assisted by computer navigation against only 50% success in the conventional group [15]. However, its use is not widespread among orthopaedic surgeons and Schröter et al found no difference between the groups and argues that equivalent surgical accuracy does not justify the increased expense and surgical time associated with navigated OWHTO [48].

PSI is based on a 3D preoperative planning achieved after the analysis of an initial CT (computed tomography) scan which acquires reference points from the centre of the femoral head, centre of the knee (that captures the distal femur and the proximal tibia) and lastly one over the centre of the ankle [32]. The simulated correction is validated by the surgeon and a patient-specific cutting guide is created. PSI allows a surgeon to produce an accurate correction [25, 49] and consequently this has been proved to potentially shorten the operative time by 70% in comparison to conventional techniques with a decrease in the number of per-operative fluoroscopic images required after a short learning curve [50]. When comparing PSI to conventional methods, the accuracy of the achieved final correction is slightly better with PSI without significant difference [51].

Robotic arm has gained popularity for assisted total knee arthroplasty without improvements in short-term clinical outcomes compared to conventional instrumentation [52, 53] with a resultant increase in operative time and higher overall costs [54]. The place for robotic surgery in creating osteotomies needs to be uncertain, however

one study which includes robot-assisted system has reported to increase the accuracy and reproducibility for closed wedge osteotomy [55] but currently any clinical evidence concerning robotic assistance and osteotomy surgery is lacking.

Navigation and PSI provide accuracy, however, they are performed with the patient in a supine position which may lead to discrepancies between preoperatively planned correction and postoperative alignment as the overall lower limb alignment under weightbearing conditions may be overcorrected if the surgeon relies solely on navigation [9] as the JLCA changes between supine and bipedal stances [56].

Finally, further studies comparing conventional methods, navigation and PSI will also endure the question of accuracy. Previously only one study has compared the results of these three techniques [57]. But the main criterion used was the HKA angle thus providing only an indirect vision of the correction resulted.

9.6 Sagittal (Un)intentional Correction and Patellar Height in Knee Osteotomy

The measurement of Posterior Tibial slope (PTS) has been widely studied for its causal relationship to the change in tibial translation [58], knee joint stability [59] and anterior cruciate ligament injuries [60]. While considerable research has been devoted toward exploring the former anatomic morphological characteristics [61], the PTS has only recently gained attention as an anatomical predictor of anterior cruciate ligament (ACL) tears. An increased tibial slope (≥12°) was shown to be a risk factor for ACL rupture [62] and failure of ACL repair [63], some authors [64, 65] advocate performing an osteotomy in order to correct the PTS after repeated failures of ACL repair.

For many authors, the correction target is a posterior tibial slope between 3° and 5° [65]. In our osteotomies, we set the correction target to give a 7° of posterior slope.

Kiapour et al. show that increased coronal tibial slope is associated with inferior clinical outcomes after ACL reconstruction. Correction of the varus deformity is an important factor for the success of the procedure [66, 67]. A combined varus high tibial osteotomy and ACL reconstruction procedure shows significant improvement in postoperative functional outcomes and low rates of complications, re-ruptures or revision surgery [68, 69]. The target is a slight overcorrection to an alignment with 1°–3° of valgus.

Three most common complications in these procedures are a lack of range of motion, deep vein thrombosis and need for hardware removal [69]. Smaller numbers of peroneal nerve or vascular injuries have been reported [68].

In our experience, we use two different approaches based on the main deformity to correct, if varus is the main target, a posteromedial opening wedge is often use (Fig. 9.4). When slope correction is predominant, an anterior closing wedge is selected (Fig. 9.5).

Finally, when a substantial correction is needed in both planes and specifically in cases where the lateral slope is more abnormal than the medial side, an asymmetric anterior closing wedge might be used.

Patellar height is often mentioned as a crucial problem in slope changing osteotomy; however, the measurement methods for patellar height are often based on the anterior border of the tibial surface as for the Blackburne-Peel or Caton-Deschamps index. Those measurements are dependent on the changes of tibial slope which may be affected by the tibial inclination and/or anteroposterior translation of the proximal fragment after osteotomy. A correlation has been found between the loss of tibial inclination and subsequent change in the ratio of patellar height [70]. Similarly, an anterior-inclined osteotomy in the sagittal plane tends to result in anterior translation of the proximal fragment which can artificially decrease the ratio of patellar height [71]. If one accepts that an opening wedge HTO leads to a decreased patellar height due to the elevation of the tibial joint surface, this concept may be challenged in futures studies with three-dimensional

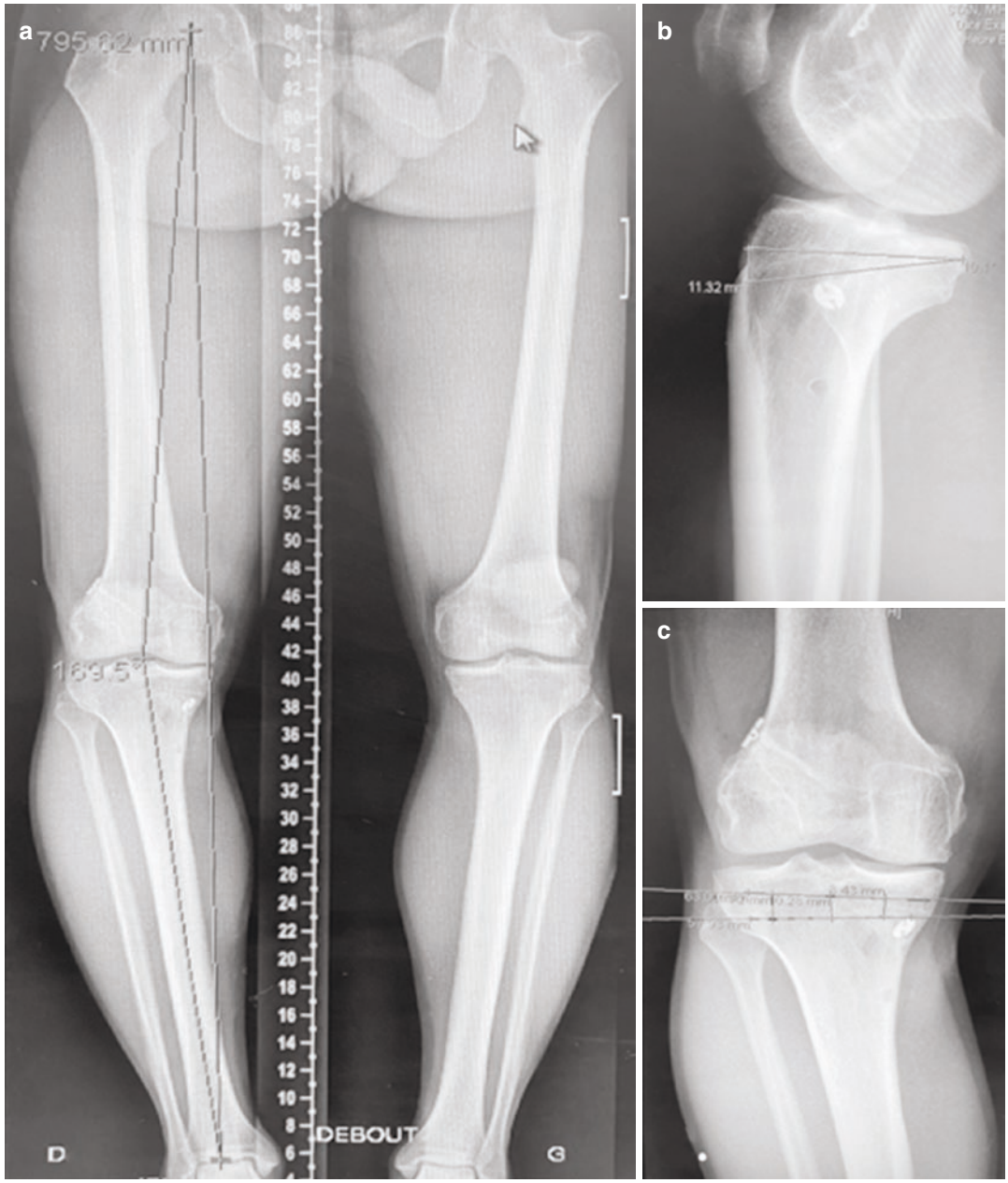

Fig. 9.4 (**a**–**c**) Planning for asymmetric anterior closing wedge high tibial osteotomy (HTO) in a 31-year-old professional athlete suffering from post-meniscectomy pain, substantial varus deformity and third anterior cruciate ligament (ACL) reconstruction re-rupture: (**a**) Preoperative varus on the HKA (hip-knee-ankle) angle (10.5°); (**b**) In this case the tibial slope is excessive and 10° of correction is planned to avoid ACL re-rupture; (**c**) The main concern of this patient is the coronal deformity, thus a posteromedial opening wedge HTO is planned

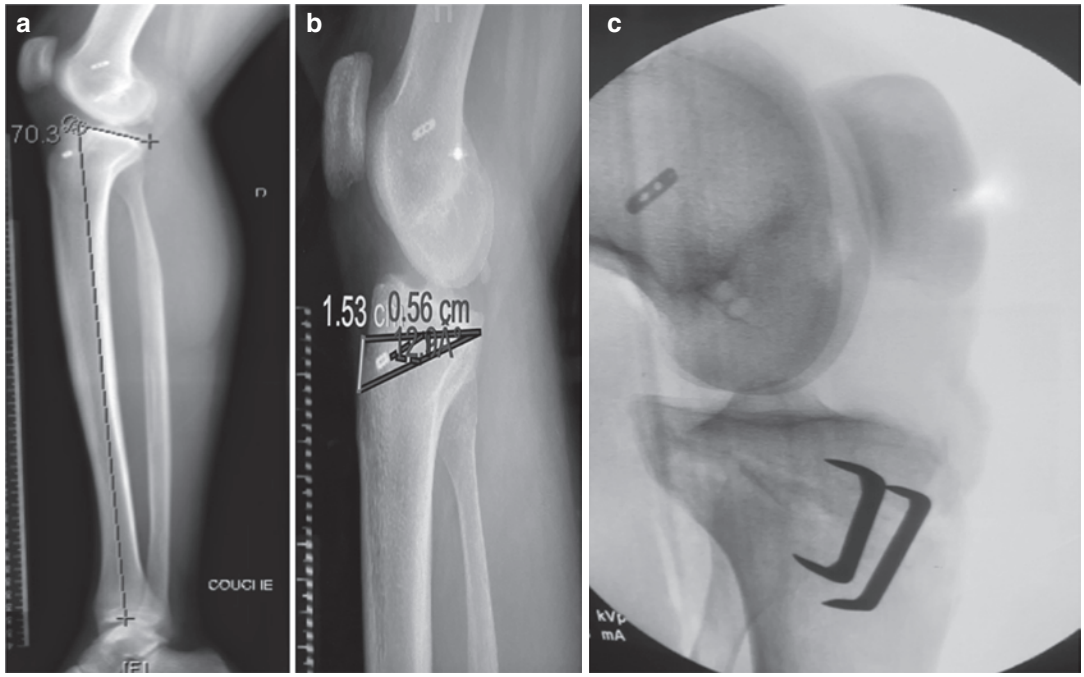

Fig. 9.5 (**a**–**c**) Patient with re-rupture of the anterior cruciate ligament (ACL) planned for anterior closing wedge high tibial osteotomy (HTO) has been selected: (**a**) In this case, the patient had a re-rupture of the ACL with an excessive posterior tibial slope of 20° (**b**); (**c**) Without major coronal deformity, an isolated anterior closing wedge osteotomy has been selected

evaluation of an osteotomy on the impact on patellar height.

9.7 Is It Necessary to Fill the Osteotomy Gap in Opening Wedge High Tibial Osteotomy?

Following the initial description of medial opening wedge high tibial osteotomy (MOWHTO), osteotomy gap grafting was advocated, primarily to prevent correction loss and reduce the risk of non-union. Currently, motivations for using void fillers are to reduce swelling and consequently post-op pain. Structural bone grafts in the form of wedges are also thought to improve construct stability, allowing for earlier full weightbearing and accelerated rehabilitation. With osteotomy gaps of <10 mm, there has been no reported difference in complication rates or loss of correction and equivalent clinical/radiological outcomes by 12–24 months when comparing no void filling to filling with autograft, allograft or synthetic graft [72–78]. The mean bony union time with either technique was 12.4–13.7 weeks [78–80]. Biomechanical studies demonstrate that osteotomy gap filling with structural filler is superior, with less alteration of tibial slope, less stress on the plate/lateral hinge, and the potential to significantly increase load to failure [81, 82].

Despite improved biomechanics, the 10-year survival of MOWHTO with or without void filling has been demonstrated to be similar at approximately 88% (with patients aged 37–72) [83]. There was no increase in long-term complications without gap filling, even when converting to total knee replacement (TKR). The advent/addition of locking plate (LP) fixation has been a major advancement in osteotomy surgery. Lansdaal et al. [84] demonstrated that immediate weightbearing in patients with no osteotomy gap filling has no detrimental effects,

equivalent functional outcome scores, VAS (visual analog scale) pain scores and no loss of correction when compared to traditional delayed weightbearing and void filling groups. Despite modern superior fixation there are circumstances when the construct stability is reduced and there is increased potential risk of non-union. In this scenario void filling is advisable and indications include lateral cortex fracture, a body mass index (BMI) > 30 and correction of >10° [85]. The threshold gap size at which void filling is necessary is more widely debated, with authors recommending gap filling above 10–14 mm [77, 79, 86–88] with a positive correlation between the size of the gap and healing time [78, 79]. When osteotomy gap filling is considered, autograft and allograft are comparable in terms of final clinical outcome. Autograft is associated with donor site morbidity, whereas allograft involves increased cost [76, 89]. Synthetic bone substitutes in comparison are associated with a small increased risk of non-union and their costs can be prohibitive [72, 77, 90]. A level 1 study comparing allograft chips and tricalcium phosphate (TCP), demonstrated no difference in union [91].

A recent meta-analysis, from the Basel Team, demonstrated that bone graft (allo- or autograft) allowed better functional results than synthetic materials [77]. We have been using femoral head allograft for 4 years now, and completely abandon calcium phosphate cement due to adverse outcomes and specific complication [25] (Fig. 9.6).

In conclusion, the osteotomy gap filling is not necessary for modest gaps if LP fixation is used. Filling of the void should be considered for large gaps/corrections, unstable hinge/lateral cortex fractures, patients with a high BMI or at increased risk of non-union. It is generally accepted in the literature that filling the osteotomy gap with allograft, autograft or synthetic grafts may be utilised with improved early clinical outcomes (at 3 months) but equivalent outcomes at 12 months, when compared to not filling the osteotomy gap.

Recent literature favours bone materials to enhance clinical outcomes and avoid specific complication related to synthetic material resorption.

9.8 Conclusions

An ideal range of postoperative mechanical axis of 2°–7° valgus is classically recommended to provide favourable clinical results after OWHTO. Correction mistakes and malalignment are well documented in previous studies and it is well known that under- or overcorrection following OWHTO can lead to complications and patient dissatisfaction. Thus, excessive overcorrection of the tibia is associated with lower functional results and may lead to an excessive JLO that could lead to detrimental stresses to the joint

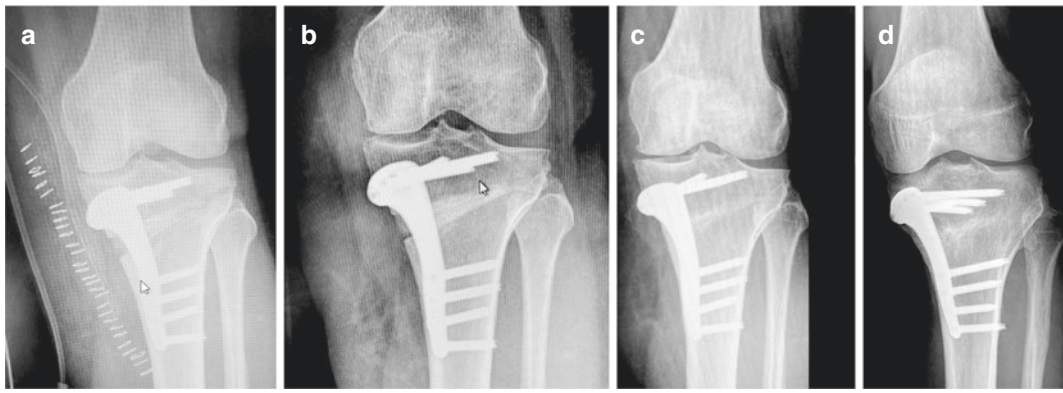

Fig. 9.6 (**a–d**) Illustrating from immediate post-op (**a**) to 3 months (**b**), 6 months (**c**) and 1 year (**d**) follow-up the osteotomy gap evolution using femoral head sculpted allograft

cartilage. It is still not clear as to what extent of an overcorrection of the MPTA after OWHTO is acceptable. To avoid abnormal tibial or femoral anatomy and an oblique joint line, osteotomies should be carried out at the location of the deformity which reiterates the importance of having knowledge of normal tibial and femoral angular values. Previous studies have shown a mean alignment of 3°–4° varus for the tibia and 3°–4° valgus for the femur in the non-osteoarthritic population.

The osteotomy gap filling is not needed for modest gaps if LP fixation is used. Filling of the void should be considered for large gaps/corrections, unstable hinge/lateral cortex fractures, patients with a high BMI or at risk of non-union. It is generally accepted in the literature that filling the osteotomy gap with allograft, autograft or synthetic grafts may be utilised with improved early clinical results (at 3 months) but equivalent results at 12 months, when compared to not filling the osteotomy gap. Recent literature favours bone materials to enhance clinical outcomes and avoid specific complication related to synthetic material resorption.

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10 Upper Tibial Osteotomy or Unicompartmental Knee Arthroplasty for Medial Compartment Knee Osteoarthritis: Evidence-Based Indications for Treatment

Alexander D. Shearman, Nicholas J. Bottomley, William F. M. Jackson, and Andrew J. Price

10.1 Introduction

Osteoarthritis (OA) is a chronic disease in which structural changes to a joint lead to progressive immobility and dysfunction. Knee OA is highly prevalent and the incidence is increasing [1]. The overall cost of osteoarthritis in the UK has been estimated to be over £4 billion, directly through treatments such as medicines or operations, and indirectly through time off work and community services [2]. There is no cure and currently available treatments aim to either delay progression of disease or to alleviate symptoms.

Total knee arthroplasty (TKA) is a highly successful treatment for end-stage knee OA. Over 92,000 TKA procedures were performed between 2018 and 2019 in the UK [3], 98% of which were for OA. However it has been estimated that up to a third of patients with knee OA have disease isolated to a single compartment of the knee [4]. Isolated medial compartment OA accounts for the majority of cases [5].

Additionally, there exists a cohort of patients with severe symptoms of OA who exhibit little in the way of radiographic disease, historically labelled the 'treatment gap' [6], as arthroplasty is associated with poor outcome and is therefore rarely indicated.

Upper or High Tibial Osteotomy (HTO) and Unicompartmental Knee Arthroplasty (UKA) are both successful treatments for isolated medial compartment OA in the varus knee. HTO is an extra-articular procedure that alters the coronal alignment of the limb such that the patient's weight-bearing axis (WBA) no longer passes through the symptomatic compartment (Fig. 10.1a), preserving the joint surfaces. UKA is an intra-articular procedure aiming to resurface the diseased joint surfaces and preserves constitutional varus alignment of the joint (Fig. 10.1b).

Despite radically different approaches in treatment there has historically been debate as to which option is preferred for patients in whom HTO and UKA could be considered equally appropriate. The surgeon's discretion often guides the decision of the patient in this scenario.

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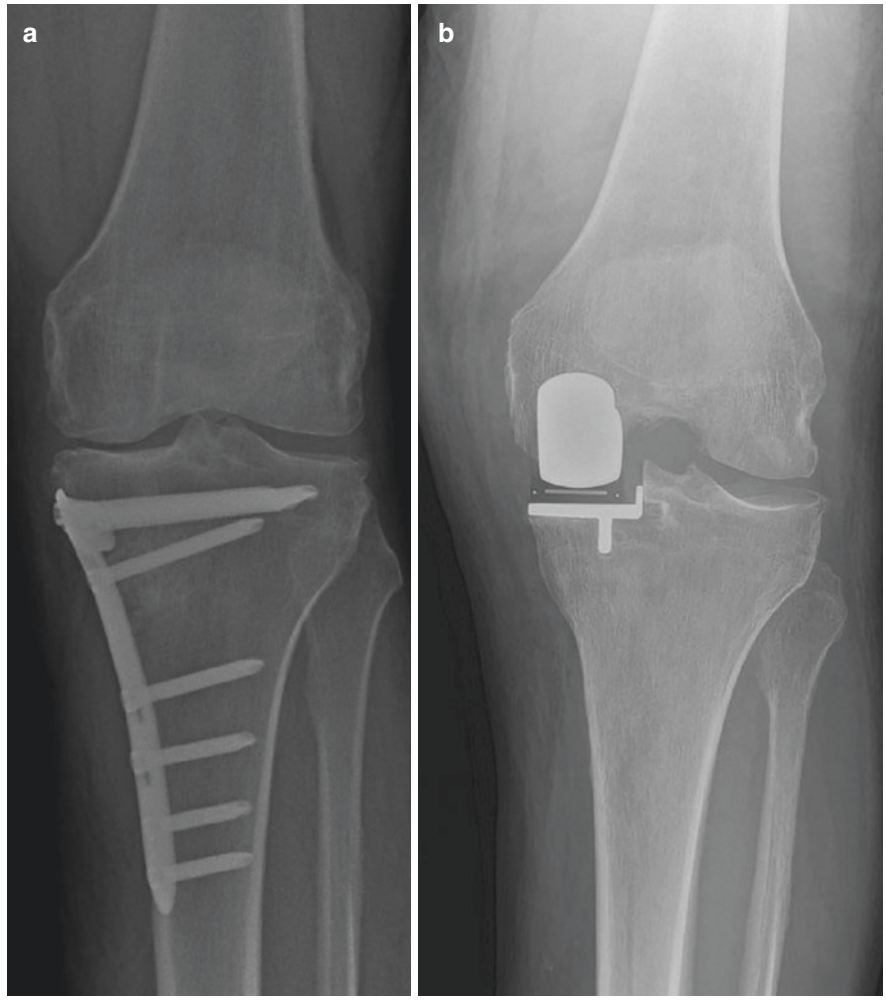

Fig. 10.1 (**a**, **b**) High tibial osteotomy (medial opening wedge) and (**b**) unicompartmental knee arthroplasty

10.2 Factors Determining Treatment in Medial Compartment OA

10.2.1 Disease Severity

Patients presenting to the orthopaedic surgeon with knee OA are often described as having 'mild', 'moderate' or 'severe' disease. Attempts to define these terms take on both clinical and radiological contexts.

Severity based on symptomatology relies on a thorough clinical assessment and will help the surgeon to frame the patient's symptoms in the context of their social circumstances. Knee related Patient-Reported Outcome Measures (PROMs) may help to quantify this [7].

Radiographic severity is typically quantified using the Ahlback or Kellgren-Lawrence Grading systems (Table 10.1), both of which rely on high-quality weight-bearing radiographs.

Clinical features often determine need for intervention, whereas radiological findings inform available treatments.

MRI imaging can be helpful in determining disease severity in some patients (Fig. 10.2) where radiographs do not detect full thickness articular loss. This may reduce the size of the

Table 10.1 Ahlback and Kellgren-Lawrence classification systems

Ahlback classification [8]		Kellgren-Lawrence classification [9]	
		I	Doubtful narrowing of joint space, possible osteophytic lipping
		II	Definite osteophytes, possible narrowing of joint space
I	Joint space narrowing (<3 mm)	III	Moderate multiple osteophytes, definite joint space narrowing, some sclerosis, possible deformity of bone ends
II	Joint space obliteration	IV	Large osteophytes, marked joint space narrowing, severe sclerosis, definite bony end deformity
III	Minor bone attrition (<5 mm)		
IV	Moderate bone attrition (5–10 mm)		
V	Severe bone attrition (>10 mm)		

treatment gap, as patients determined to have full thickness disease are more likely to report satisfactory outcome with arthroplasty.

10.2.2 Disease Chronicity

In addition to severity patients with knee OA can be defined by the time point in their disease process at which they develop symptoms. As OA is a chronically progressive condition patients may be presenting to the orthopaedic clinic at an early or late stage of the disease process.

Early knee OA can be defined as knee pain associated with radiographic change (Kellgren-Lawrence 0-2) and arthroscopic or MR evidence of articular cartilage degeneration [10]. Severity of symptoms does not correlate with stage of disease and the pain suffered by patients early knee OA can often be as severe and debilitating as those with end stage disease [7].

The fate of early knee OA can vary: symptoms may stabilize without structural progression, symptoms may deteriorate without structural progression or there may be structural progression with or without symptom change. It is difficult to predict which path a patient will follow. It is important from the history to try and determine which course a patient is following as this may impact on treatment choices.

10.2.3 Deformity Analysis

Lower limb alignment has previously been shown to be both highly variable and predictive of knee OA [11]. Patients within the treatment gap who have significant metaphyseal varus of their tibia are highly likely to develop structural progression of knee OA over a 24 month period [12]. Correcting metaphyseal varus using HTO is therefore an attractive method of preventing OA progression but of also unloading the affected compartment and improving their current symptoms.

There are a relatively small number of patients in whom deformity leading to varus knee OA originates from the femur and not the tibia. In these cases, corrective femoral osteotomy may be indicated. Equally, double osteotomy has been described for patients with femoral and tibial deformity, or in those with such significant malalignment, correction of the WBA by HTO alone would lead to severe obliquity of the joint line [13].

10.3 HTO and UKA in the Treatment of Medial Compartment OA

10.3.1 Upper Tibial Osteotomy

In 1961 Jackson and Waugh described the first use of HTO to treat compartmental osteoarthritis without internal fixation [14]. Early treatments using lateral closing wedge techniques, described by Gariépy and Coventry among others, have given way to more modern techniques [15, 16]. Digitally planned biplanar osteotomies using

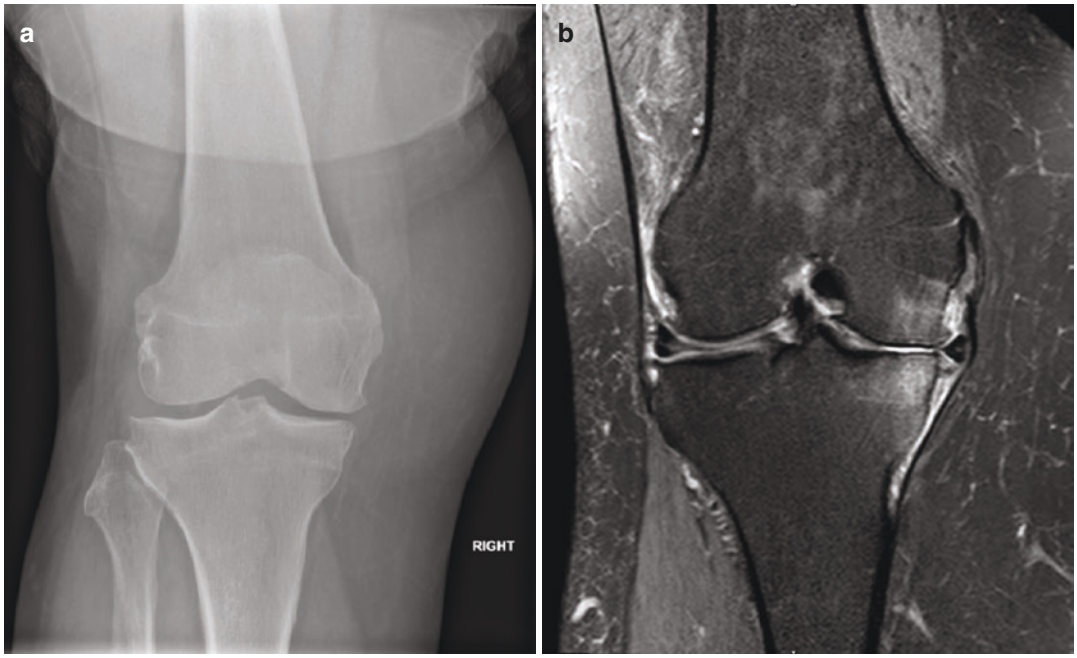

Fig. 10.2 (**a**, **b**) XR (**a**) and MRI (**b**) imaging of the same knee: full thickness chondral loss visualized on the MRI despite Ahlback 1 appearances on the plain film radiographs

locking plates have increased accuracy and reduced surgical variation [17]. Combined with a greater understanding of deformity analysis [18] and required correction point [19, 20], the similarities of modern-day osteotomy to its historical counterparts are almost non-existent. This can make assessment of long-term treatment outcomes challenging.

Indications for modern knee osteotomy are varied, including treatments for instability, deformity and arthrosis. The United Kingdom Knee Osteotomy Registry (UKKOR) first annual report examined a cohort of 620 patients undergoing osteotomy surgery in the UK over a 3 year period [21]. The majority of these (526) were HTOs. Osteoarthritis was the recorded indication in 79.1% of cases. In these cases, radiographic disease grade was Kellgren-Lawrence 2 or 3 in 62% of cases and Grade 4 in 18% of cases.

The International Society of Arthroscopy, Knee Surgery and Orthopaedic Sports Medicine (ISAKOS) has previously published guidelines referring to 'ideal', 'possible' and 'not suited' patient groups for HTO [22] (Table 10.2).

HTO for varus is most commonly performed using a medial opening wedge or lateral closing wedge technique. A randomized study of 92 patients undergoing either technique demonstrated a higher complication rate in opening wedge techniques although lateral closing wedge HTO was associated with a higher conversion to TKA [23]. Osteotomy is used in end-stage OA [21] although an Ahlback score of >II has been shown to independently predict dissatisfaction with HTO [24]. Lobenhoffer has demonstrated satisfactory increases in Oxford Knee Score (OKS) in patients regardless of disease severity although final OKS was lower in patients with worse pre-operative structural disease [25].

10.3.2 Unicompartmental Knee Arthroplasty

Initially an interpositional metal implant [26] and then a hemiarthroplasty of the tibial plateau [27, 28], early UKA design expanded significantly in the early 1970s, with multiple implants reflecting

Table 10.2 ISAKOS (International Society of Arthroscopy, Knee Surgery and Orthopaedic Sports Medicine) guidelines for knee osteotomy

Ideal candidate	Possible but not ideal	Not suited
Isolated medial joint line pain	Flexion contracture <15°	Bicompartmental (medial and lateral OA)
Age 40–60 year old	Previous infection	Fixed flexion contracture >25°
BMI <30	Age 60–70 or <40	Obese
High demand activity (not running/jumping)	ACL/PCL/PLC insufficiency	Meniscectomy in other compartment
Malalignment <15°	Moderate patellofemoral OA	
Metaphyseal varus TBVA >5°	Wish to continue all sports	
Full range of movement		
Normal lateral and PF compartments		
Ahlback Grade I to IV		
No cupula		
Normal ligament balance		
Non-smoker		
Some level of pain tolerance		

OA Osteoarthritis, *ACL* Anterior cruciate ligament, *PCL* Posterior cruciate ligament, *TBVA* tibia bone varus angle, *PF* Patellofemoral

an increase in popularity among surgeons. Mixed results in the medium term reflected a lack of appropriate selection criteria [29, 30] by surgeons, leading to a strict and limited description of indications by Kozinn and Scott in 1989 [31]. Results were subsequently seen to improve. However, the number of patients meeting these criteria was estimated to be as low as 6% [32], leading to a critical review of indications for UKA.

Currently medial UKA is recommended for patients who are symptomatic with bone-on-bone anteromedial OA in the medial tibiofemoral compartment, preserved full thickness cartilage in the lateral compartment, a functional medial collateral ligament (MCL) and a functional anterior cruciate ligament (ACL) [33]. Patellofemoral (PF) disease is not a contraindication to medial UKA, provided there is no significant lateral facet disease. Survival of up to 91% at 15 years has been shown in the Oxford knee by adhering to these indications [34].

UKA is not however recommended in patients who do not have end-stage knee OA. This is on the basis that improvements are unpredictable and the reintervention rate is higher [35–37].

10.4 Comparison of HTO vs UKA

Despite fairly separate evolutions resulting in different indications, HTO and UKA have often been compared with each other across similar patient groups.

10.4.1 Pain and Functional Outcomes

A meta-analysis of comparative studies found ten appropriate studies examining the difference between the two groups [38]. In this study, osteotomy technique was not standardized, and radiological severity was either unclear or included patients with partial thickness disease (Kellgren-Lawrence 3/Ahlback 1). Two randomized controlled studies were included [39, 40], both of which employed a traditional lateral closing wedge technique and included patients with variable radiographic disease. Neither detected a significant difference between procedures in terms of functional improvement. In a comparative study of over 100 patients undergoing medial opening wedge HTO or UKA, Dettoni reports better knee society scores in patients undergoing UKA, whilst

patients undergoing HTO reported better function [41]. Patients in the HTO cohort were on average 10 years younger than the UKA cohort.

HTO has been seen to be an operation for patients with high functional demands including sports activities. The impact that these activities have on arthroplasty is uncertain, and previously may have deterred surgeons from offering UKA to younger or more active patients, despite end stage disease.

A recent pooled analysis of 1622 UKAs and 401 medial opening wedge HTOs reported an average age of 48.4 in the HTO group and 60.6 in the UKA group [42]. In these groups average increase in OKS was similar in both HTO and UKA but there was a better improvement in Lysholm and Tegner functional scores seen in patients undergoing UKA. However, patients receiving HTO tended to have better functional scores pre-operatively, and radiographic grade of disease at the time of surgery was not reported.

UKKOR has reported an average improvement in OKS by 11.7 points at 1 year (25.11–36.82) and a mean change in EuroQol-5D (EQ-5D) score from 0.55 to 0.70 at 1 year and 0.74 at 2 years.

Comparatively, the recently published TOPKAT study reported 5-year functional outcomes in over 200 UKAs in a multicentre trial comparing UKA to TKA for medial compartment OA. OKS saw on average an increase of 19.2 points (18.8–38.0). EQ-5D improved similarly (0.428–0.744) [43].

10.4.2 Survival

HTO survival has been reported as 80% and 56% at 5 and 10 years, respectively. Patients who were older and with co-morbidities were more likely to be revised to TKA [44].

UKA is reported in multiple longitudinal studies to have survival rates between 82 and 85% at 10 years [45–48]. UK Registries report cumulative revision rates as low as 5.9% at 10 years for specific implants [3].

Although UKA is technically possible after HTO, the most common surgical treatment for failed HTO is total knee arthroplasty. TKA following reconstruction either with UKA or HTO is more complex, potentially requiring revision augments or stems. There is some evidence that TKA after closing wedge HTO or UKA has a higher risk of re-revision compared to primary TKA [49].

Average time to revision is similar in both groups (8.2 years for UKA versus 9.7 years for HTO) [50]. Patient reported outcomes including satisfaction are similar for TKA following UKA or HTO.

10.5 Shared Decision Making in the Surgical Treatment of Medial Compartment OA

In light of the Montgomery vs Lanarkshire ruling, there has been further emphasis in the UK on involvement of patients in their own care [51]. Shared decision making (SDM) is the process by which patients are ‘supported to (a) understand the care, treatment and support options available and the risks, benefits and consequences of those options, and (b) make a decision about a preferred course of action, based on evidence-based, good quality information and their personal preferences’ [52].

Embedding SDM in clinical pathways is critical to ensure patients remain satisfied with the care they receive and are not potentially harmed by treatments without evidence-based indications. This is relevant to the case of medial compartment osteoarthritis, where non-operative treatments such as physiotherapy may have clinical effects that approach those of surgery [53]. Equally, by taking a patient’s personal preferences and social circumstances into account, different treatment options may be more appropriate for similar conditions.

10.5.1 Summary

The independent evolution of HTO and UKA over time has led to altering indications for each procedure which may have inadvertently led to

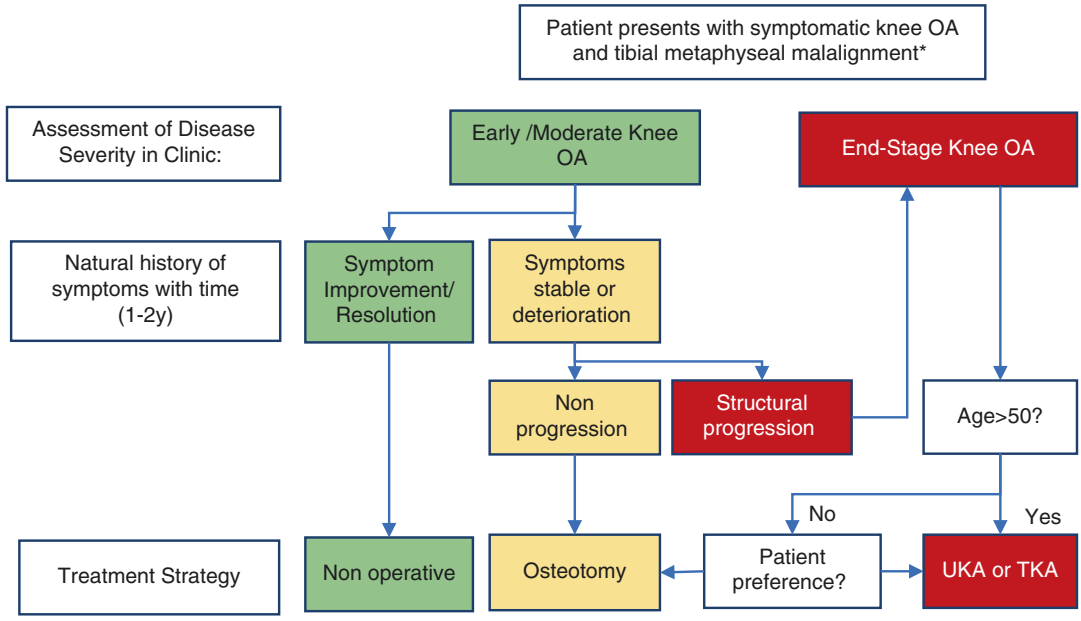

Fig. 10.3 Suggested flow diagram for patients presenting with symptoms from medial compartment OA and metaphyseal malalignment. *Defined using long leg radiographs TBVA >5°

Table 10.3 Variable indications for HTO or UKA, or both

Discriminator:	HTO	UKA	HTO or UKA
Radiographic severity	Variable thickness disease	Full thickness disease	Full thickness disease
Alignment	Metaphyseal varus	Metaphyseal or intra-articular varus	Metaphyseal varus
ACL status	Not required	Functional	Functional

HTO High tibial osteotomy, *UKA* Unicompartmental knee arthroplasty, *ACL* Anterior cruciate ligament

some overlap in opinion as to which is the best treatment option for patients suffering with medial compartment osteoarthritis. The reality is that HTO and UKA are both excellent treatment options for different patient groups. Measuring one treatment against the other is not helpful.

Having separately reviewed indications for HTO and UKA in medial compartment OA, it is apparent that HTO may be indicated for variable radiographic disease severity in patients with metaphyseal varus, whereas UKA is indicated in patients with full thickness (severe) radiographic disease in a functionally stable knee. A proposed flow diagram is shown in Fig. 10.3.

The group of patients in whom both procedures are appropriate (Table 10.3) are those with full thickness disease, metaphyseal malalignment, a functionally stable joint, and are of an age where joint replacement is not ideal. This is a small group of patients to treat and outcomes are variable regardless of the selected treatment. Shared decision making is a critical step in these challenging cases.

10.6 Conclusions

In older patients UKA or TKA is recommended for symptomatic end-stage osteoarthritis of the knee as outcomes are reliably excellent. MRI can help determine full thickness disease in some cases.

In patients with structural tibial deformity and evidence of early or moderate knee OA, HTO is recommended for patients who have failed non-

operative treatment. Further studies into the natural history of early knee OA are required to fully understand the optimal time point for surgical intervention.

In reality, the cohort of patients in whom HTO and UKA are equally indicated is very small. Younger patients with end-stage knee OA may be suitable for either HTO or UKA but outcomes can be variable in both options.

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11 Unicompartmental Knee Arthroplasty vs Total Knee Arthroplasty

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11.1 Introduction

The burden of knee osteoarthritis (OA) is substantial. Epidemiological studies suggest that the lifetime risk of developing symptomatic knee OA is approximately 50% [1]. For most patients with knee OA, the disease is restricted to the medial compartment [2]. The increasing prevalence of risk factors such as obesity, and an ageing population have led to projections that the number of knee arthroplasties performed each year will increase significantly (by up to 600% by 2030 [3]).

End-stage knee OA can be managed using two treatment options. Unicompartmental knee arthroplasty (UKA) replaces only the arthritic part of the joint, preserving normal joint surfaces and both cruciate ligaments, whereas total knee arthroplasty (TKA) replaces the entire knee joint [4].

For individuals with end-stage osteoarthritis of the knee, a substantial proportion (estimated to be between 25 and 47% of patients) could be candidates for UKA [5–7]. The evidence available in relation to UKA and TKA is interpreted differently and has resulted in significant variation between surgeons in the use of UKA ranging from 0% to over 50% [8].

In this chapter, the evidence in relation to factors including the indications, complications, reported revision/re-operation rate and functional outcomes of UKA and TKA is summarized.

11.2 Indications

The seminal paper on UKA by Kozinn and Scott [9] suggested very strict patient and disease criteria for the procedure. The authors state that patients who were younger than 60 years old, weighed over 82 kg, had exposed bone in the patellofemoral compartment, were highly physically active or demonstrated chondrocalcinosis on preoperative plain radiographs, or at arthrotomy, should not be offered UKA for fear of early failure of the implant. These strict selection criteria were based on their experience with early fixed bearing UKAs, where the principal mode of failure was aseptic loosening, and no empirical data were presented [10]. When the contraindications to UKA as proposed by Kozinn and Scott are applied to the knee arthroplasty population, only 6% would qualify [7].

There has been great progress in implant design over the intervening years. The development of new polyethylenes and the widespread use of mobile bearings [11] have rendered aseptic

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loosening uncommon as a mode of failure following UKA. This has led to a change in approach; rather than reserving UKA for a small, specific group of patients with 'ideal' characteristics, advocates of UKA suggest that it is a mainstream intervention which should be offered to all patients with suitable pathoanatomy, regardless of other patient characteristics [12]. The main indication for UKA is anteromedial osteoarthritis (AMOA) [13]. In AMOA, there should be bone-on-bone osteoarthritis of the medial compartment, a functionally normal medial collateral ligament and anterior cruciate ligament, and preserved full thickness cartilage in the lateral compartment [11]. Suitability for UKA can be confirmed by the presence of an anterior wear scar on the lateral radiograph and preservation of joint space in valgus stress or Rosenberg radiographs.

When a suitable implant is used with appropriate indications, early failure can be avoided in spite of these broad criteria for eligibility. Pandit et al. [10] studied the long-term survival in a prospective series of 1000 medial UKAs with a mobile bearing; 68% of the patients in the series had at least one of the contraindications described by Kozinn & Scott [9]. Within that sub-group the survival at 10 years was 97.0% (95% Confidence Interval (CI) 93.5–100%). The 10-year survival in the cohort of patients that did not fulfil any of Kozinn & Scott's contraindications was 93.6% (95% CI 87.2–100%). Additionally, Hamilton et al. [14] published a study on 458 patients with an average follow-up of 10.5 years. They found that in the context of full thickness cartilage on the lateral side at the time of surgery, the presence of lateral osteophytes did not compromise the long-term functional outcome or implant survival.

Of all the criteria for offering UKA, the presence of full thickness joint space loss in the affected compartment is the most important. Knifsund et al. [15] followed up 294 UKRs for an average of 8.7 years. The knees with a preoperative Kellgren-Lawrence grade of 0–2 OA on the pathological side had a higher risk of re-operation than those with Kellgren-Lawrence grade 3–4 (odds ratio = 1.89; 95% CI 1.03–3.45; $p = 0.04$). The authors concluded that UKR should only be performed in cases showing severe osteoarthritis in preoperative radiographs, with medial bone-on-bone contact, and a medial/lateral ratio of <20%.

A number of authors have explored the influence of patellofemoral wear or symptoms on the outcome of UKA, finding little evidence of an effect of clinical symptoms [16], radiological findings or intraoperative findings [17, 18] of patellofemoral disease. Most recently, Hamilton et al. [19] analysed the long-term outcomes of a group of patients that underwent UKA, a proportion of whom had anterior knee pain and patellofemoral joint (PFJ) OA. Preoperative anterior knee pain did not compromise the functional outcome or survival and the authors stated that PFJ OA should not be considered to be a contraindication. One exception to this was in the presence of severe damage to the lateral side of the PFJ with bone loss and grooving which was described as a contraindication to mobile-bearing UKA. Konan et al. [20] reiterated that topographical location and severity of cartilage damage of the patella can influence function after successful Oxford medial UKA. Patients documented lower mean satisfaction with pain and function and more difficulty climbing stairs when cartilage lesions were located centrally or laterally on the PFJ. The authors found that patients with medial chondral PFJ lesions behave in a similar way to patients with no chondral lesions.

11.3 Complications

UKA represents a substantially smaller intervention than TKA and would be expected to be associated with a lower rate of early adverse outcomes. This is supported by a comparison of adverse outcomes in over 100,000 UKAs and TKAs matched using a propensity score analysis based on 20 variables [21]. The study utilized data from the National Joint Registry (NJR) [8] and UKAs were found to have many advantages. Major medical complications such as thromboembolism, stroke, infection and myocardial infarction occurred between 25 and 50% less frequently

with UKAs. Additionally, intraoperative complications and the need for transfusions were a quarter of that found in TKA. The re-admission rate was also found to be one-third less. Mortality following UKA was also significantly lower with survival curves progressively separating for the first 4 years and remaining parallel thereafter. Subsequently, a large, multicentre pragmatic randomized trial comparing outcomes of UKA and TKA involving 528 patients, the TOPKAT trial, has been reported [22]. 5-year follow-up data found that patients receiving a TKA had more complications than those receiving a UKA, with the most common complications being unexplained pain and knee stiffness.

11.4 Revision Rate

Unadjusted data from international joint registries [8, 23] demonstrate that the revision rate of UKA is higher than for TKA, leading some to suggest that UKA is an inferior intervention to TKA and should not be offered to patients [24]. Whilst revision of the implant is a 'hard' outcome measure which is easy to measure, it is highly imperfect as a measure of patient-relevant outcome [25]. If implant survival is considered in isolation, patients who have died, undergone amputation, or have unsatisfactory, but unrevised implants are considered to be success [26]. Implants that are easier to revise (as is the case in UKA) will be revised more often than those which are not, and by considering unadjusted analyses, implants that are offered to younger, more active patients (as is the case in UKA) will have inferior overall rates of survival, as will those that are more dependent on surgical skill or patient selection than others.

Detailed investigation of these factors brings some clarity to the comparison of revision rates. As outlined above, the rate of complications and mortality are lower for UKA than TKA. Patient reported outcomes are higher overall but the threshold for revision of UKA is many times lower than that for TKA—unsurprising as revision of UKA is normally a conversion to a 'primary' TKA. Data from the New Zealand Joint Registry (NZJR) [23] supports this suggestion, as results demonstrate that despite UKAs having more excellent and fewer poor post-operative functional outcomes 6 months after surgery, the overall revision rate for UKA is approximately 5 times higher than the revision rate for TKA. The rate of revision is strongly related to surgical volume, with the highest-volume UKA surgeons having similar rates of revision for UKA and TKA, in spite of the additional modes of failure associated with UKA [27].

11.5 Functional Outcomes

The NJR [8] and NZJR [28] also collect patient reported outcome measures (PROMs) using the Oxford Knee Score 6 months after surgery. The data from the NZJR demonstrates that UKAs have more excellent outcome and less poor results than TKA [23] and similarly, a study analysed PROMS data of 14,000 matched patients (using propensity scores) from the NJR and found that UKA patients are more likely to get excellent results or be highly satisfied [29].

Burns et al. [30] assessed functional outcomes in UKA and TKA 10 years post-surgery. 590 UKAs were matched with the same number of TKAs. PROMS for UKA were better and continued to be so demonstrating the long-term impact [30]. In addition, hospital stays are significantly shorter for patients undergoing UKA [31] and gait studies have found that UKA results in a more physiological gait compared with TKA and a higher top walking speed [32].

11.6 Effect of Surgeon/Unit Volume

Systematic reviews [33, 34] and unadjusted data from national registries [8] confirm that the revision rate for UKA is much higher than for TKA [24]. Data from the NJR shows that the most common number of UKAQs implanted per surgeon per year is one, and the second most common is two [12]. A separate study found that 81.4% of surgeons performed fewer than 10

UKAs per year [27]. Among surgeons who perform both TKA and UKA, the mean usage of UKA was only 11.0% (SD 13.4%).

Liddle et al. [12] used NJR data [8] to demonstrate the importance of surgical caseload in determining the rate of revision and found that surgeons performing a small number of UKAs per year had the highest revision rate. For surgeons performing one or two UKAs per year, the revision rate equated to approximately 4% per year. Surgeons performing approximately 10 UKAs per year had a revision rate of 2% per year, whereas surgeons performing more than 30 UKAs per year achieved a revision rate of 1% per year, similar to that after TKA (HR = 1.10, 95% CI = 0.99–1.22).

The reasons for this effect are complex and not fully explained by variables recorded in the National Joint Registry; however, the patient selection and revision threshold of lower-volume surgeons may be a factor. Data suggests that higher-volume surgeons operate on older patients, with more comorbidities but a lower level of deprivation [12]. Low-usage surgeons implant UKAs in younger patients than high-usage surgeons and all joint registries report poorer survival in younger patients, whatever arthroplasty they receive [28, 35, 36].

11.7 Cost-Effectiveness

There are also economic implications to be considered in relation to UKA and TKA [37]. The typical length of stay for UKA is significantly shorter [21], therefore patients receiving UKA can be expected to require fewer perioperative resources and offer a short-term cost-saving in comparison to TKA patients. This initial saving could potentially be offset by the need for additional operations and revisions over the medium and long-term.

The TOPKAT clinical trial [22] presented a cost-effectiveness analysis for cohorts of patients receiving UKA and TKA. UKA resulted in better outcomes (0.24 additional QALYS, 95% CI 0.046–0.434), lower surgical costs and lower follow-up health costs in comparison to TKA. Overall, UKA was found to be more cost-effective and less expensive than TKA (−£910, 95% CI −£1503 to −£317) during the 5 years of follow-up presented. A number of other studies have demonstrated similar outcomes [37–40], leading to suggestions that UKA should be considered the primary treatment option for unicompartmental knee OA [5].

11.8 Conclusion

In conclusion, despite systematic reviews and registry data demonstrating that UKA has a higher revision rate than TKA, evidence has found that if surgeons aim for usage of 20% or more, with an implant that can be used for broad indications, patients should be able to experience the benefits associated with UKA without the higher revision rate.

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12 Bilateral Simultaneous Versus Bilateral Staged Total Knee Arthroplasty and Unicompartmental Knee Arthroplasty

Luke D. Jones

12.1 Introduction

The incidence of knee arthritis and demand for effective intervention continue to rise as the population ages. Severe bilateral knee arthritis is seen in as much as 10% of the population presenting to knee clinic and patients understandably often request bilateral arthroplasty. Both total knee arthroplasty (TKA) and unicompartmental knee arthroplasty (UKA) are recognised as successful procedures to treat end stage knee arthritis, however historically they also entail significant risks. Despite dramatic improvements in pre-operative optimisation and both intraoperative anaesthetic and surgical techniques, concerns regarding risks rightly persist and are heightened when bilateral surgery is considered. This chapter seeks to highlight the current evidence on safety, function and cost in bilateral simultaneous and bilateral staged total and partial knee arthroplasty.

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12.2 Bilateral Total Knee Arthroplasty

The development of total condylar knee replacements in the early 1970s transformed the management of severely deformed and painful knees [1]. Whilst the indication was often osteoarthritis, inflammatory arthropathy and other conditions that have since been effectively controlled by medical management such as sickle cell disease or haemophilia [2], were others.

As with any new procedure, the procedure was initially reserved for those with the most severe disease. Consequently, performing bilateral total knee replacement in a single sitting has been considered from very early in the development of the procedure [3]. It was already clear that preoperatively, patients with bilateral knee disease exhibited a greater degree of physical disability and limitation of activity due to multiple joint involvement and that this would have implications for both the anaesthetic and the postoperative recovery and hence length of stay [4]. Hardaker et al. in the earliest report of bilateral TKAs from 1978 [5] describe 26 patients with severe rheumatoid arthritis and osteoarthritis. Twelve had simultaneous operations bilaterally and fourteen had separate, staged procedures. They reported comparable relief of pain and function between the two groups. Importantly, it was clear even at this early stage that both com-

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plications and costs were of concern— despite the small numbers in each group the authors reported no difference in intra- or post-op complications. However, costs were significantly higher in the staged group. Forty years following these early reports, the debate regarding the safety and efficacy of simultaneous bilateral TKA continues.

As TKA entered the mainstream of medical practice, utilisation increased dramatically, and now over 100,000 are performed per year in the UK [6] and more than 1,200,000 per year in the USA. A significant percentage of patients undergoing primary unilateral TKA complain of bilateral knee involvement, with approximately 7% of patients undergoing surgical treatment of both knees simultaneously during the same hospitalisation, and 15% seeking treatment of the contralateral knee within 1 year [7]. In Sweden, registry data suggests that the incidence of simultaneous bilateral TKA can be as high as 25% [8]. With the utilisation of TKA rising exponentially with the ageing population, the number of patients seeking surgical treatment of both knees will inevitably rise as well.

Patients may elect to undergo both procedures performed under the same anaesthetic, either by one surgical team working sequentially or two surgical teams in parallel. This is referred to as simultaneous bilateral TKA (SBTKA). Alternatively, a staged bilateral TKA (StBTKA) may be performed under two anaesthetic events, defined as being at least 90 days but not more than 365 days apart [9]. Potential benefits of a simultaneous procedure in patients with bilateral disease are clear.

Only a single admission to hospital is required and the overall rehabilitation is shorter. Proponents also report greater patient satisfaction, similar functional gains [10] and decreased costs [11]. In those with severe bilateral varus or valgus, or indeed windswept knees, reconstructing unilaterally and then waiting 3 months before reconstructing the second side means significant difficulty with rehabilitation of the knee due to the apparent leg lengthening of the newly aligned knee. In order to walk, the prosthetic knee must now adopt a flexed position to minimise a limping gait. In these difficult situations, a bilateral restoration of mechanical alignment is attractive.

Rosenberg, at the turn of the century [12], emphasised the prevailing opinion at that time. In his report of 229 SBTKA compared to 69 StBTKA both requirement for allogenic blood transfusion and the incidence of significant postoperative cardiac complications was significantly higher in the SBTKA group. He considered the benefits of the procedure to be firstly time saving for the patient and secondly reduction in overall costs. Despite this, he concluded that the risks of the procedure were too high to justify the routine performance of SBTKA.

In the first and early second decade of this century, concerns regarding complications of SBTKA limited utilisation. In 2013, the Consensus Conference on Bilateral Total Knee Arthroplasty Group released a consensus statement concluding that SBTKAs are more invasive and complex procedures associated with increased risk for perioperative adverse events compared with TKA in an unselected group of patients [13]. Experts perceived that SBTKA increases medical risk, and thus a systematic approach to the management of patients should be taken to minimise complications.

These concerns were again highlighted by the American Academy of Orthopaedic Surgeons(AAOS) who concluded that there was only limited evidence to support simultaneous bilateral TKA, and even then only in patients aged 70 or younger of with ASA (American Society of Anaesthesiologist's) status of 1–2 [14]. Retrospective reviews of the Swedish Knee Arthroplasty Register [15] revealed higher 30-day mortality if bilateral knee arthroplasties were done at the same time versus staged within a year. Multiple retrospective reviews [16] showed adverse cardiovascular outcomes in patients with simultaneous bilateral knee arthroplasties. Memtsoudis et al. [16] helped to define the higher risk patient by showing that patients who suffered a major complication had a higher prevalence of comorbidities including, specifically, chronic lung diseases, congestive heart failure and pulmonary hypertension.

More recently, in response to concerns regarding safety of the procedure, Seo et al. [17] reported their series of 2098 consecutive patients who underwent SBTKA using extramedullary referencing and overlapping surgical teams to reduce anaesthetic times. In. this study, despite lack of a control group, there was acceptably low rate of complication at 1 year follow-up, including 0.33% for symptomatic pulmonary embolism, 0.62% for deep surgical infection requiring revision surgery, 0.05% for 14-day mortality, 1.14% for adverse cardiac events and 0.76% for postsurgical delirium. Wong et al. [18] in their retrospective review of 826 knees in 413 patients found low overall mortality rate, no cases of acute post-operative mortality and few medical complications. They concluded that, in contrast to earlier literature, using modern surgical and anaesthetic protocols SBTKA is safe.

In a review of data of 36,000 bilateral TKA from the Australian Orthopaedic Association National Joint Registry, Chua et al. [19] compared rates and causes of revision and 30-day mortality between SBTKA and StBTKA procedures with intervals of 1 day–6 weeks, 6 weeks–3 months and 3–6 months. Whilst simultaneous and staged bilateral TKA were demonstrated to have similar rates of revision over the medium term, 30-day mortality was lower in the 6 weeks–3 months staged group suggesting this is the optimum time delay in high risk patients.

In a meta-analysis of 18 studies covering 73,617 participants in the SBTKA group and 61,838 in the StBTKA group, Liu et al. [20] concluded that SBTKA showed a lower risk of deep infection and respiratory complications, but increased mortality, pulmonary embolism (PE) and deep-vein thrombosis (DVT) compared with StBTKA. There were no significant differences in revision, superficial infection, arthrofibrosis, cardiac complications, neurological complications and urinary complications between procedures.

When assessing patient suitability for bilateral surgery, the surgeon must consider the combined risks of two-staged procedures versus the risk of a single bilateral procedure, rather than comparing the risk of one bilateral procedure to just one unilateral TKA. For example, Barrett et al. [21] noted an 80% higher risk of pulmonary embolism in the 3 months after a bilateral TKA compared to a unilateral TKA but noted that the sum of the risks associated with two procedures for staged bilateral TKAs may equal or exceed the risk of simultaneous bilateral surgery.

Richardson et al. [22] using the PearlDiver Patient Records Database performed a study comparing patients who underwent SBTKA with those undergoing StBTKA within 12 months. They evaluated the complications associated with SBTKA versus StBTKA subgroups divided by delay between the first and second TKA: Less than 3 months, 3–6 months or 6–12 months. They hypothesised that after controlling for comorbidities, the simultaneous group will have the highest rate of complications and complications would diminish in the staged group as the amount of time between the two surgeries was increased. In this study of over 7000 patients, they found higher rates of blood transfusion and readmission in patients who underwent SBTKA, while there were higher rates of mechanical complications and infection in patients who underwent StBTKA. Whilst their study highlighted inherent risks to simultaneous bilateral TKA, it also emphasised the risks associated with staging procedures.

In a similar study utilising the New Zealand Joint Registry Database, Wyatt et al. compared 30 day mortality, all cause revision rate and function between unilateral TKA, SBTKA and StBTKA with intervals of 1–90 days, 90–1 year and >1 year [23]. StBTKA had lower mortality than unilateral TKA at three time interval groups unless performed within 90 days (adjusting for age and ASA grade). Revision risk with SBTKA was lower compared to unilateral TKA. Six-month Oxford scores were superior in SBTKA versus unilateral TKA. They concluded that SBTKA is at least as safe as unilateral TKA or StBTKA in appropriately selected cases and that surgeons should wait at least 90 days before the second procedure in those patients selected for StBTKA.

In a propensity matched study of SBTKA and StBTKA from the Danish patient registry, Lindberg-Larsen et al. [24] found no significant differences in 30-day readmission rates and mortality between simultaneous and staged bilateral TKA, but the in-hospital complication rate and re-operation rate were higher after the simultaneous procedure.

12.3 Bilateral Unicompartmental Knee Arthroplasty

Epidemiological studies show that knee osteoarthritis is not one uniform disease but rather affects the individual compartments of the knee joint; medial tibiofemoral, lateral tibiofemoral and patellofemoral to varying degrees [25]. In a study of all knees referred to secondary care in the UK, Bottomley et al. [26] determined that the predominant pattern of disease was medial (62–70%) followed by bicondylar (19–27%), lateral (8–9%) and then isolated patellofemoral (2–3%). Anteromedial knee osteoarthritis (AMOA) is a distinct phenotype of knee osteoarthritis first formally defined in 1991 [27]. In this specific disease, the articular cartilage in the medial compartment experiences degeneration, the lateral compartment remains unaffected and the anterior cruciate ligament remains intact. When established AMOA is present, the used of UKA is an effective treatment option [28]. UKA was introduced to the orthopaedic community by McIntosh in the 1950s when a metal spacer was used in a single tibiofemoral compartment [29]. In the 1970s the Marmor Prosthesis [30] and the St Georg Sled [31] were introduced with good outcomes. In 1974, the introduction of the Oxford unicompartmental knee replacement, with its unconstrained and highly conforming meniscal bearing design, transformed the use of UKA with excellent results reported for both designer and non-designer surgeons, and more recently the successful introduction of uncemented femoral and tibial components [32, 33]. Comparisons of outcomes in patients with medial disease consistently demonstrate improved outcomes with UKA compare to TKA [34]. Despite early concerns regarding revision rates, a more detailed understanding of registry data demonstrates that in surgeons who perform at least 20% of knee arthroplasty as UKA, outcomes [35] and survival favour UKA over TKA [36]. Understandably therefore, the popularity of UKA has increased over the last decade.

In the UK, the National Institute for Health and Care Excellence (NICE) has recently updated their guidance on knee arthroplasty [37]. A clinically important benefit of UKA over TKA was found for PROMs outcome, length of stay in hospital and deep vein thrombosis (DVT), minor revisions and re-operation after 5 years. Recovery from UKA tends to be faster and this procedure is usually associated with less post-operative pain and faster mobilisation resulting in people often going home sooner after surgery. NICE suggests UKA saves money compared with TKA. Whilst TKA makes up the majority of current practice, offering a choice of both procedures is likely to result in more UKA operations.

With knee osteoarthritis frequently presenting bilaterally, and most commonly isolated to the medial compartment, understanding the risks associated with both simultaneous bilateral UKA (SBUKA) and staged bilateral UKA (StBUKA) is of increasing importance.

Compared to other knee replacement procedures, UKA may be better suited to single-stage surgery, given the less invasive and shorter operative and anaesthesia times.

In the earliest report of bilateral UKA surgery, Chan et al. [38] performed a retrospective analysis of 159 patients SBUKA and 80 StBUKA. The groups were comparable in age and ASA grade, but more women were in the two-stage group. No statistical differences between the groups were found regarding the tourniquet time or minor complications. The anaesthetic times were longer for the StBUKA, and although no complications were reported in the StBUKA group, major complications were seen in 8.2% of SBUKA. Due to the significantly higher risk of major complications associated with SBUKA group, the authors advocated caution before undertaking the procedure.

In another early study comparing SBUKA (35 patients) with StBUKA (141 patients), Berend et al. [39] retrospectively reviewed cases to evaluate perioperative complications and short-term results. Results demonstrated a low risk of perioperative complications when performing SBUKA in a surgeon selected cohort. There were no increased perioperative risks identified and no increased mortality. Although SBUKA was performed in younger and less obese patients, the data suggest simultaneous UKA can be performed safely in this group. Limitations identified by the authors included lack of randomisation and significant selection bias.

In a study of total 220 bilateral simultaneous and 347 unilateral UKAs, Romagnoli et al. [40] compared complication and revision rates, length of hospital stay and the use of transfusion of allogeneic and autologous blood. Simultaneous bilateral UKAs significantly reduced, in patients requiring bilateral arthroplasty, the overall length of hospital stay and, therefore, patient management costs. There was no difference between groups in terms of revisions or complications. The authors concluded that blood loss differences could be reduced with the use of modern anaesthetic techniques.

In a smaller but more recent study, Ma et al. [41] prospectively compared SBUKA and StBUKA and followed patients for a minimum of 50 months. There was no difference between groups in terms of death, PE, DVT, prosthetic infection, total tourniquet time, or pre- and post-operative haemoglobin levels. Patients undergoing SBUKA had a shorter cumulative anaesthetic time and a quicker cumulative recovery. The authors recommend SBUKA based on patient selection including age and pre-operative fitness.

Ahn et al. [42] compared SBUKA with unilateral TKA in two retrospectively matched cohorts with all knees having the same full thickness anteromedial knee arthritis pattern. Patients undergoing SBUKA demonstrated fewer perioperative complications, less blood loss, less transfusion and better functional outcomes at 6 months post-operatively than unilateral TKA. This data, despite the small study size, suggests that SBUKA can be performed safely and results in acceptable clinical outcomes even when compared to unilateral TKA.

In a retrospective study of 44 SBUKA and 26 StBUKA knees performed over a 6 year period, Siedlecki et al. [43] compared firstly the short-term complication rate and secondly total hospital stay lengths and post-operative range of movement. SBUKA was not inferior to StBUKA in terms of the total post-operative haemoglobin level decrease, short-term complication rate, time to full range of movement recovery, or implant position regardless of patient age. Single-stage surgery was associated with shorter total inpatient stay and substantially lower costs.

Clavé et al. [44] retrospectively analysed data from 50 patients who underwent SBUKA compared to a hundred patients (100 knees) with unilateral medial osteoarthritis (OA) who underwent unilateral UKA. Blood loss incidence of blood transfusions, and complication rates were compared. Clinical results were assessed at 6 month and at a 2-year minimum follow-up. No significant difference was observed between groups regarding the blood loss, post-operative transfusion rates, complication rates, functional results or patient satisfaction.

In a further retrospective review of SBUKA and STBUKA, Biazzo et al. [45] found that SBUKA did not increase the risk for perioperative complications. Whilst total blood loss at discharge was higher in the SBUKA group than in the first stage StBUKA group, cumulative haemoglobin loss was significantly lower in SBUKA group. In this study, patients with bilateral end stage disease benefited from a single hospital admission and anaesthetic time, a shorter total inpatient stay and a reduction in hospital costs.

These results were reproduced by Feng et al. [46] in a retrospective analysis of matched cohorts undergoing SBUKA and StBUKA. Whilst total anaesthesia time, post-operative length of hospital stays and hospitalisation expenses in the SUBKA group were significantly less than in the StBUKA group, haemoglobin levels in SBUKA group were lower than in the StBUKA group at post-op day 3. However, no significant differences in the rate of transfusion, complications or

functional outcome scores were detected between groups at 4 years post-op.

Pujol et al. [47], in a recent systematic review designed to compare the clinical outcomes associated with SBUKA and StBUKA, identified only ten retrospective cohort studies that address this question. Whilst acknowledging the poor quality of the available studies, namely low number of studies, retrospective nature and non-randomised, the authors concluded that in patients with severe symptomatic bilateral unicompartmental OA, a one-stage bilateral UKA can be considered as a comparably safe operation and may be a better treatment option when compared with a two-stage procedure in terms of cumulative complication rate and cost effectiveness.

12.4 Conclusions

Whilst advocates of SBTKA cite benefits including single anaesthetic, shorter cumulative hospital stays, patient convenience and satisfaction and increased cost effectiveness for the healthcare system, it appears that SBTKA is also associated with increased perioperative complications, including pulmonary embolism, major cardiac events, higher transfusion rates and increased mortality when compared to StBTKA. In light of this, surgeons should consider patient profile carefully before advocating this treatment approach. In patients undergoing StBTKA, an operative interval of 90 days is commonly advocated in the literature.

In contrast to the concerns regarding bilateral TKA, SBUKA, presumably due to its less invasive nature and reduced requirement for intramedullary instrumentation, appears safe with no increased perioperative risks. Despite increased blood loss when compared to StBUKA, requirements for blood transfusion do not increase. Functional outcomes can be expected to match those achieved with StBUKA. Anaesthetic time, total length of stay and overall hospital costs are all likely to be less making this a clinically viable option for patients with bilateral unicompartmental disease.

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13 Late Acute Hematogenous Infection Following Total Knee Arthroplasty: Debridement, Antibiotics and Implant Retention (DAIR), One-Stage Revision or Two-Stage Revision?

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13.1 Introduction

Infection is one of the worst complications of total knee arthroplasty (TKA). Late acute hematogenous periprosthetic joint infection (PJI) occurs via hematogenous spreading after a period in which the prosthesis had functioned properly [1]. The best therapeutic modality for treatment of this infection remains controversial. For acute postoperative infections, there is now strong evidence for the use of debridement, antibiotics and implant retention (DAIR); two-stage revision is considered to be the gold standard for the treatment of chronic late infections. However, there is a paucity of data presently available on the treatment and results of patients treated for late acute hematogenous PJI [2].

The purpose of this chapter is to review recent literature in order to know the best current treatment alternative for late acute hematogenous infection after TKA: arthroscopic or open debridement, antibiotics and implant retention (DAIR) with or without polyethylene exchange, one-stage revision or two-stage revision.

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13.2 Incidence of Late Acute Hematogenous PJI After TKA

Late acute hematogenous infection is rare. In 2007 Cook et al. published a late acute hematogenous infection rate of 0.5% at 10 years mean follow-up after primary TKA. In a series of operated patients of 3013 primary TKAs they found 15 late hematogenous infections in 14 (0.5%) patients [3]. In a small 2018 study of complex cases, Westberg et al. found that the incidence of late acute hematogenous PJI following TKA was 5/100 overall. This was broken down into 1/33 (3%), 1/45 (2%), and 3/22 (14%) following complex primary TKA, aseptic revisions, and septic revisions, respectively [4].

13.3 Arthroscopic DAIR

Arthroscopic DAIR is, undoubtedly, the least invasive surgical option and can be considered in a small number of patients who meet several criteria. It is only suited to acute infective presentations of well-fixed implants [5]. Success is far from guaranteed and is only likely in streptococcal infection. The arthroscopic surgery is only the beginning of treatment, and it represents a tool to facilitate sup-

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pression with prolonged antibiotic therapy: it has a limited role as complete biofilm clearance is theoretically impossible. It is most effective in the very early phase of acute presentations of infected TKA. It can be of use in cases where the organism is not associated with strong biofilm, in patients of extreme frailty, as an adjunct to suppressive antimicrobial medical therapy or as part of a diagnostic workup. If performed, high volumes of fluid and accessory portals should be used [5].

13.4 Open DAIR

According to Encinas-Ullán et al., of the methods used for the treatment of PJIs, open DAIR is technically the least demanding, the most economical, and with lower morbidity in comparison with one-stage or two-stage revision arthroplasty [6]. However, the failure rate of open DAIR can be high and can compromise outcomes of the two-stage revision. Indications for an open DAIR are summarized in Table 13.1.

Open DAIR should not be recommended in chronic infection (>4 weeks postoperatively, insidious onset of symptoms) [6].

13.5 One-Stage Revision

Table 13.2 shows rigorous inclusion criteria that must be used to recognize patients most likely to profit from one-stage revision arthroplasty [7]. Table 13.3 shows main criteria not to indicate an one-stage revision arthroplasty in acute hematogenous infected TKA [8, 9].

Table 13.1 Indications of open debridement, antibiotics and implant retention (DAIR) in late acute hematogenous infection of total knee arthroplasty (TKA)

Duration of clinical signs and symptoms is less than 3 weeks
Patients who have a well-fixed implant and local soft tissues in good condition (no abscess or sinus tract)
Low-virulence bacteria
Elderly patients with less bone stock and multiple comorbidities, for whom anesthesia and more invasive/complex surgery could be dangerous
Non-immunocompromised patients

Table 13.2 Inclusion criteria that must be used to recognize patients most likely to profit from one-stage revision arthroplasty in late acute hematogenous infection of total knee arthroplasty (TKA)

Minor bone loss and a soft tissue deficiency that can be closed primarily
Absence of immunocompromise
Low virulent bacteria which are sensitive to accessible bactericidal antibiotic therapy recognized preoperatively
Patients should be able to allow an esthetic

Table 13.3 Main criteria not to indicate a one-stage revision arthroplasty in late acute hematogenous infected total knee arthroplasty (TKA)

The existence of generalized sepsis
Infections in which the bacteria is not determined
Infection produced by drug-resistant bacteria
The existence of a sinus tract
The existence of severe soft tissue defect over the articulation

13.6 Two-Stage Revision

Two-stage revision TKA remains the gold standard for the treatment of PJI [10]. Multidisciplinary collaboration between the orthopedic surgeon, infectious disease, microbiology, and pathology departments is crucial for obtaining high rates of infection eradication in a two-stage revision TKA. For that reason, these procedures should only be performed in hospitals that offer such specialties. The purpose of two-stage revision is to resolve the infection and reconstruct the joint in order to achieve a knee that is pain-free, stable, and well aligned with the new revision prosthesis. Surgery should begin with an appropriate approach and careful component removal, minimizing bone loss at this first surgical stage. The use of dynamic spacers with antibiotic-loaded cement has resulted in shorter systemic antibiotic treatment and an improvement in patient function in the period prior to implantation of the new prosthesis. The most commonly used parameters to determine the best time for implantation are still C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) values. Intraoperative histologic analyses are not conclusive enough to

rule out the presence of infection during the second surgical stage [10].

13.7 Comparative Studies: DAIR, One-Stage Revision or Two-Stage Revision?

The treatment of PJI is a major challenge for orthopedic surgeons [11, 12]. Open DAIR is considered a low-aggression intervention that attempts to preserve a functional implant, avoiding the morbidity associated with implant removal and subsequent necessary surgical procedures. Although its indications are narrow, DAIR is the preferred first intervention in patients with acute hematogenous PJI who fit the criteria as it is associated with significantly less morbidity than formal revision procedures [1, 13, 14]. The success rates of DAIR are highly variable in the literature (between 30 and 80%) [15–23]. However, most studies were performed before a standardized definition of PJI was available [24], and there was great diversity in how treatment failure was defined. Although DAIR remains a viable and less aggressive alternative to two-stage revision arthroplasty, recent studies have shown that a failed DAIR is strongly related to the failure of a future two-stage revision arthroplasty [25, 26]. The reasons for this are unclear, but it may be that early intervention with two-stage revision is more likely to result in an effective debridement and ultimately successful outcome; alternatively, it may be that patients with failed DAIR have more aggressive or resistant organisms which may have resulted in poorer outcomes after revision either way.

In 2019 Leta et al., in a series of 644 TKAs reviewed for deep infection (i.e., surgically treated PJIs) and reported to the Norwegian Arthroplasty Register (NAR) between 1994 and 2016, evaluated their prosthetic survival rates, risk of revision and mortality rate following the different surgical strategies used in the treatment of PJIs (one-stage revision versus two-stage revision and DAIR) [27]. During follow-up, 19% of DAIR cases, 14% of one-stage revision cases and 12% of two-stage revision cases were subsequently revised due to a PJI. The 5-year survival rate with infection screening as the end point was 79% after DAIR, 87% after one-stage screening, and 87% after two-stage screening. There were no significant differences between one-stage and two-stage revisions with subsequent revision for any reason as the end point and no difference with revision because of infection as the end point. In patients over 70 years old the risk of revision for any reason was 4 times higher after one-stage revision than after two-stage revision. In knees treated with DAIR age had no significant effect on the risk of subsequent revision. The 90-day and 1-year mortality rates after revision for PJI were 1.2% and 2.5%, respectively. DAIR yielded good results compared with previous published studies. Although the one-stage revisions resulted in a fourfold increase in risk of subsequent revision compared with the two-stage revisions in older patients, the overall outcomes after one-stage and two-stage revisions were similar [27].

In 2013, Hermann et al. analyzed the outcomes of DAIR after acute hematogenous TKAs infections that had produced symptoms for up to 4 weeks [28]. The surgical technique included arthrotomy, synovectomy, inlay removal, jet lavage, instillation of polyhexanide, replacement of the polyethylene insert, drainage and infusion-aspiration-drainage if necessary, wound closure with plastic surgery if necessary. Postoperative treatment included infusion-aspiration-drainage with polyhexanide for 3 days or drainage for 3 days; continuous passive motion (CPM) with increased range of motion (ROM) 0–0–30°; and removal of the drainage at 5 days, followed by mobilization with increased ROM and full weight load. The success rate of his surgical technique was 70% [28].

In 2014 Konigsberg et al. presented their experience on the use of DAIR in the management of acute hematogenous infections after TKA and total hip arthroplasty (THA). They analyzed 40 patients (42 joints; 22 TKA, 20 THA) [15]. Following surgery and as directed by an infectious disease specialist, patients received 6 weeks of intravenous antibiotics specific for the cultured organism, followed by a course of oral

antibiotics. An obvious source of hematogenous seeding was identified in 19 patients (45%; including cellulitis, urinary tract infection, dental work, infected hematoma, and others). Nineteen patients (45%) had documented fever above 38.5 °C. The blood culture was positive in 8 of the 25 patients (32%) in whom the test was performed; in all cases the blood culture coincided with the culture obtained during surgery. Recurrent infection requiring further surgery developed in 9 of 42 joints (21%) after an average of 56 months (range, 25–124 months), eight of whom had a staphylococcal infection. Recurrence of infection after DAIR developed at an average of 7 months (range, 1–17 months). Reoperations included two two-stage revision arthroplasty in eight patients. One patient (who had an infected THA and chronic renal failure treated with hemodialysis) was treated by a permanent resection arthroplasty. Ten of the 40 patients (25%) died within 2 years of infection. The DAIR for the treatment of acute hematogenous infection was successful in most patients (76% survival at 2 years). Non-staphylococcal infections had a very low failure rate (96% 2-year survival) [15].

In 2016 He et al. published their results for 11 acute hematogenous infections following TKA treated with DAIR [2]. To improve the efficiency of irrigation, a vacuum closure device was used and the most sensitive antibiotics were injected into the irrigation saline. The mean age of the 11 patients was 56.3 years; there were 2 men (18.2%) and 9 women (81.8%). Before the symptoms appeared in the operated knees, the patients had a history of bacteremia and a blood culture coinciding with the culture of the local infection; the most common infectious organisms were staphylococci and streptococci. Of the 11 patients, 9 were counted as successes in terms of implant survival at 2 years, with all non-staphylococcal infections and none of the staphylococcal infections being successfully treated. The duration of symptoms before the operation and the type of pathogen influenced the outcome [2].

In 2018 Swenson et al. published a retrospective review of their series of patients with acute and acute hematogenous PJI undergoing DAIR [29]. They attempted to identify factors from preoperative laboratory values and history leading to success or failure at 6 months (defined as retention of a well-fixed implant with no need for further surgery or suppressive antibiotic treatment, and with at least 6 months' follow-up). In 53 out of 72 patients (73.6%) the DAIR was successful. Of the 19 failures, 14 required two-stage revision arthroplasty, one of which failed due to recurrent infection. Again, Staphylococcus aureus infection was associated with a higher likelihood of failure after DAIR compared to other organisms (48.3% vs 11.6%). The rate of success with acute hematogenous PJI was similar to that seen in the acute group ($p = 0.616$). Patients with low preoperative hematocrit values (≤32.1) were also more likely to fail (55% vs 16%). When none of the risk factors was present, 97.1% of the PJI were successfully treated with DAIR. Of those who failed DAIR, two-thirds went on to be successfully treated with two-stage revision arthroplasty [29].

In 2019, Iza et al. evaluated the results of DAIR and attempted to identify possible predictors of outcome [30]. They retrospectively reviewed all acute postoperative infections (≤3 months from the index procedure) and acute hematogenous infections treated with DAIR over 12 years ($n = 12$). Twenty-six knees were analyzed, with an average age of 73.4 years. The average follow-up was 41 months. The overall success rate was 77%, but in contrast with the study of Swenson et al., acute postoperative infections (93%) did substantially better than acute hematogenous infections (58%). Infections in which Staphylococcus aureus was isolated had only 33% success, compared to 82% when the microorganisms were not Staphylococcus aureus [30]. This was a small study and so it is difficult to determine whether the difference between acute and acute hematogenous was true. It is sometimes difficult to distinguish between a chronic subclinical infection and a late, acute hematogenous infection—just one misdiagnosed chronic infection would make a substantial difference when the cohort is this small.

In 2019 Kuo et al. conducted a retrospective review of 49 patients with acute hematogenous infection and positive blood cultures undergoing DAIR [31]. The minimum follow-up was 1 year.

44.9% (22/49) of the blood cultures obtained were positive. A high level of comorbidity (defined using the Elixhauser criteria) was a significant risk factor associated with positive blood culture. A positive blood culture was the only significant factor predicting treatment failure in acute hematogenous PJI. Kaplan-Meier survival for implant survival without infection was 53.1% per year in all patients, 66.7% in patients with negative blood cultures, and 36.4% in patients with positive blood cultures [31].

In 2019, Shohat et al. investigated the failure rates of DAIR in patients with acute hematogenous and acute postoperative PJI, and attempted to identify risk factors associated with failure [32]. They retrospectively reviewed 199 patients with TKA who required DAIR for acute postoperative PJI (<3 months postoperatively) and acute hematogenous PJI (equal to or greater than 3 months postoperatively, with abrupt symptoms lasting <3 weeks). Only patients who met the Musculoskeletal Infection Society (MSIS) criteria for PJI were included. Treatment failure at 1 year was defined according to the Delphi criteria. The failure rate at 1 year was 37.7% (75 of 199). In patients with acute hematogenous infections, the failure rate (56%, 29 of 52) was almost twice as high as that of patients with acute postsurgical infections (31%, 46 of 147). Again, given that acute hematogenous infections were diagnosed only on the duration of symptoms, not requiring any predisposing event or positive blood culture, it is possible that a proportion of these were actually chronic subclinical infections. Predictors of failure after DAIR are summarized in Table 13.4 [32].

Table 13.4 Predictors of failure after debridement, antibiotics and implant retention (DAIR): failure rate 56%

Previous revision surgery
Higher Charlson comorbidity rate
Specific comorbidities (chronic obstructive pulmonary disease, diabetes, and a history of malignancy)
Patients with polymicrobial infections were also more likely to have treatment failure
Presence of intraoperative purulence
Elevated systolic blood pressure
Tachycardia
High C-reactive protein (CRP)

13.8 Conclusions

There is good evidence for the treatment of late acute hematogenous infection using DAIR. On the basis of the studies available, it appears that the risk of failure in late hematogenous infections is higher than that in acute postoperative infections, but this may reflect miscategorization of chronic subclinical infections as acute hematogenous infections. A high level of comorbidities increases the chance of failure. Specific comorbidities associated with DAIR failure are chronic obstructive pulmonary disease, diabetes, and a history of malignancy. Patients with polymicrobial infections or infections involving staphylococci were also more likely to have DAIR failure. Clinical and laboratory risk factors associated with DAIR failure are the presence of intraoperative purulence, elevated systolic blood pressure, tachycardia and high CRP, with one study suggesting that a positive blood culture was associated with increased risk of failure.

In the Cochrane Central Register of Controlled Trials there is currently a trial under way entitled "How to improve the results of irrigation and debridement for PJI through the use of intraosseous antibiotics" (https://clinicaltrials.gov/show/NCT03713528, 2018 | added to CENTRAL: 28 February 2019 | 2019 Issue 2). This is a two-arm, multi-center, randomized, superiority clinical trial.

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14 Management of Distal Femoral Periprosthetic Fractures: Plate, Intramedullary Nail or Arthroplasty?

Edward Matthews, Ian Sinha, and Alexander D. Liddle

14.1 Introduction

Mirroring the increase in the number of primary arthroplasty procedures being performed, the incidence of fractures around a knee replacement is increasing in their incidence and complexity [1]. The distal femur is exposed to significant mechanical stresses and this is altered when there is a total knee arthroplasty (TKA) in situ, resulting in distal stress shielding and a stress riser at the bone implant interface. The most common place for periprosthetic fracture is at the supracondylar level of the distal femur. The incidence of this is fortunately low and is quoted from 0.3 to 2.5% of TKAs [1].

Fractures commonly occur as a result of trauma in the presence of a well-fixed component or fracture as a consequence of osteolysis around a loose TKA. These both pose significant but differing challenges in treating patients with a wide range of medical co-morbidities and character of the fracture.

In this chapter, we will revise the current concepts, management and outcomes of these challenging and rare injuries around the distal femur.

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14.2 Basic Concepts

The distal third of the femur is trapezoidal and has coronal slopes of both the medial (~25°) and lateral condyle (~10°). The femoral component of a TKA causes a stress riser to this area of metaphyseal bone and can cause shielding beneath it.

The main deforming forces acting upon the distal femur are quadriceps, hamstrings, adductor magnus and gastrocnemius, producing the characteristic deformity of varus, adduction and internal rotation. The deforming forces are powerful and difficult to outcome by conservative methods, particularly in more distal fractures.

14.2.1 Risk Factors

Periprosthetic fracture is a risk in all arthroplasty and pre-disposing factors that can be sub-divided into factors that give rise to poor host bone stock, local stress risers and patient-specific factors such as propensity for falls and co-morbidities. Distal femoral fractures in this subtype are generally of low energy.

Patient and fracture specific variables have been highlighted as pre-disposing risk factors for periprosthetic fracture of the distal femur [2], highlighted in the table below (Table 14.1).

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Table 14.1 Pre-disposing risk factors for periprosthetic fracture of the distal femur

Poor bone stock	Osteoporosis, steroids, smoking, vitamin D deficiency, rheumatoid arthritis
Local stress risers	Stiff TKA, notching, previous cortical screw holes, implant interface
Patient	BMI, neurological disorders and dystonias, age

TKA Total knee arthroplasty, *BMI* Body mass index

14.2.2 Local Stressors and Notching

TKA design, degree of constraint and presence of anterior cortical notching have all been postulated as risk factors for periprosthetic fracture but no firm clinical evidence has been provided to establish a causal effect. Biomechanical studies have established that notching of the anterior femoral cortex weakens the femur by 18% with bending loads and 39% in torsional loading [3], but there is no firm clinical evidence that notching is associated with a higher incidence of fracture.

Other factors include the stress riser from the shielding effect of the anterior flange of the femoral implant/cortex interface. The design of the implant including whether they have a large bony resection for a box for a posterior stabilised implant also plays a role.

The stress riser effect is heightened by the presence of an ipsilateral total hip replacement which also renders management more challenging.

14.3 Classification Systems

Most classification systems are based upon the anatomical site of the fracture, the degree of displacement and whether components are loose or well-fixed. These classification systems are simple and assume that the component is a primary TKA without significant stem to the femoral prosthesis.

Lewis and Rorabeck's classification (1997) has become widely accepted. It is based on the degree of displacement and the quality of fixation of the component (Table 14.2).

Table 14.2 Lewis and Rorabeck [4]

I—Undisplaced, component intact
II—Displaced, component intact
III—Displaced, component failing or loose

Table 14.3 Su et al. [5]

1. Proximal to femoral component
2. Originates at the proximal aspect of the component and extends proximally
3. Any part of the fracture is distal to the anterior flange of the component

The most common type of fracture reported in the literature is type II. Su et al. [5] outlined a system of classification which describes these fractures from an anatomical perspective (Table 14.3).

The Unifying Classification System [6], derived from the Vancouver classification of fractures about the hip, also adds to this categorisation of distal femoral fractures and covers a greater range of situations including interprosthetic fractures, where both a hip and knee arthroplasty are in situ. All of the systems of classification available are useful in highlighting anatomical or fracture specific components, but do not draw all the factors together and it is unclear as to how effective they are in guiding management. In particular, patient-specific features such as age, co-morbidity and function are important when considering fixation or revision surgery and when determining the likely prognosis of the fracture.

14.4 Treatment

The aims of treating these fractures are to achieve early range of movement, permit early weight bearing and rehabilitation. The majority of these fractures occur in an elderly, frail population and they can be considered to be analogous to hip fractures, where tolerability of the surgery and ability to bear weight fully following surgery are important aspirations.

Overall, there are three principal methods of operative treatment: retrograde or antegrade femoral nail; open reduction and fixation with a lock-

ing plate; and replacement of the distal fragment with a revision knee replacement or distal femoral replacement. Occasionally, nail and plate are used in combination.

In most cases, the decision as to which method to use will be based on the character of the fracture. For most surgeons the more comminuted distal fracture associated with loosening will be for many not considered for fixation and the type I fractures in the Rorabeck and Lewis classification will be a simple decision to fix.

The surgeon still needs to consider the quality of bone when aiming for fixation, the presence of any stiffness within the TKA, the condition of the TKA in terms of wear and any possibility of lysis may push a surgeon towards revision or distal femoral replacement.

Patient-specific features such as age, comorbidity and function are important considerations when thinking about failure of implant or fixation and whether the patient can tolerate the surgical insult of surgery.

14.4.1 Intramedullary Fixation

Retrograde femoral nail is used commonly with native distal femoral fractures and is advocated by a review of registry trauma data [7]. This study reviewed 297 patients treated with intramedullary nail (IMN) or locked plate, which found better quality of life scores for IMN (in terms of the EQ-5D index) and a very small difference in alignment as compared to a locked plate.

Commonly the patient is positioned supine with a wedge or triangular shaped bolster to allow the knee to be flexed to 30°, this must be radiolucent. Ideally a closed reduction is performed with traction and rotation is confirmed. An arthrotomy is then performed via image intensifier guidewire placement and entry reaming through the prosthesis.

There are important technical considerations when IMN is chosen to treat this type of periprosthetic injury. The most important is the anatomy of the intercondylar notch in the TKA. There is much published regarding diameter of nail and notch size [8]. The other important consideration is the position of the notch and the ability to enter the nail at the correct anatomy in the distal segment so as to not cause a mal-union. The distal bone must be adequate to allow fixation within it with the distal locking screws; in the same way, the distal locking screws within the nail must be distal enough to hold the fracture and there is biomechanical evidence that this is better if this are angle stable.

The potential advantages of IMN fixation are well established. They are a load sharing device that can be used without periosteal stripping and blood supply injury. The process of intramedullary reaming stimulates blood supply and fracture healing. The advantage of avoiding a large approach to the joint replacement in contused and injured soft tissues and fracture site is significant. Where a closed reduction is possible, a minimally invasive approach can be taken to fixation to reduce the physiological burden of surgery.

14.4.2 Locking Plate Fixation

Rigid fixation can be achieved with locking distal femoral contoured plates. Position and setup is the same for intramedullary nailing. The authors prefer a lateral parapatellar approach or use of the most lateral scar which provides good access to both the anterolateral femur for plate and can be used as a utility incision for medial/adjuvant plate fixation.

Many of these contemporary designs offer variable angle locking screws for fixation into the plate. These can offer an excellent device with which an experienced surgeon can reduce and fix these fractures. Plate fixation however is vulnerable to its design as an extramedullary, load bearing device and does not have the same mechanical advantage as an IMN. Its use in osteoporotic, comminuted bone around the implant means that it is at risk of varus collapse and progressive deformity.

Both plate fixation and IMN can be augmented with an accessory plate either on the medial column of the distal femur or as 90° plate construct. This further adds to the metal burden of the distal but may offer more stability in fixation of a highly comminuted fracture. Another adjuvant to fixation is use of injectable bone substitute or even polymethylmethacrylate bone cement.

There is biomechanical advantage to orthogonal plane fixation of dual locking plates of the distal femur [9]. However, there is little clinical data to support this as routine practise but does confer biomechanical advantage and should be considered when treating osteoporotic patients.

14.4.3 Results of Fixation

The large variation in patient co-morbidity, function and fracture anatomy, when combined with a relative infrequency of this type of fracture, means that there is a paucity of prospective clinical data on the outcome of fixation of periprosthetic distal femoral fractures.

Much of the published literature is from retrospective cases series and as a result any recent syntheses of the data are limited by this in their conclusion.

In a recent systematic review, the most reported fracture subtype, classified by the Rorabeck classification system, is Type 2 (363/488) [10]. The review reports outcomes of fracture healing with rates of union reported for IMN at 84% and with locking plates at 87%. Complications were found with a high incidence in both subgroups—35% for locking plates and 53% in IMN fixation. The most common is mal or non-union.

Other systematic reviews have shown little difference in the rate of non-union between IMN and plate fixation but suggested that malunion was more common with IMN fixation [Odds Ratio (OR) 2.37] as compared with plate fixation [11].

Li et al. [12] in a meta-analysis of locked plates against retrograde intramedullary nails found no statistically significant difference in the 6 month union rate, operation time, complication rate and time to union. A randomised controlled trial (TrAFFix) has been designed to compare nail and plate fixation in native and periprosthetic distal femoral fractures and a feasibility study has been undertaken [13]. Differences in surgeon expertise and preference are expected to render recruitment challenging, but plans are in place for a definitive randomised controlled trial (RCT) on this issue.

More recently, the use of a combination of nail and plate has been proposed to overcome the disadvantages of either technique (Fig. 14.1). The rationale is that by achieving fixation with both devices, the strain applied to each is reduced, reducing in turn the likelihood of failure. Liporace and Yoon [14] report the results of 15 patients with periprosthetic ($n = 9$) or native ($n = 6$) fractures of the distal femur. All were made full weight bearing as tolerate post-operatively. Results were akin to those seen in hip fractures, with half (8/14) losing a degree of mobility, but with no non-unions, failure of hardware or return to theatre.

Failure of fixation is a complication with significant risk of infection and challenges in an already frail population. The main decision is between continuing with the aim for union with further fixation or conversion to distal femoral replacement (DFR) arthroplasty (Fig. 14.1).

14.5 Primary Endoprosthetic Replacement

Revision arthroplasty for fracture, whereby the distal femur is resected proximal to the fracture and replaced by a stemmed, constrained prosthesis and the tibial component is revised, is indicated where there is loose prosthesis, inability to stabilise with fixation and where previous efforts to fix have failed. The contraindications for this are where there is suspected or confirmed infection and where the patient is deemed too frail for the physiological insult of the surgery (Table 14.4).

Primary endoprosthetic replacement (EPR) for these fractures in frail patients may offer an opportunity to retain their independent mobility by allowing immediate weight bearing and this in itself can offer a significant advantage over fixation. Clearly this option is better suited where bone stock preservation is not desirable and in the majority of cases is directed to elderly patients without a significant burden of co-morbidity.

Where DFR is performed the patient is set up supine, with access to the proximal femur avail-

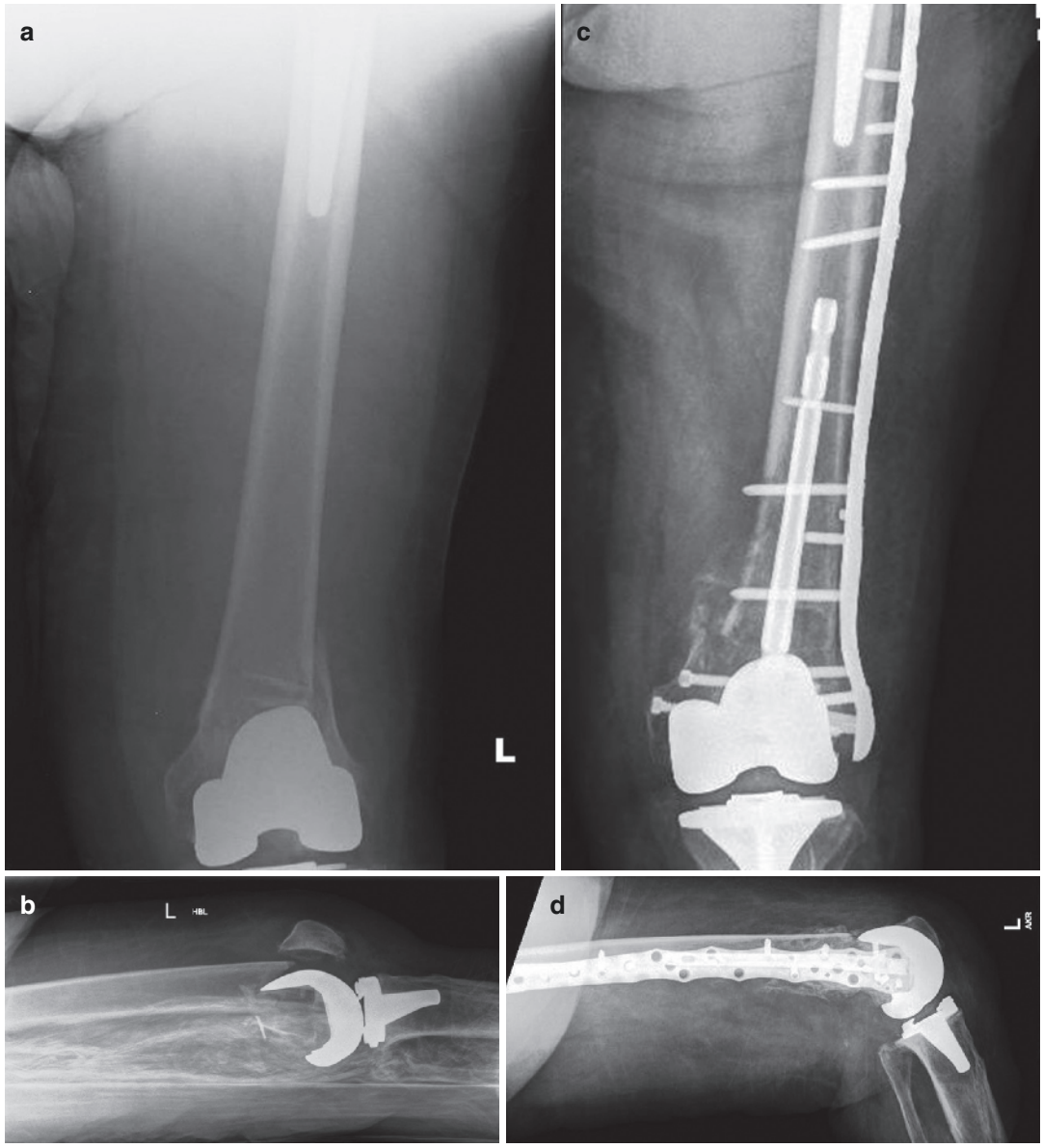

Fig. 14.1 Nail-plate fixation of periprosthetic distal femoral fracture. (**a** and **b**): AP and lateral views of displaced distal femoral fracture in an elderly osteoporotic patient. (**c** and **d**): AP and lateral views following nail-plate combined fixation

Table 14.4 Indications and contraindications for endoprosthetic replacement (EPR) in periprosthetic fractures of the distal femur

Indications	Contraindications
Loose prosthesis	Infection
Inability to fixation due to bone stock	
Failure of prior repeated ORIF	
Relative indications	
Age and TKA function prior to injury	

ORIF Open reduction and internal fixation, *TKA* Total knee arthroplasty

able. An extended parapatellar approach either lateral or medial is performed with incision extending into rectus femoris muscle belly. Tourniquet is difficult to apply as height of application may encroach onto the surgical field. A sterile tourniquet on standby is often a more pragmatic approach.

The proximal part of the femoral fracture site is held by large reduction forceps and protected to avoid injury to the popliteal fossa and neuro-

vascular bundle. The soft tissues attached to the distal fracture site are then dissected at a subperiosteal plane to gain access to the posterior femur and the distal femur is excised.

Cemented DFR is the authors' preferred implant (Fig. 14.2), given that by definition bone quality is often poor in this patient group. The stem length in the distal femur is dependent of

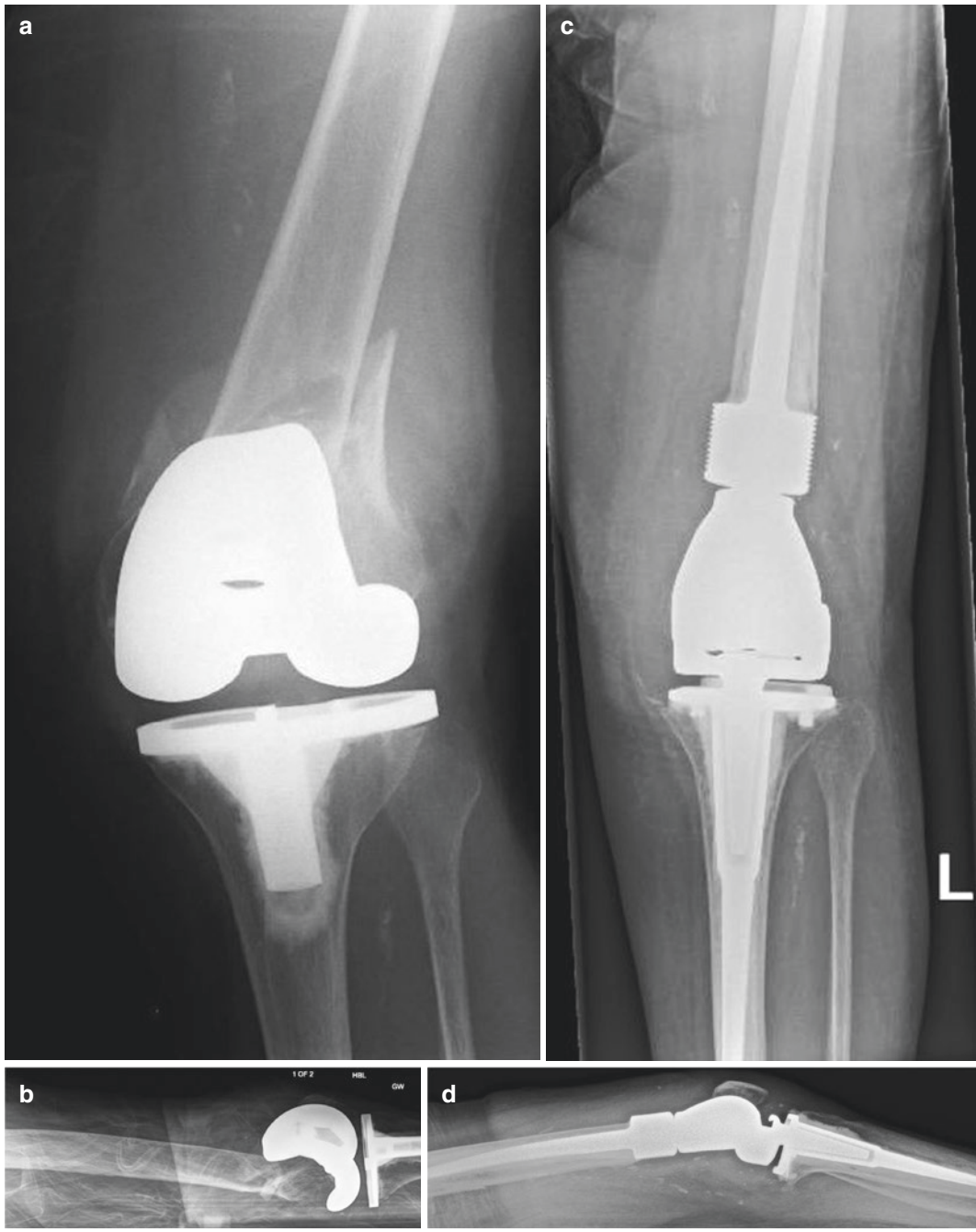

Fig. 14.2 Distal femoral periprosthetic fracture treated in a 93-year-old patient with cemented distal femoral replacement. (**a**, **b**) AP and lateral views of low periprosthetic distal femoral fracture in an osteoporotic patient. (**c**, **d**) AP and lateral views of a distal femoral replacement (METS, Stryker, Stanmore, UK) in situ

fracture level and ideally engages the diaphysis although this may be less important with cemented narrow stems [15].

The outcomes of DFR in trauma are not well published. The more frequent indication for this is failed TKA or failed prior fixation, infection and tumour surgery. Clearly these indications have a significant impact upon the outcome of the prosthesis. Again, much of the published literature is limited to extended cases series with no control group.

The failure of DFR is most commonly from infection or aseptic loosening and periprosthetic fracture. Much of the published case series available have numbers of 30 patients or less, without a control group. Lokikere et al. [16] reported in 2016 a review of 25 consecutive patients with a mean age of 72 years, finding a re-revision rate in the early postoperative setting (less than 2 years) of 8% with an additional 3 patients sustaining further periprosthetic fracture within the early postoperative course. They did not report any early infections however.

Springer et al. [17] reported a case series with infection as a complication in 5/26 knees (19%) with a significant morbidity associated and limited options for revision in this situation.

Korim et al. in 2013 [18] performed a systematic review, reporting on 241 EPRs performed for non-tumour indications. They describe re-operation in 17% for any reason, with infection being the most common at 15% and aseptic loosening and fracture both being at 5% of the cohort. It reported a mortality at 22% over a 3 year period reflecting the frailty of the patients in this group. This highlights the important point that distal femoral replacement is a salvage procedure that has a significant mortality and morbidity associated with it although has advantage regarding early post-op rehabilitation.

A feasibility study for a randomised, controlled trial, (KFORT), comparing internal fixation with distal femoral replacement, was performed in 2019. Significant challenges in recruitment and retention of patients were encountered, rendering the study unfeasible. It is likely that further evidence on this subject will come from observational studies [19].

14.6 Conclusion

Distal femoral fractures are a challenging and infrequent injury. With a wide variety of patient and surgical factors to consider there is no high-level evidence data to support one strategy over another. What is well established that by far the most common presentation is a displaced supracondylar fracture with adequate bone stock. There appears to be equipoise as to whether this should be treated with a IMN or a locked plate. There is also consensus in the literature that non-surgical treatment is best avoided and that distal femoral replacement is a viable alternative to both unsalvageable fractures and where rehabilitation necessitates immediate mobilisation but is burdened with a significant risk of serious complication.

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15 Total Knee Arthroplasty in Patients with a History of Metal Allergy: Conventional Implant or Hypoallergenic Implant?

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15.1 Introduction

It is well known that current conventional total knee arthroplasty (TKA) materials (cobalt-based alloys containing cobalt, chromium and nickel) have good biocompatibility [1]. However, such materials can cause an immune response whose role in the TKA outcome is not clear yet [1, 2]. Some allergic reactions have been published, such as eczema, urticaria, continuous swelling or aseptic loosening of the prosthesis [3]. Although the presence of sensitivity to the metals used in TKA is widespread, few patients exhibit symptoms. Nickel, chromium and cobalt are the most typical sensitizers, but allergic reactions to titanium and vanadium have been reported as well [1].

The immune response is characterized by infiltration of perivascular T and B lymphocyte tissue around the TKA. The infiltrates are predominantly surrounded by high endothelium venules. This response may be associated with periprosthetic osteolysis and aseptic loosening of the implant. The differentiation between hypersensitivity and low-grade infection is a diagnosis by elimination, made by aspiration cultures and histological analysis of the synovial tissue [4]. Whether the patient develops symptomatic hypersensitivity to metal implants is unpredictable. Despite the fact that 20–25% of patients who have a TKA (and a higher proportion of women) have a clinically testable sensitivity to metal, hardly any (<1%) have symptoms [5, 6].

The purpose of this chapter is to answer the following questions: What should we do if a patient who needs a TKA tells us that he/she has a history of metal allergy? What tests should be done to confirm or exclude the diagnosis? Should we implant a conventional TKA (made of cobalt-based alloys) or a "hypoallergenic" implant?

15.2 Diagnosis of Metal Allergy: What Tests Should Be Done? Are They Reliable?

The diagnosis of metal hypersensitivity in patients who have undergone TKA is challenging. Conventional testing for cutaneous allergy is by skin patch tests (SPTs), however, it is not clear how reliably SPTs diagnose allergy related to TKA. The diagnosis should be made after excluding other sources of pain and swelling, such as low-grade infection, instability,

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loosening or mal-rotation of components, referred pain and complex regional pain syndrome [7]. Metal hypersensitivity following TKA presents in two principal ways: dermatitis or a continuous painful synovitis of the knee joint. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and knee aspiration are usually negative.

In 2016 Bravo et al. investigated whether patients with a history of metal allergy with a positive SPT performed worse after a primary TKA than those with a negative SPT and controls [8]. They concluded that a positive SPT for metals was of little practical value in anticipating the medium-run result after TKA. Therefore, they did not recommend SPT as a method to guide the selection of TKA type in the primary scenario.

SPT, leukocyte migration inhibition test (LMIT) and lymphocyte transformation tests (LTT) are commonly utilized to evaluate metal hypersensitivity [9, 10]. Many patients will give a history of metal allergy–self-reported metal allergy (SRMA) and this is frequently utilized as a screening tool prior to TKA [11]; however, again, a history of SRMA is not a reliable predictor of problems following TKA.

In 2019 Yang et al. analysed the relationship between a positive LTT test and histopathological findings and clinical and functional results [12]. They studied 27 primary, well-fixed, aseptic TKAs in which patients had continuous pain and/or stiffness. Patients were screened for suspicious nickel allergy, as determined by a positive LTT. Periprosthetic tissue samples taken at the time of revision surgery were scored utilizing the aseptic lymphocyte-dominated vasculitis-associated lesion (ALVAL) scoring system. Eight patients were considered as barely reactive; 8 patients, moderately reactive; and 11 patients, strongly reactive to nickel by LTT. The prevalent findings in the routine histopathological study were fibrosis and various degrees of lymphocytic infiltration in 17 (63%) of the 27 cases. The conclusion was that a positive LTT test may not demonstrate that an immune reaction is the source of pain and stiffness following primary TKA.

15.3 The Clinical Impact of Metal Allergy on the Outcomes of TKA

In 2008 Granchi et al. assessed the clinical impact of metal allergy on the outcomes of TKA [2]. Ninety-four patients underwent SPTs, involving representative haptens of cobalt-based alloys (chromium–cobalt–molybdenum) and titanium-based alloys (titanium–aluminium–vanadium). There were 20 who had not yet undergone arthroplasty, 27 with well-functioning TKA, and 47 with loosening of prosthetic components. The incidence of positive skin reactions to metals increased significantly following TKA, regardless of whether the implant was stable or loose (no implant 20%; stable TKA 48.1%, $p = 0.05$; loose TKA 59.6%, $p = 0.001$, respectively). A higher incidence of positive vanadium SPT was found in patients with stable TKA with at least one titanium–aluminium–vanadium component (39.1%, $p = 0.01$). According to Granchi et al. the clinical history of metal allergy seemed to be a risk factor, as TKA failure was four times more probable in patients with preoperative symptoms of metal hypersensitivity. The prognostic value was supported by the survival analysis, albeit in a very small population sample. This study confirmed that in patients with TKA the incidence of positive SPT was higher than in the general population; however, no prognostic value was ascribed to sensitization, because SPT could not differentiate between stable and loose implants. Granchi et al. stated that the existence of metal allergy symptoms before primary TKA surgery should be contemplated as a plausible risk factor for implant failure.

In 2008 Schuh et al. analysed 300 patients (100 men, 200 women) with total hip arthroplasty (THA, $N = 214$) or TKA ($N = 86$) using a standardized questionnaire of the Implant and Allergy Working Group with respect to allergies, especially to different metals. The objective was to determine the incidence of allergic reactions to alloy components [3]. The follow-up was 33.3 months on average (range: 3–174 months). Different allergies were observed in 39 patients.

By SPT, in 12 patients (4%) had allergic reactions against nickel, in 4 patients (1.3%) against cobalt, and in 2 patients (0.7%) against chromium. One patient each suffering from a nickel allergy exhibited signs of osteolysis or recurrent effusions after THA with a metal-on-metal bearing (although this may or may not have been related to allergy). One patient each suffering from recurrent effusions or eczema after TKA exhibited allergic reactions to benzoyl peroxide. In the rest of patients with allergies to the alloy constituents, no adverse events were observed. The majority of the patients with allergies tolerated the TKA without problems. However, Schuh et al. concluded that further research was needed to recognize the patients with allergy who do not tolerate the conventional TKA, and thus decide whether to use hypoallergenic implants.

In 2016 Nam et al. assessed the relationship between allergy and patient-reported outcome. In patients reporting metal allergy preoperatively, functional outcomes and postoperative mental health state were inferior to those who did not report such allergies [13]. Patients (N = 1494; 906 primary THA; 589 primary TKA) operated on over a 2-year period completed a preoperative questionnaire asking about metal allergy. Groups with and without metal allergy were compared. The incidence of metal allergy reported by patients was 2.3% in THAs and 4.1% in TKAs; 97.8% of metal allergy patients were women. After TKA, postoperative knee society function, symptoms, satisfaction, and expectations were lower in the metal allergy group ($P < 0.001$–0.002). After THA, patients with metal allergy had a worse mental component score of SF-12 and a smaller degree of improvement of their mental component score of SF-12 compared to the non-metal allergy group ($P < 0.0001$ and $P = 0.001$, respectively).

In 2019 Schmidt et al. analysed the effect of SRMA on TKA [11]. Over a 4-year period, 168 patients with SRMA underwent TKA; 150 (89%) received nickel-free implants and 18 (11%) received chromium–cobalt implants containing nickel. The mean age was 67 years, and 95% were women. The control group were 858 patients with TKA (mean age, 68 years) without SRMA, matched by sex. No differences were observed between the nickel-free and chromium–cobalt SRMA groups. Patients with SRMA and those without SRMA showed similar early functional results.

15.4 Should We Implant a Conventional Primary TKA or a Hypoallergenic TKA?

In 2013 Thomsen et al. published a survey conducted among members of the Joint Replacement Working Group in Germany (86.7% response), observing that 0.6% of patients with TKA had hypersensitivity to nickel or cobalt after surgery [14]. Only a third of them required revision TKA. Although patients with hypersensitivity were uncommon, 84% of surgeons preferred to implant coated TKA in patients with self-reported allergies. Thomsen et al. advised that prior to performing a revision TKA, arthroscopic synovial biopsy should be performed to exclude infection and allergy, with samples being sent for histology and microbiology. In 2015 Mitchelson et al. performed a literature review suggesting that there was a probable causal relationship between metallic TKA and hypersensitivity reactions that can possibly result in aseptic failure [15].

It has been reported by Lachiewicz et al. that if metal hypersensitivity is suspected following TKA and non-surgical treatment has failed, revision TKA with components made of titanium alloy or zirconium coating can be successful. However, surgeons must inform patients that no evidence-based guidelines are available for the treatment of this problem, in particular for screening decisions. The results of such revisions are unpredictable. Taking into account the limitations of testing methods available, the extensive screening of patients for metal allergies prior to TKA is not warranted [7].

In 2016 Ajwani and Charalambous identified 15 “hypersensitivity-friendly” systems suitable for patients with metal hypersensitivity: 10

implants were chromium–cobalt prostheses with a "hypersensitivity-friendly" outer coating and 5 implants were made entirely of non-chromium–cobalt alloys [16]. Moreover, some of the aforementioned systems offer the same surgical designs and techniques as conventional implants.

In 2018 Eftekhary et al. stated that there was no evidence-based support for either preoperative testing or routine utilization of hypoallergenic TKA [17]. In 2019 Saccomanno et al. did not recommend routine allergy testing or patch testing before TKA, except if a clear history of local or systemic reactions had been informed. The reason was that there was still a lack of evidence concerning relationship between metal hypersensitivity and implant-related adverse events. In patients with positive history and positive tests, a "hypersensitivity-friendly" TKA should be contemplated. In fact, after failure of primary TKA, one-stage revision TKA for metal hypersensitivity should be considered only after excluding most common causes of such a failure, and even after a short-run treatment intending to resolve skin dermatitis and pain [18].

15.4.1 TKA Using Alternative Materials

Taking into account that there is no validated screening method to recognize patients at risk for complications of metal allergy following TKA, in patients at risk some surgeons have advised to consider the routine use of implants that do not contain nickel, chromium and cobalt [19]. In primary TKA, the use of an all-polyethylene tibial component avoids exposure to any metal alloys; for the femur, the use of oxidized zirconium (Oxinium, Smith and Nephew, London, UK), or ceramic components is viable options. Of these, oxidized zirconium is an established, mainstream alternative which is used as standard in a number of primary total and partial knee designs, albeit that it is proprietory to a single manufacturer.

In 2014 Innocenti et al. assessed the risk of metal hypersensitivity in 24 TKA patients (25 knees) [20]. A cemented, fully anallergic implant with an oxidized zirconium femoral component and a tibial base plate made entirely of polyethylene was utilized. Four (16.6%) of the 24 patients were considered hypersensitive to metals. Mean follow-up was 79.2 months. No patient presented any reaction related to hypersensitivity or complications after TKA. These authors made the following recommendations: careful investigation of medical history for metal hypersensitivity, SPT and laboratory tests should be carried out in case of doubtful sensitization; and that the selection of a hypoallergenic implant can avert any potential complications.

In 2014 Hofer and Ezzet analysed 109 TKAs with an oxidized zirconium femoral component in 82 patients with a minimum follow-up of 5 years. Their objective was to determine the survival of the TKA and to assess whether any complication was due to this bearing [21]. Survivorship free of bearing-related complications was 100%. There were revisions for loosening, osteolysis, implant failure or deep infection. There were no TKAs with radiographic failure, visible wear, loosening or osteolysis. The conclusion was that oxidized zirconia was an interesting alternative for patients with nickel sensitivity.

In 2015 Bloemke and Clarke assessed the rate of self-reported cutaneous metal allergy, or sensitivity, in 194 patients experiencing TKA, and whether there was a higher incidence in females [19]. The frequency of self-reported metal allergy or skin sensitivity was 14%; 22% (19/86) of women and 2% (1/53) of men reported a positive history. Fourteen percent of patients experiencing TKA self-identified as having a cutaneous metal allergy or sensitivity. These authors advised that until validated screening tests exist to recognize patients at risk of symptomatic metal allergy following TKA, selective use of prostheses that do not contain nickel, chromium or cobalt may be contemplated for patients who self-identify as having a metal sensitivity. Table 15.1 shows non-coated metal "hypersensitivity-friendly" TKAs.

Table 15.1 Some non-coated metal "hypersensitivity-friendly" primary TKAs available

Company	TKA System	Femoral component	Tibial component	Same design and intrumentation as the conventional system
Smith and Nephew	Genesis II	Oxinium oxidized zirconium (available off the shelf)	Titanium	Yes
Smith and Nephew	Genesis II	Oxinium oxidized zirconium (available off the shelf)	All-Poly® tibial (made entirely of polyethylene without metal-back)	Yes
Smith and Nephew	Legion primary	Oxinium oxidized zirconium (available off the shelf)	Titanium	Yes
Zimmer	NexGen	Titanium (available off the shelf)	Titanium (available off the shelf)	Yes

Table 15.2 Some coated metal "hypersensitivity-friendly" primary TKAs available

Company	TKA system	Femoral component	Tibial component	Same design and intrumentation as the conventional system
B. Braun and Aesculap	Columbus AS implant system	Complete zirconia nitride coating of the standard implant (available off the shelf)	Complete zirconia nitride coating of the standard implant (available off the shelf)	Yes
Biomet	Vanguard	Complete titanium niobium nitride coating of Vanguard knee (available off the shelf)	Complete titanium niobium nitride coating of Vanguard knee (available off the shelf)	Yes
Depuy	PFC Sigma	Complete titanium nitride coated (custom-made)	Complete titanium nitride coated (custom-made)	Yes
Stryker	Triathlon	Complete titanium nitride coated (available off the shelf)	Complete titanium nitride coated (available off the shelf)	Yes

15.4.2 Surface Coatings

To avert or diminish the local and systemic consequences of the metal ions released by metal implants, i.e. to prevent a hypersensitivity reaction, the alternative approach is to coat implants to prevent the exposure of metal alloys [21–23]. A potential extra benefit of these implants is wear resistance—in vitro tests have demonstrated a decrease in polyethylene wear for these coatings—but it is not known whether this translates to a clinical benefit commensurate with the increased cost of these implants [24].

In 2013 Lutzner et al. compared coated TKA (N = 60) and conventional TKA (N = 60), in patients with no history of hypersensitivity and no other metal implants. They concluded that sensitization had no influence on clinical results [22]. The hypersensitivity SPT for chromium, cobalt, molybdenum and nickel and plasma ion concentrations was assessed before and 1 year after surgery. A new weakly positive reaction to cobalt was found in the coated TKA group and two doubtful skin reactions to nickel (one in each group). Even with sensitization to the TKA materials no skin reactions were encountered.

In 2016 Beyer et al. randomly assigned 120 patients to undergo a new seven-layer coated TKA or a conventional TKA [24]. A revision TKA was carried out in the conventional group, resulting in a calculated 5-year survival of 100% in the coated group and 98.1% in the conventional group. No adverse effects were observed with the new coating during mid-run follow-up. Table 15.2 shows coated metal "hypersensitivity-friendly" TKAs.

15.4.3 Comparison of Outcomes of Conventional and Hypoallergenic Implants

In 2015, Thienpont compared 40 titanium–niobium–nitride coated TKAs and 80 conventional chromium–cobalt implants [23]. The average follow-up was 2 years. No differences were observed between the groups in terms of clinical, radiological or patient-reported outcomes. No patients required short and medium-run revision TKA.

In 2016, Bergschmidt et al. evaluated the clinical and radiological outcomes of a TKA system, comparing a ceramic (BIOLOX® delta) and metallic (cobalt–chromium–molybdenum) femoral component over a 5-year follow-up period [25]. Forty-three patients with TKA (17 metal and 26 ceramic femoral components) were analysed. No differences were found between the two groups. Therefore, Bergschmidt et al. stated that ceramic knee implants may be a promising solution for patients with metal sensitivity.

In a level I evidence-based study published in 2018, Postler et al. compared coated to conventional TKA in patients with no known hypersensitivity reaction [26]. They compared conventional, Cobalt–Chromium Balansys TKA ($N = 59$) with TKA of the same design, but with titanium–niobium–nitride (TiNbN) coating ($N = 59$). Patient-reported outcome measures (PROMs) showed substantial improvement after TKA, with no difference between groups.

15.5 Is There a Justification to Use Primary Hypoallergenic TKA in Patients with Metal Allergy?

In 2016, Middleton and Toms reviewed the literature on whether allergy and hypersensitivity have a clinical basis for implant selection at TKA [27]. Although a relationship existed, they could not encounter any evidence of implant failure due to allergy. With the lack of evidence, these authors stated that there can be no justification for utilizing "hypoallergenic" implants in patients with pre-existing skin sensitivity to the metals used in TKA.

Ultimately, there is conflicting evidence to guide our practice in this area. The link between patient-reported or SPT-evidenced cutaneous hypersensitivity on the outcome of TKA is not supported by strong evidence. However, in a patient who reports cutaneous allergy, and using implants which have comparable outcomes compared to conventional implants, the use of coated implants is certainly justifiable. Figure 15.1 shows the authors' recommended preoperative diagnostic algorithm to select patients requiring hypoallergenic TKA.

15.6 TKA Failure Due to Metal Allergy: Should We Perform a "Hypoallergenic" Revision TKA

This is a difficult question to answer given the challenges with diagnosing clinically relevant metal allergy; however, some small studies exist to guide our protocol.

In 2013, Thakur et al. reported a series of five patients (six knees) with persistent pain and hypertrophic synovitis after TKA with cobalt–chrome components [6]. Infection was excluded in all cases. None underwent metal allergy testing but in all cases there was synovitis and an aseptic inflammatory reaction on histological examination. All patients received an oxidized zirconium revision implant with a titanium tibial tray (Genesis II, Smith and Nephew). In all cases, there was good pain relief and recovery of function. The authors recommend the use of this implant as it is in widespread use with good long-term survival data in the general population.

Zondevan et al. reported a retrospective comparative series of 46 patients presenting with a painful TKA of unknown aetiology [28]. All patients underwent LTT and those with a positive test ($n = 39$) were revised to a coated implant; those with a negative test were revised to a conventional implant. Overall, they report a high degree of satisfaction following revision surgery.

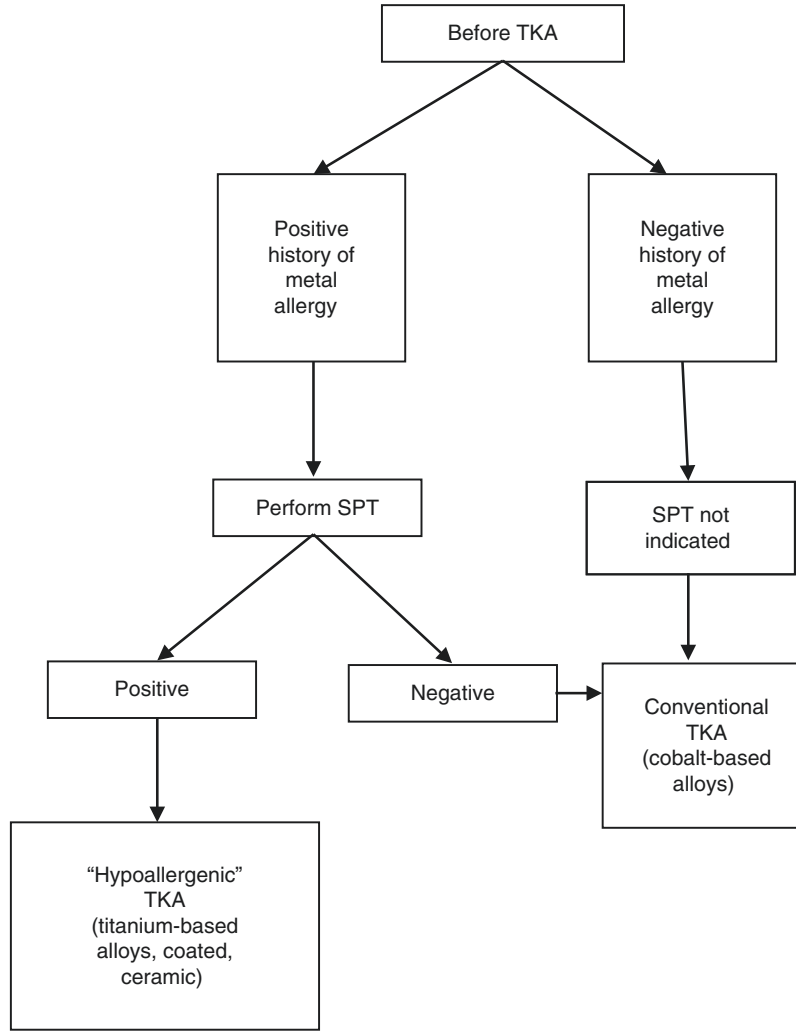

Fig. 15.1 Preoperative diagnostic algorithm to select patients requiring "hypoallergenic" primary total knee arthroplasty (TKA). *SPT* skin patch test

The magnitude of the improvement in pain and function was greater in those revised for a diagnosis of hypersensitivity and reached statistical significance in this group; the group with unexplained pain was smaller and, whilst there was still a substantial improvement in symptoms, this did not reach statistical significance. The authors suggest that metal hypersensitivity is a reason for pain following TKA and that revision to a hypoallergenic component is an effective form of management.

By contrast, in 2019 Sasseville et al. found no statistically significant difference in the result of revision surgery between patients with positive versus negative SPT or LTT [29]. Despite this, Sasseville et al. considered that patients with a history of suggestive allergy to metals, acrylate or aminoglycoside should be tested preoperatively to avoid hypersensitivity-related postoperative adverse events. Given the availability of well proven hypoallergenic alternatives to cobalt chromium components, we recommend the use of such components in patients with proven hypersensitivity; the use of such components should also be considered in those with high clinical suspicion in the absence of a test. Figure 15.2 shows our recommended algorithm for diagnosis and treatment for metal allergy-related complications after TKA.

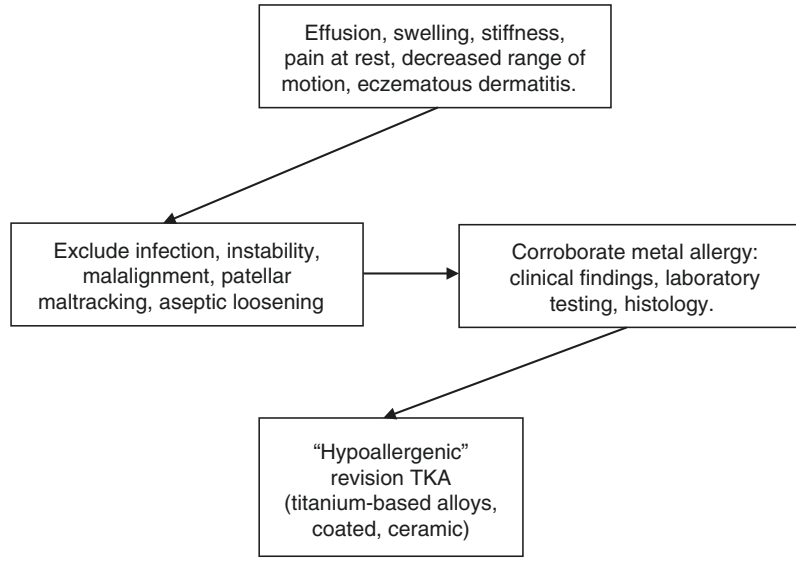

Fig. 15.2 Algorithm for diagnosis and treatment for metal allergy-related complications after conventional primary total knee arthroplasty (TKA)

15.7 Conclusions

Although 20–25% of TKA patients develop sensitivity to metals following TKA, fewer than 1% exhibit symptoms. For some authors a history of metal allergy appears to be a risk factor, as TKA failure may be four times more likely in patients with metal hypersensitivity. Other authors point to the fact that most patients with allergies tolerate the conventional chromium–cobalt implant without problems and suggest that there is no justification for using "hypoallergenic" TKA in patients with skin sensitivity to metals. There are several options for TKA in cases of hypersensitivity. One option is to use implants that do not contain nickel, cobalt and chromium; be they oxidized zirconium or ceramic with an all-polyethylene tibial component. Another possibility is to use implants that have been coated with substances such as titanium–niobium or nitride. In view of the existing controversy, we believe that it is currently safer to implant a nickel-, cobalt- and chromium-free TKA in patients who report themselves to be allergic to metals. Although it is advisable to perform a SPT for metals, a positive SPT has little predictive value of the medium-term outcome of conventional TKA. Patients in whom a primary TKA fails due to confirmed or highly suspected hypersensitivity may benefit from hypoallergenic prosthetic revision. However, prior to performing it, it is advisable to carry out knee arthroscopy to get tissue to allow microbiological and histopathological studies to exclude low-grade infection. Further studies are required to achieve a conclusion on the influence of metal ions in sensitization and development of TKA-related metal hypersensitivity.

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16 Ankle Arthroplasty Versus Arthrodesis: Making the Right Choice

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16.1 Introduction: Background and Current Practice

The prevalence of osteoarthritis varies amongst joints in the body, even amongst those with similar loadbearing properties. From experience we know that osteoarthritis is a common occurrence within the knee, whilst comparatively it is relatively uncommon in the ankle joint, despite their similar loadbearing properties [1–6]. The reason for this is unknown but is likely to be related to the differences in the joint morphology and congruency which is much higher in ankles as well as the cartilage properties. Ankle cartilage (1.0–1.7 mm) is much thinner than knee cartilage (4.0–6.0 mm), stiffer, more resistant to compression and has a much higher percentage of superficial layers for absorption of compressive force [7–9]. With age, there is a reduced decline in tensile strength of ankle cartilage compared to the hip and knee [3].

Trauma is one of the commonest causes of end-stage ankle arthritis, with genetic, developmental and metabolic factors also playing a role [10]. Given that the ankle is one of the most commonly injured joints in the body and the incidence of ankle injuries is increasing, it is prudent to anticipate this will represent a significant future health burden [11, 12].

The mainstay of surgical treatment until recently has been arthrodesis, in which the ankle joint is fused, preventing movement and thus pain. However, total ankle arthroplasty is becoming an increasingly recognised treatment option as an alternative to ankle arthrodesis, preserving functional range of movement [13].

Despite accounting for a small proportion of the overall arthroplasty market, total ankle replacement is a growing sector with over 15,000 performed in the USA alone, rising 12-fold from 2007 to 2014 and accounting for 45% of all end-stage ankle arthritis operations [14]. The United Kingdom has been comparatively more modest, with little over 1000 total ankle arthroplasties being performed in 2019 [15]. Given that total ankle arthroplasty has been an option since the 1970s, it is unclear what has driven its recent increased popularity. However, understanding how these implants have been refined over this time may in part explain their rise in clinical practice.

To date there have been three distinct generations of ankle arthroplasty implants, evolving over time (Fig. 16.1). The first generation of implants were two-component cemented prostheses, with a polyethylene tibial compo-

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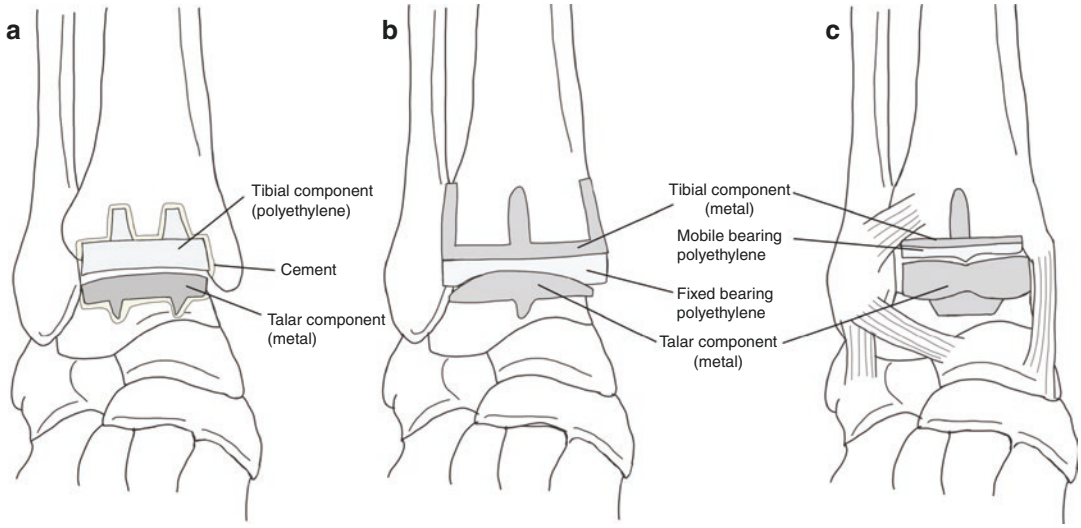

Fig. 16.1 (**a**–**c**) Total ankle arthroplasty—prosthesis evolution (**a**) First generation, (**b**) Second generation and (**c**) Third generation

nent and metal talar component, either highly constrained or semi-constrained. The constrained design was expected to provide better resistance to wear and surface deformation due to improved pressure resistance [16]. Like all first-generation arthroplasties, early failure was guaranteed by poor understanding of biomechanics and tribology. Rapid osteolysis occurred causing early failures, with few implants lasting more than a few years. The poor outcomes continued to persuade the orthopaedic community to avoid ankle replacement [17]. One of our arthroplasty pioneers, Mike Freeman stated in 1985 that "the overall results and long-term outlook of ankle arthroplasty is so poor as to warrant offering only arthrodesis as the surgical treatment of the disabling arthritic ankle. Unless the design and method of fixation of ankle prostheses are improved, we feel that ankle arthroplasty should not be performed, even in patients with rheumatoid arthritis" [18].

Second-generation implants again utilised a two-component basis but introduced a fixed bearing polyethylene surface into either the talar or tibial component. In addition to the design changes of the components themselves, the operative technique was also adapted.

Preservation of the stronger periarticular metaphyseal bone was accepted, and more conservative bone cuts were undertaken, retaining much of the natural ankle architecture in comparison to the first-generation components. A porous press-fit design was opted for allowing for bony ingrowth that was not possible with cementation.

The second-generation implants provided evidence for successful outcomes in ankle replacements showing acceptable long-term outcomes [19]. Although the majority of replacements were, in a group of rheumatoid patients with low demand on their implants [19]. Unfortunately, these designs again failed to restore characteristic three-planar rotation and ankle gliding motion [20, 21].

Third-generation implants aimed to address this, whilst also providing congruence at the joint line. There were further design modifications, with talar components becoming more anatomical to match the differing radii of curvature of the medial and lateral talar dome.

There were further advances in the design of the insert, with improved freedom for valgus and varus movement, increased congruency and with the addition of an independent mobile bearing polyethylene insert to form a three-part modular

ankle replacement. These advances aimed to address the dilemma of combining congruence, with minimally constrained components and allow for ligaments and soft tissues to control physiological movement at the joint [22, 23].

The operative technique was further modified, impressing upon the need to minimise bone resection and undertake anatomic balancing and focus on retaining ligament stability [16, 20]. With the improvements in design and greater understanding of the kinematics of the ankle, the majority of third generation ankle replacements are expected to last more than 10 years. Enough time has not elapsed yet to confirm this, however intermediate-term results are promising.

16.2 Ankle Arthrodesis Versus Total Ankle Arthroplasty—Is There Really a Gold Standard?

While many may advocate ankle arthrodesis as the gold standard for treating end-stage ankle arthritis, it is not without its limitations [24–27]. There is a significant incidence of non-union and although this is much reduced with arthroscopic surgery, it is still present. There are also the biomechanical effects on the other joints in the body, not only those joints down-stream from the ankle but also proximally at the knee and spine. The exacerbation of symptomatic arthritis in other joints in the foot is well established and whether present or not pre-fusion surgery, this needs accounting for in the decision-making process [28]. Understandably, an ankle fusion will project abnormal forces on the surrounding joints and these may be combatted by the use of rocker-bottom shoe or trainers, which have become more fashionable.

Several systematic reviews comparing total ankle arthroplasty and ankle arthrodesis have been undertaken in an effort to answer this question. More recently, these have focussed on third-generation implants compared either directly to ankle arthrodesis or by pooling results [12, 29–31]. Various validated outcome scores were utilised across these studies, to document the severity of the impact that end-stage ankle arthritis had pre- and post-operatively on a patient's quality of life. However, there are many confounding factors and given the heterogeneity of the data presented it is difficult to come to a conclusion. The studies involve a varied patient cohort, with ankle arthritis being not just a single joint disease. On top of this there are varied prostheses, none of which have a long-term pedigree for their outcomes. Many of the studies are absent of pre-operative scores, with a focus solely on post-operative scores. Nonetheless, focussing on those with both pre-operative and post-operative scores there are comparable results reported for both arthrodesis and total ankle arthroplasty [29, 30].

In addition to quality of life, many studies commonly utilised AOFAS and SF-36 questionnaires to assess post-operative functional improvement. A recent systematic review showed a statistically significant difference between pre- and post-operative functional scores for total ankle arthroplasty, both in AOFAS and SF-36 [30]. Ankle arthrodesis, however, was only shown to have significant improvement in SF-36 scores, with total ankle arthroplasty showing improved function in the longer term, at 2-year follow-up [30]. Whilst this review attempted to compare both treatment groups, they were unfortunately not matched, and therefore caution is needed before drawing wide conclusions from this. With regard to pain relief, total ankle arthroplasty has been shown to be more effective than arthrodesis, with better pain relief post-operatively and improvements in quality-adjusted life years from ankle arthroplasty [32–35].

There are well established biomechanical and gait advantages with ankle arthroplasty, not only with the range of motion, but also a more normalised gait pattern, better walking velocity and a reduction in the energy expenditure [36–39]. Theoretically, all of this is beneficial, and it may be the deciding factor in choosing between the two procedures.

Given the comparative results for quality of life and improved functional outcomes and pain relief from total ankle arthroplasty, one would assume that this would easily be the favourable

treatment option. Unfortunately, it is complicated somewhat when analysing complication and revision rates. Total ankle arthroplasty showed slightly worse outcomes with regard to revision than arthrodesis, whilst complications were higher in patients undergoing ankle arthrodesis [29, 30]. However, a recent study has shown no difference in revision rates between ankle arthroplasty and arthrodesis across a cohort of 238 patients [40].

It would appear that both ankle arthroplasty and arthrodesis are affected by patient characteristics, including bone quality, age, diabetes and joint deformity, and all factors that might increase the likelihood of failure [41–44]. This suggests that an ideal gold standard treatment does not exist and therefore consideration of several other patient factors is required when choosing the correct treatment option.

16.3 Key Considerations for Choosing Between Ankle Arthrodesis and Total Ankle Arthroplasty

When choosing operative interventions, there are often several key considerations that need careful assessment before the correct procedure can be decided upon. These will include, although not comprehensively, the surgical suitability of the limb and the patient, as well as the patient's environment.

Often when trying to delineate if one treatment is superior to another, studies will focus on outcome measures such as pain, revision or reoperation as the sole determinants to success. However, in the case of ankle arthrodesis versus total ankle arthroplasty, this is not always a simple or fair comparison. Studies undertaken often show improvements in both cohorts independently but when compared to each other most studies have shown little or no difference, or if a difference is found it may be in part explained by differences in patient demographics. In this section we attempt to unravel some of the main considerations that may influence choice between ankle arthrodesis and total ankle arthroplasty. Primary concepts to consider when deciding on a treatment include the specific risk profile, the desired range of motion, post-operative rehabilitation goals and duration of immobility, whether revision surgery may be necessary and if the underlying bone stock is amenable to this, as well as what further stress you may impose by altering the natural biomechanics.

16.3.1 Does Range of Motion Matter?

There are over 30 mobile joints in the foot and ankle and the complex interplay between them makes treating arthritis in this region a particular challenge [45]. The biomechanics of the foot and ankle should therefore be taken into consideration when planning any operative intervention.

Key movements of the ankle joint occur in three planes and combination of these motions across the subtalar and tibiotalar joints creates the three-dimensional motions of supination and pronation [46, 47] (Fig. 16.2). The complexity of ankle motion is further exemplified by the differences in radial curvature across the medial and lateral aspects of the talar dome causing multiple axes of rotation that are dynamic throughout motion [48].

The range of motion within the ankle joint is predominantly within the sagittal plane with a range of 65–75°, from 10 to 20° dorsiflexion through 40–55° of plantarflexion [49, 50]. However, the actual range of motion in the sagittal plane required for activities of daily living is far less, with a maximum of 30° when walking, 37° when ascending and 56° when descending stairs [47]. As such from a functional perspective, any treatment options employed can accept a somewhat reduced range of motion while still preserving activities of daily living for most individuals.

Since its inception the idea of total ankle arthroplasty has been to recreate normal joint kinematics, biomechanical have shown that implants should have a comparable range to normal physiology [45, 51]. Various studies have individually assessed total ankle arthroplasty and pre-and post-operative range of motion; all show-

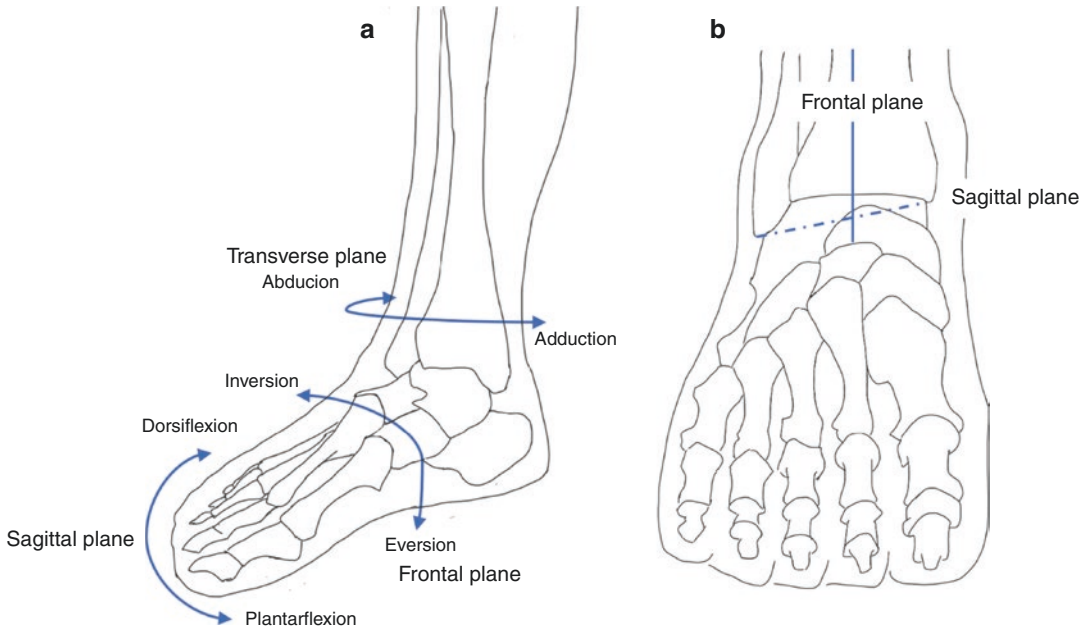

Fig. 16.2 Illustration demonstrating ankle motion in three planes (**a**) Key movements of the ankle occur in three planes—sagittal (plantarflexion and dorsiflexion), transverse (abduction and adduction) and frontal (inversion and eversion). (**b**) Axis of motion for frontal (solid) and sagittal (dashed) planes, intersection of the two is the centre of rotation for inversion and eversion (51)

ing improved walking velocity, more normal first and second rockers during the gait cycle and improved sagittal dorsiflexion, when compared to a control group with no intervention [37, 38]. However, from real-world practice, the actual clinical and radiological range of motion of total ankle arthroplasty is less than the expected physiological range. This may in part be due to a combination of implants not functioning as designed, soft tissue limitations or tightness and patient compliance with post-operative rehabilitation and physiotherapy.

A study undertaken by Pedowitz et al. expanded on this by comparing range of motion and functional outcomes of total ankle arthroplasty and arthrodesis directly. In this, patients undergoing ankle arthroplasty maintained a significantly greater range of motion (34.2°) compared to those undergoing arthrodesis (24.3°) [45]. While total ankle arthroplasty provides benefit over arthrodesis, given that many patients with end-stage disease may have little range of motion at presentation due to joint space loss, the aim of achieving at least 10° of dorsiflexion and 30° plantarflexion would allow most to function well for the majority of activities of daily living [52].

16.3.2 Post-operative Rehabilitation

Post-operative rehabilitation protocols for both arthroplasty and arthrodesis vary considerably. Generally, consideration of the procedures undertaken, and any concomitant procedures need to be factored into weightbearing, range of motion and functional restrictions. Ideally with surgery, the aim is to return to full function as quickly as possible whilst balancing the initial need to heal the surgical incision and soft tissues and in the intermediate term, promote bone healing and integration with any prosthesis utilised.

Patients undergoing arthrodesis typically have a long period of post-operative immobilisation. Although there is a range of recommendations, commonly the patient is kept non-weightbearing for a period of 6–8 weeks, before a removable boot is applied [53]. Only after a further 4-week

period is the patient allowed to fully weightbearing with restrictions often imposed on full daily activities until approximately 12 weeks, subject to clinical and radiological evidence of fusion [54–56].

Total ankle arthroplasty offers the opportunity of earlier mobilisation compared to ankle arthrodesis. The period of non-weightbearing is much less and typically for only 10–14 days, with full weightbearing allowed after 3–6 weeks. This again varies with some surgeons allowing weightbearing immediately after surgery [52].

Arthroplasty can be very beneficial in elderly patients, who may struggle to non-weightbearing for several weeks and where early mobilisation can make a big difference to early recovery. This has the added benefit of significantly reduced immobility and bed rest, with benefits in maintaining levels of activity, strength and health in this susceptible group of patients. This also reduces the need for ongoing venous thromboembolism prophylaxis [57]. Conversely, with earlier mobility, the risks of non-union, increased wound problems, need for further surgery and issues with underlying prosthesis or metalwork are all a greater risk in comparison to arthrodesis [57].

16.3.3 Long-Term Concurrent Joint Osteoarthritis

We have discussed the comparative clinical outcomes in the short and intermediate term with both total ankle arthroplasty and ankle arthrodesis. However, long-term outcomes must also be considered. Ankle arthrodesis has for a long time been considered the treatment of choice due to the poor longevity of earlier ankle arthroplasty implants. Nonetheless, a major reported risk of ankle arthrodesis has always been adjacent joint degeneration.

There are conflicting reports within the literature as to the extent to which it afflicts patients, and some studies have gone as far as to suggest that it may in fact be a pre-existing change at the time of arthrodesis being undertaken [58]. Unfortunately, it would appear that this may not be the entirely true and the fact is that it remains a significant concern, especially in younger patients who may not be appropriate for total ankle arthroplasty.

A large retrospective cohort study by Yasui et al. investigated factors that may influence postoperative adjacent joint arthritis following arthrodesis. In this, those undergoing open ankle arthrodesis were found to have a significantly higher rate of adjacent arthritis than those undertaken arthroscopically [59]. The exact reason for this was not fully addressed by the authors and many subsequent reviews have failed to account for this observation, or indeed for the reason behind increased arthritis in ankle arthrodesis in general. However, if we consider the basic biomechanics of the foot and ankle, as discussed previously we may be able to explain the differences in arthroplasty and arthrodesis.

When assessing range of motion between arthroplasty and arthrodesis cohorts we identified an expected improvement in range of motion in the total ankle arthroplasty group. However, surprisingly the arthrodesis group seemed to have more range of motion than one would expect, approximately 24.3° [45]. The movement within the arthrodesis group arises from compensatory hyper-mobility of adjacent articulations, particularly at the midfoot. Studies showed an increased movement at the midfoot (22.8°) in the ankle arthrodesis cohort when compared to a relatively normal range of motion (10.5°) in the arthroplasty cohort [45]. It is clear therefore, that by undertaking ankle arthrodesis, there is increased motion at adjacent joints that would otherwise not be present in the arthroplasty cohort. As such, increased loading and motion at these joints may predispose to the progressive arthritis within adjacent joints in patients undergoing ankle arthrodesis. Finite element analysis undertaken in biomechanical studies for both arthroplasty and arthrodesis showed that total ankle arthroplasty provided a more stable plantar pressure distribution than ankle arthrodesis [60]. Based upon these findings, total ankle arthroplasty may not be subject to the same long-term issues.

Secondary arthritis affecting the surrounding joints of an ankle arthrodesis is common, with

many patients having restrictive symptoms. This often affects the subtalar joint but also the talonavicular and midfoot joints. Initial management is focussed on symptomatic relief, with injections and footwear adaptations such as rocker-bottom soles. Beyond this, there are few options and a secondary fusion is usually required, rendering the foot with similar function to a patient that has undergone either a tibio-talo-calcaneal (TTC) or pan-talar fusion. Importantly, the success rate of a secondary subtalar fusion, below an ankle fusion, is much lower than in primary surgery, with only a 62% fusion rate [61].

There is a paucity of evidence on the functional outcomes after TTC or pan-talar fusions, although from our experience this treatment is essentially a salvage operation that allow recipients at best to mobilise limited distances and manage the normal activities of daily living.

There are a few published case reports that have described 'taking down' ankle fusions for concurrent joint osteoarthritis [62, 63]. In these case reports surgeons have revised the ankle arthrodesis to an ankle arthroplasty whilst at the same time performing a subtalar fusion. The ability to 'take-down' an ankle fusion may be dependent on whether the fibula was preserved at the time of the original ankle fusion and therefore when performing an ankle fusion on a younger patient some caution needs to be taken before employing a fibula sacrificing approach as this may potentially limit options later on in life.

The addition of a subtalar fusion for osteoarthritis in patients who have already had an ankle arthroplasty or who underwent simultaneously arthroplasty and subtalar fusion does not appear to have a significant impact on functional outcomes and therefore this should be taken into consideration when deciding between ankle arthroplasty and arthrodesis [64].

16.3.4 Revision Surgery

One of the main rationales for choosing ankle arthrodesis over total ankle arthroplasty has been the unacceptably high rates of revision that earlier generation implants were subject to. Short- to intermediate-term outcomes for first- and second-generation ankle arthroplasty implants showed failure of up to 90% within 5 years [11, 13, 16, 20]. A lot of the reluctance to undertake total ankle arthroplasty has been as a result of this, as well as a paucity of long-term outcome data from newer implants.

In the last 5–10 years, however, a number of reviews have been undertaken which look at comparing newer generation implants directly against ankle arthrodesis. From this we have seen that the revision rates of total ankle arthroplasty are still higher than those undergoing arthrodesis [30]. Krause et al. found complications as high as 54% in those undergoing arthroplasty versus 26% in those with arthrodesis [65]. A large multicentre trial has been undertaken which shows reoperation rates in the arthroplasty group to be 17% across a 7 year period, over twice that of the arthrodesis group, which saw revision at around 7% [66].

A meta-analysis of total ankle arthroplasty in 2012 showed 10-year survival rates of arthroplasty to be 89% [12] however in order to guide decision making in younger patients longer term outcomes are still needed and additional larger, multicentre RCTs are underway [31]. The results of these are still yet to be published, but many inferences can be taken from our current knowledge of outcomes as to who may be more susceptible to revision. A systematic review undertaken analysing failures found that revision surgery was more common in patients with ankle osteoarthritis associated with valgus tilting, medial laxity, posterior tibial tendon or deltoid insufficiency [30, 41–44].

Much like any other arthroplasty, components are subject to wear, causing osteolysis. While improvements have been made in the latest generation of ankle replacements, osteolysis will still occur and the long-term effects of arthroplasty need to be considered. For revision, the loss of bone stock is an important factor and can cause severe additional complexity to a revision procedure. For this reason, prosthesis monitoring is important to avoid any catastrophic changes in the joint foundations. Earlier intervention, with grafting of bone cysts can be a very useful and small procedure to avoid this [67].

Certainly, aseptic loosening remains a risk and the success of revision surgery, either to a revision arthroplasty or arthrodesis, can be dependent on sufficient bone stock. The development of dedicated revision ankle prosthesis goes some way to addressing this problem although long-term results of revisions remain unknown [68]. However, the old adage of ankle arthroplasty being unsuitable for younger, overweight male patients may not be as true as they once were. Newer literature has shown that revision surgery was reportedly higher in women, under the age of 60 and those with poor glycaemic control [30, 69, 70]. Therefore, we must explore other factors that need to be considered when weighing up both treatment options.

The complications of revision surgery also apply to ankle arthrodesis, with data from the Swedish registry showing a revision rate of 8% across 1716 ankles in 9 years [71]. The reasons for revision were varied and did not include all non-unions, as not all were symptomatic enough to warrant revision. The published rates for non-union of an ankle arthrodesis range from 7 to 15%, surprisingly with arthroscopic fusions being less successful than open surgery in some reports [24, 72–74]. Revision of ankle fusion is similarly complex and the results are understandably less successful than in primary arthrodesis, with at best an 80% fusion rate and an often prolonged post-operative recovery [75]. The effects of this should be comprehended as they may well have a significant effect on a patients' recovery and wellbeing.

16.4 Factors Influencing Decision to Perform Either Ankle Arthrodesis or Total Ankle Arthroplasty

When debating ankle arthrodesis versus ankle arthroplasty, the debate often moves quickly to patient selection and demographics. Should ankle arthroplasties not be performed in the young, in men, in the overweight? These ideas may be outdated.

16.4.1 Patient Demographics

Classically, clinicians may be reluctant to undertake arthroplasty in a young patient, with concern over rapid wear in an active patient and the complexities of revision surgery, either to a fusion or another replacement. The alternative of ankle arthrodesis in this group is not without risk either and there is the guarantee of progressive concurrent joint arthritis. In younger patients, whilst the success and function after ankle arthroplasty or fusion are similar, it is the next operation that becomes the important consideration.

In the case of ankle arthrodesis, the next procedure is likely to be a hindfoot fusion with variable success rates and the functional loss that ensues from a rigid hindfoot. With an ankle arthroplasty, the next procedure may be a revision arthroplasty or a revision to an arthrodesis. Certainly, there are well documented successes recommending revision to an arthrodesis, with good outcomes [76, 77]. Treatment with a revision arthroplasty, although technically possible, has little published evidence to support or refute its use, and this needs to be discussed carefully with the patient. In older age groups, these decisions become easier as patients become less active with both arthroplasty and arthrodesis lasting longer without the requirement for revision.

With ageing, the range of motion of the ankle also changes and biomechanical studies have shown that younger females, aged between 20 and 39 years, had a higher range of motion compared to males [78]. However, with increasing age, older females showed 8° less dorsiflexion but 8° greater plantar flexion comparative to their male counterparts between 70 and 79 years old [51, 78]. Additionally there was a reduction in range of motion in both of the oldest age groups, as would be expected [51].

When we compare this clinically, it is surprising that there was no difference in survivorship or revision rates in ankle arthroplasties between those aged below and over 50 years old [79]. The Norwegian Joint Register also shows no significant difference with age [80]. With regard to gender, registry data from Norway and Sweden both show no difference in patients

undergoing total ankle arthroplasty or ankle arthrodesis [80, 81].

16.4.2 Relative Demographics and Co-morbidities

Relative patient demographics such as obesity and smoking, as well as co-morbidities such as diabetes are important factors to consider for total ankle arthroplasty or ankle arthrodesis.

Given the underlying predisposition of ankle osteoarthritis being secondary to repeated insults or trauma, compared to other joints such as the hip or knee which are more afflicted by weight-bearing, obesity might be thought to be less of an issue in this select group of patients. However, worldwide, obesity has tripled since 1975 and it is now estimated that more than 1.9 billion adults are overweight, and this number is set to rise [82]. As such, many patients are likely to have obesity and there is concern that this may increase the risk of aseptic loosening or lead to delayed wound healing [83]. However, surprisingly, many papers have shown the relatively effectiveness of ankle arthroplasty in patients who are obese. A review paper by Gross et al. prospectively identified 455 primary total ankle arthroplasties, comparing 266 who were of a normal BMI (<30) and the remainder who were diagnosed as overweight or obese. This study showed that ankle arthroplasty across these two groups was not prone to increased complications and had comparable efficacy, with the obese group having slightly lower functional outcome scores initially in the short term [67].

The results for patients with diabetes undergoing total ankle arthroplasty were less promising. A study undertaken by Choi et al. reviewed 173 total ankle arthroplasties in which 43 diabetic patients were included, 18 of which had uncontrolled diabetes. Functional outcome scores were significantly better in the non-diabetic group, with clinical failure and delayed wound healing being half that when compared to diabetic patients [69].

Much like diabetes, smoking is a significant risk factor for many perioperative complications including delays in wound and bone healing. It is well established that smoking or illegal drug use promotes a higher risk of non-union after ankle arthrodesis [84]. With respect to total ankle arthroplasty this has also been shown, with higher wound complications and worse functional outcome scores compared with non- or ex-smokers [85]. Interestingly, within this same study, cessation of smoking was shown to reverse the effects and allowed ankle arthroplasty to be an effective, safe procedure.

16.4.3 Lifestyle Factors

There are no specific literature recommendations on this topic, but common belief is that if a patient has a high impact job or activity, then the prosthesis may wear out faster and therefore a fusion may be preferable. Schuh et al. compared postoperative recreational activity and sports in patients undergoing total ankle arthroplasty versus ankle arthrodesis. There was no difference in the two groups with the arthrodesis cohort activity decreasing from 90 to 75% and arthroplasty cohort decreasing from 86 to 76% postoperatively. There was also no difference in the AOFAS score or the UCLA activity score [32].

Patients should be counselled on what to expect after an ankle arthroplasty and these figures alone do not account for the reality of individual activities patients may not be able to perform. Further analysis of the paper reveals that the majority of patients returning to activity were in those swimming or cycling, with very few undertaking running, dancing or football [32]. Based upon cross-sectional data, 71% are able to drive at 3 months and 76% of patients are able to return to work by 6 months [86]. Setting realistic targets with patients is important prior to planning any intervention.

16.4.4 Local Pathology

There is a belief that aetiology of the ankle arthritis will have a factor on the treatment outcome. In some cases, especially due to previous trauma

surgery and implants used, this can be true. Indeed, patients with post-traumatic arthritis have been shown to have poorer outcomes and higher complication rates following total ankle arthroplasty than patients with primary osteoarthritis [87, 88]. However, other studies have found no difference in outcomes and survivorship between primary arthritis, traumatic arthritis, and rheumatoid arthritis [89, 90].

Primary bone stock loss occurs in avascular necrosis and in severe cyst formation with arthritis. The degree of bone loss needs full assessment of both the tibia and talus, ideally with a computed tomography (CT) scan. If the majority of the bone loss is within the resection margins of the implant, then a successful replacement should still be possible [91]. In more severe cases, it may be more prudent to arthrodese the joint (although this will not be without its own complications) or in some circumstances to use a stemmed implant.

16.4.5 Bilateral Ankle Disease

Registry data from Sweden has shown that 91% of patients undergoing bilateral arthrodesis were satisfied with the outcome in the short and intermediate term. However, in bilateral ankle arthritis, undertaking ankle arthrodesis is controversial and many surgeons would opt to avoid this due to associated problems in severe gait abnormality and loss of motion in both talocrural joints [92].

The optimum treatment for patients with bilateral ankle arthritis is therefore unclear, however many studies in the last 5 years have shown that total ankle arthroplasty can be beneficial, restoring gait mechanics and achieving good functional outcomes. Several studies have shown comparable results with good patient outcome scores and satisfaction across both unilateral and bilateral total ankle arthroplasty groups and this is further confirmed by the Swedish Joint Registry [81, 93, 94].

16.4.6 Cost Effectiveness

With an ageing population global health costs are increasing and the cost effectiveness of total ankle arthroplasty in comparison to ankle arthrodesis must be considered. A study by Courville et al. devised a model to determine the cost effectiveness of arthroplasty compared to arthrodesis in a hypothetical cohort. They concluded that although the initial cost of ankle arthroplasty was higher, 28,000 USD v 8000 USD for arthrodesis, it was cost effective once the increased quality-adjusted life years (QALY) was taken into consideration [95]. With respect to arthroplasty in general, total ankle arthroplasty has been shown to be comparable in cost to total hip or total knee arthroplasty [96].

16.4.7 Patient and Surgeon Expectations

When considering any orthopaedic procedure, we are often driven by outcome scales based upon pain and function. Outcomes based upon patient expectation and satisfaction may be far more useful [97]. However, patient satisfaction is also intrinsically linked to expectation and there may be disparity between patient and surgeon expectations.

Patients undergoing total ankle arthroplasty appear to have higher expectations prior to surgery than those undergoing ankle arthrodesis [97]. Pre-operative expectations were shown to be independent of pre-operative functional scores in both arthrodesis and arthroplasty; however, post-operative satisfaction was directly linked to functional scoring, with ankle arthroplasty and arthrodesis showing similar patient satisfaction post-operatively [97]. Consideration of patient expectations and any possible disparity to surgeon expectations should prompt better pre-operative education.

In recent years registry data for total ankle arthroplasty has been increasing, particularly in the United Kingdom. As mentioned, this is somewhat smaller in comparison to the USA. However, when you consider the disparity of this data you might find that fewer individual surgeons in the USA are undertaking large numbers of ankle arthroplasties, so while numbers may be high, we know that this may be dispersed.

Certainly, as surgeons we know what works well within our hands and for any established surgeon who is used to ankle arthrodesis, the prospect of learning how to refine ankle arthroplasty might not be an attractive option. Conversely, the opposite is also true for more novice surgeons. Ankle arthrodesis is an established technique and thought of by many as a gold standard option. While we may have presented examples of why this may no longer be true throughout this narrative, it is, without doubt a simpler operation with a much quicker learning curve. For the newer surgeon, attempting to undertake ankle arthroplasty and acquire the requisite skill to perform replacements entails a steep learning curve [98].

16.5 Making the Right Choice

When choosing between total ankle arthroplasty and ankle arthrodesis for end-stage ankle arthritis, clinicians may refer to the latest published evidence. Unfortunately, deriving definitive conclusions can often be conflicting and confusing. All too often studies focus on short- to intermediate-term outcomes, however, when faced with a younger patient, long-term outcomes should play a greater role in the decision-making process, as they may have a greater cumulative impact on the patient during their lifetime. Table 16.1 summarises considerations affecting decision to undertake either ankle arthrodesis or arthroplasty.

Table 16.1 Summary of considerations affecting decision to undertake either ankle arthrodesis or arthroplasty

Considerations	Ankle arthroplasty	Ankle arthrodesis
Range of motion (ROM)	Improved ROM, attempting to match normal physiology but still slightly reduced	Reduced, but may be in keeping with normal functional ROM
Rehabilitation	Early weightbearing	Prolonged immobility and potentially poor compliance
Activity	Return to work and function earlier, often only to low-impact sports	Preferable in high impact job or activity to avoid prosthesis wear
Adjacent arthritis	Low in short-term studies, unknown in long term	Increased risk due to altered foot biomechanics
Revision surgery	89% survival at 10 years Suitable bone stock for revision needed, limited long-term data in younger patients	7–15% non-union rate requiring revision Few case reports reporting taking down arthrodesis after failure, may require fusion of adjacent joints. Similar complications to arthroplasty but unmatched cohorts
Bilateral disease	May be beneficial in bilateral disease to preserve kinematics. Good outcomes compared to unilateral arthroplasty in registry data	Patent satisfaction good in short term, however bilateral loss off talocrural joints bilaterally and severe gait abnormality may not be good long term
Avascular necrosis	Few case reports, relative contraindication	Established treatment option for AVN with good outcome data
Obesity	Slightly lower functional outcome scores in short term than arthrodesis	Similar outcomes to arthroplasty
Diabetes	Poor outcomes with respect to wound impairment and clinical failure	Risk of wound healing problems, infection and non-union
Smoking	Poor outcomes compared to non-smokers	Poor outcomes compared to non-smokers
Patient expectations	Higher pre-operative expectations, good post-operative satisfaction	Lower pre-operative expectations, satisfactory post-operative patient outcomes
Surgeon expectations	Steep learning curve, reluctance to undertake based upon earlier arthroplasty results	Not subject to registry data, potential selection bias in patients suitable for this procedure
Cost	Overall higher initial cost, better long-term QALY	Lower overall cost

16.6 Conclusions

The success rates of both procedures are well documented and the decision of which is best depends on multiple factors—there is no one answer for all. The right choice will depend on several patient factors both pre- and post-operatively and the long-term effects of the surgery. Having an awareness of the next steps after either arthrodesis or arthroplasty is critical to ensure that as clinicians, we are not storing up problems for the future, however far away they may be. That said practical short-term relief as well as the ability to return to work and mobilise independently is equally important. A careful and measured approach encompassing the strategic aims of surgery is imperative, in combination with a detailed discussion with the patient to ensure informed decision making. This in turn should result in a bespoke, patient-centred treatment plan and better managed expectations.

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17 Achilles Tendon Ruptures: Nonoperative Treatment, Open Repair or Percutaneous Repair?

Inmaculada Moracia-Ochagavía
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17.1 Introduction

The Achilles tendon is the largest tendon in our body and is composed of the confluence of two muscles: the soleus muscle and the medial and lateral heads of the gastrocnemius muscle. Both are innervated by the tibial nerve. There are several characteristics that increase the stress on the Achilles tendon: (a) It is the only tendon muscle unit that crosses two major joints. (b) The fibers of the tendon go through an internal rotation of 90°, in such a way that the fibers of the medial gastrocnemius are later in their insertion in the calcaneus. (c) It is surrounded by a paratenon instead of a true tendinous sheath. As a result of the lack of synovial sheath together with other elements of the local anatomy mean that there is precarious vascularization in the area between 2 and 6 cm from the insertion of the tendon in the calcaneus.

Another important aspect to consider in the later approaches of tendon of Achilles is the anatomy of the sural nerve. The sural nerve is located medial to the gastrocnemius-soleus muscle unit until the union of the tendon muscle, where it crosses to a lateral position to the tendon.

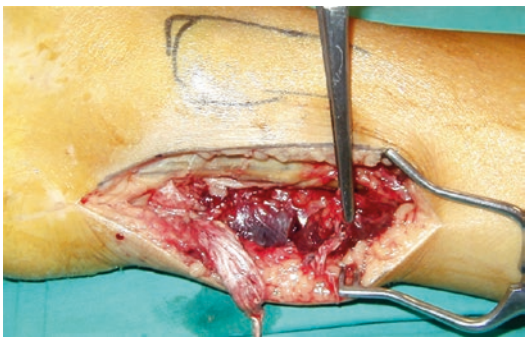

Fig. 17.1 Acute Achilles tendon rupture. It usually occurs at 2–6 cm of their insertion in the tuberosity of the calcaneus. Note the degeneration of the tendon with deflection and deterioration of the tendon fibers

Acute Achilles tendon ruptures occur most frequently between the ages of 30 and 40, predominantly in males, and are associated with occasional sporting activities and poor physical preparation. Up to 15% of patients may have prodromal symptoms, with degenerative changes observed in the area of the ruptured tendon in some cases. Most ruptures occur 4–6 cm from the insertion of the Achilles tendon into the calcaneus, in the hypovascular anatomical region (Fig. 17.1).

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17.2 Nonoperative Treatment

17.2.1 Nonoperative Treatment and Early Active Rehabilitation

Nonsurgical treatment was historically reserved for sedentary or elderly patients with medical comorbidities, or who did not wish to undergo surgery.

Treatment in this case includes a functional brace or plaster cast immobilization in equinus at 20° of plantar flexion of the ankle, followed by early functional rehabilitation with appropriate protection. As time has passed, traditional long-term plaster immobilization has been superseded by more active treatment which prioritizes early rehabilitation. In patients who have not undergone surgery but have followed an accelerated functional rehabilitation protocol, clinical results have been similar to those found in patients treated surgically, and also with fewer skin complications.

These early rehabilitation and loading protocols contrast with previous treatment of immobilization and unloading, for at least 6–8 weeks, to protect the healing of the Achilles tendon. However, mechanical studies have shown that mechanical loading stimulates tendon repair and the production of growth and strength factors in the repair tissues [1–3]. This explains the lower rate of ruptures than with classical conservative treatments.

The problem with this option is that, although there are various studies that publish rehabilitation protocols after conservative treatment, these are very heterogeneous. The time of immobilization, the time to start loading, and the type of orthosis used are variable. In fact, regimens can be divided into three main types: (a) Controlled early loading with initial immobilization [4]. (b) Early mobilization with active dorsiflexion and passive plantar flexion without early loading (Twaddle and Poon [5], using such a regime, showed a rate of ruptures and functional results similar to Ecker's studies [4], in which the foot was immobilized for 6 weeks). (c) Immediate early loading with controlled early mobilization (Barford et al. have published good functional results with this strategy, with improved quality of life compared to patients who were not allowed to load [6]).

Brumann et al. in 2014 conducted a systematic review and concluded that the combination of early loading and early mobilization results in better rehabilitation outcomes, with a higher degree of satisfaction, earlier return to work and preinjury activities, increased calf muscle strength and reduced muscle atrophy and tendon elongation, and finally less resource use [7].

Heikkinen et al. observed increased soleus muscle atrophy in patients treated non-surgically with a rehabilitation protocol based on early mobilization and loading compared to patients treated surgically [8]. The Achilles length was 19 mm longer in those who underwent surgery. These structural changes could explain their findings that those treated surgically had 10–18% more strength in the calf muscles.

In a prospective study published in 2019, a nonsurgical treatment regimen (Leicester protocol) for Achilles tendon ruptures was presented that appears to be effective [9]. In the Leicester Achilles Management Protocol (LAMP), compared to other studies, the boot is maintained less time, with lower complication rates and similar results. There were 9 (2%) ruptures in the 442 patients treated non-surgically. The assessment scale used was the ATRS (Achilles Tendon Rupture Score) with a result of 75.5 at 23 months mean follow-up. There was still a significant difference in calf circumference and heel elevation height when compared to the uninjured side at 12 months after the rupture ($p < 0.05$). According to the study, although the ATRS is lower than in previous studies [10, 11], it is the first with such long follow-up, consistent rehabilitative treatment, and a large population sample [9].

A negative correlation between age and outcome has been observed in one study, which was also observed in a previous study by the same author that concluded that women and older patients have poorer functional outcomes in non-surgical Achilles tendon ruptures treated with a fully dynamic load functional rehabilitation regimen [12].

Despite these encouraging results in terms of conservative treatment, early functional rehabilitation still does not have a consistent definition in the current literature, even though studies recognize that such protocols are safe, result in a high level of patient satisfaction, improve function, and allow a faster return to work and sports. In addition, these early rehabilitation protocols require coordination and ongoing attention from the Department of Physical Medicine and Rehabilitation. In some hospitals, these departments are in great demand and it is difficult to carry out such early and comprehensive treatment and follow-up.

17.2.2 Nonoperative Treatment Versus Open Surgical Treatment

Multiple randomized clinical trials comparing surgical and nonsurgical treatment and meta-analyses of these clinical trials were published before 2005. They concluded that with nonsurgical treatment the risk of rupture was higher and, however, surgical treatment showed an increase in other complications (such as surgical wound healing problems and infections) [13–15]. After assessing these risks, these studies recommended surgical treatment for the management of Achilles tendon ruptures.

Clinical trials published later, on all those based on a functional orthosis and early active mobilization protocols, showed discordant clinical results with a similar rupture index between surgical and conservative treatment [16].

Lim et al. published a study in which they compared the functional outcomes of surgical and nonsurgical treatment, following a similar rehabilitation treatment protocol [17]. In this program, loading was not allowed until 4 weeks and the ankle was kept immobilized in equinus with a below-knee cast. With this protocol, an attempt was made to balance early mobility with protection of mobility in noncompliant patients. There were no significant differences in the number of ruptures between the two types of treatment, nor in the ATRS functional scale at 2 years follow-up. There was no correlation between the ATRS scale and patient age. However, in women, there was a significant negative correlation between ATRS and age, such that older patients had worse functional outcomes. They concluded that their study did not support the surgical treatment of Achilles tendon ruptures.

Lantto et al. in 2016 published a randomized clinical study in which they compared surgical and conservative treatment in acute Achilles tendon ruptures using the same early loading and rehabilitation protocol [18]. They concluded that the results were similar in terms of subjective, functional and calf muscle strength scales. However, with surgery, calf muscle strength was restored earlier in the full range of motion of the ankle, with a 10–18% difference in strength in favor of surgery at 18 months of evolution. Surgery can also result in patients perceiving a better quality of life in relation to physical function and body pain, compared to nonsurgical treatment.

In a systematic review and meta-analysis by Ochen et al. it was shown that surgical treatment of Achilles tendon rupture reduces the risk of rupture compared to nonsurgical treatment [19]. However, the rate of ruptures was low and the difference between the two treatment groups was small (risk difference 1.6%). On the other hand, it should be noted that surgical treatment resulted in a high risk of other complications (risk difference 3.3%).

Therefore, the final decision in managing acute Achilles tendon ruptures should be based on patient-specific factors and shared decision making.

A meta-analysis of 2017 carried out by Deng et al., in which the rate of ruptures in the operated group was significantly lower than in the non-operated group ($p < 0.001$), should be noted [20]. There were no significant differences in the number of deep vein thrombosis, return to sport, ankle range of motion, and physical activity scales. They considered that surgical treatment may be the best choice for the treatment of acute Achilles tendon ruptures. However, they recognized some limitations in their work such as the presence of some relatively small studies and a short follow-up period (15.4 months).

17.3 Surgical Treatment

17.3.1 Suturing Techniques

Many suture techniques have been described. In general, they are performed in classic open surgery, although some minimally invasive or percutaneous techniques also use them. The following stand out: (a) The blocked Krackow-type suture has been one of the most widely used for tendon repair with widely documented success in terms of allowing early mobility with a stable suture [21–25]. (b) There are other suture techniques such as the Kessler suture, the Bunnell suture, the continuous suture, the triple bundle, which all have varying degrees of usage within the literature. (c) The "Gift box technique," introduced by Labib et al. as a modification of the Krackow-type suture, being biomechanically twice as strong as the traditional Krackow in corpse models [26]. A study in which this type of suture was performed on 44 patients concluded that the technique is reproducible, with good patient satisfaction and return to activity. No ruptures or lesions of the sural nerve, wound dehiscence, or infections were observed.

According to previous studies, the Krackow technique [27] is a stronger suture than the Kessler or Bunnell frame, and the triple bundle suture [28] is stronger than the Krackow technique.

These aspects were confirmed in a systematic review of human biomechanical studies [29]. It was observed that in cases of Achilles tendon reinsertion techniques, the maximum failure load was significantly higher when a double-row technique was used instead of a single row. In the midline of the tendon, the Bunnell and Krackow suture techniques were significantly stronger for tendon repair.

In another cadaveric study published by Manent et al., it was observed that the rate of tendon rupture was similar with the Bunnell and Krackow techniques. However, with Bunnell's technique, the tendon was less elongated. For this reason, Manent et al. recommended the latter suture technique [30].

17.3.2 Surgical Approaches

There are three main types of approaches: (a) Open posteromedial approach (usually a variable incision from 6 to 18 cm). (b) Minimally invasive or mini-incision approach (the incision can be from 2 to 6 cm posterolateral, protecting the sural nerve). (c) Percutaneous approach (in which small multiple incisions are made).

Most studies comparing the different types of approaches have similar results and complication rates.

17.3.2.1 Open Surgery Versus Minimally Invasive Surgery

Tejwani et al. presented a retrospective study in which they compared the posteromedial standard technique and the posterolateral minimally invasive technique. They observed that both techniques were effective and safe for the treatment of acute Achilles tendon rupture [31]. However, there were significant differences between the approaches in terms of dorsiflexion and postoperative plantar flexion although the full arch of motion was similar. In the standard posteromedial approach group there was a higher rate of statistically significant skin complications. In the minimally invasive surgery group there was a higher rate of sural nerve injury, also statistically significant. A trend towards better results (improved single heel raise at 6 months) was also observed in patients operated with minimally invasive approach but this was not statistically significant.

There is a minimally invasive technique described by Muezzinoglu et al. in 2013, known as SIIS (semi-invasive internal splinting) technique [32]. This technique consists of making two incisions separated by 2 or 3 cm from the area of the tendon rupture. The sural nerve is exposed and protected. The surgery is performed in such a way that the ends of the rupture are not exposed or manipulated. A Krackow-type suture is made on the medial and lateral sides in the proximal area of the tendon and passed distally using a tendon gripper. The appropriate tension is applied to the muscle-tendon joint and the foot is kept in plantar flexion. A blocked Krackow suture is also performed on both sides of the tendon at the distal level.

In 2016, Serman et al. conducted a retrospective study of 45 patients in which they compared the SIIS technique (semi-invasive "internal splinting") with classic open surgery [33]. At the end of the median follow-up (43.7 months), a larger number of patients in the SIIS group returned to their normal daily activities ($p<0.05$). However, there were no differences in the ankle AOFAS (American Orthopedic Foot and Ankle Society) scale, in the calf or thigh diameter or in the range of motion.

A systematic review and meta-analysis published in 2017 by Alcelik et al. appraised articles comparing minimally invasive surgery and classic open surgery [34]. In it, they corroborated the existence of significant differences in terms of the higher rate of skin complications in the open surgery group. However, minimally invasive surgery and open surgery had similar results in terms of rupture rates, sural nerve injury, and return to sports activity.

17.3.2.2 Open Surgery Versus Percutaneous Surgery

As for the percutaneous technique, there are different types of instruments on the market that facilitate the approach.

Hsu et al. reviewed patients operated on with a percutaneous Achilles tendon repair system (PARS [Arthrex, Inc., Naples, FL]) and compared them with patients in whom a traditional open technique was performed [35]. A very low rate of complications was noted in comparison with previous publications (8.5%). There were no ruptures and most patients were able to return to their previous activity 5 months after the intervention. There was also no significant difference in the rates of post-surgical complications between the percutaneous system and open Achilles tendon rupture repair.

In another prospective, randomized study published by Kolodziej et al. another percutaneous surgery system (Achillon®) was compared to traditional open surgery with Krackow-type suture [36]. There were no reruptures or lesions of the sural nerve in either group. The only statistically significant difference between the groups was the length of the scar. Kolodziej et al. stated that although percutaneous surgery with this system can limit the rate of serious skin complications, there were no significant differences with the traditional open surgery group in their study.

17.3.2.3 Surgical Technique Preferred by the Authors of This Chapter

For the authors of this chapter, open surgery remains the gold standard in most patients with acute Achilles tendon rupture.

One of the reasons for continuing with open surgery despite the good results presented with percutaneous surgery is that with open surgery we can evaluate the condition of the tendon. In most cases of acute Achilles tendon ruptures there is a previous degenerative process and tendinosis. With percutaneous surgery or conservative treatment we cannot assess this and therefore we would be treating a damaged tendon with poor quality tissue.

With open surgery we evaluate the tendon, we can debride it, remove devitalized tissues and even in cases of large residual defect, we can reinforce it with a tendon transfer from the flexor hallucis longus performed in the same intervention (Fig. 17.2).

One of the causes of this tendon deterioration is the existence of a twin shortening (gastrocnemius contracture). Therefore, we usually perform a calf lengthening by means of a modified Strayer technique (gastrocnemius recession), in order to reduce the tension on the Achilles tendon.

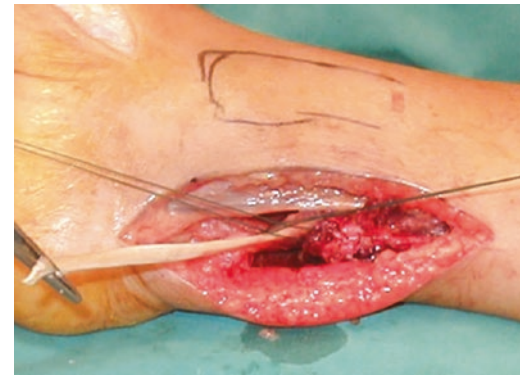

Fig. 17.2 Transfer of tendon flexor hallucis longus for reinforcement of ruptures of Achilles tendon which present great tendinous deterioration and poor quality of the tendon ends

In general, all studies report a higher rate of skin complications with open surgery and this is one of the main drivers for surgeons to adopt percutaneous or minimally invasive techniques. We believe that skin complications can be minimized or almost eliminated if the correct surgical technique is used [37]. As Hansen points out in his book [38], the best incision is a medial incision in the safe area of fat that is anterior to the Achilles tendon, placing the incision between the Achilles tendon and the neurovascular package (Figs. 17.3, 17.4 and 17.5). The approach is made from the front to maintain good soft tissue coverage over the repair and to avoid the formation of adhesions to the skin. The tissues must also be handled delicately, avoiding automatic separators and separating the skin only with little retractors.

As for the type of suture, we use a resorbable monofilament suture such as polyglyconate (Maxon) or polydioxanone (PDS), generally making a Krackow-type suture and adding loose stitches on the circumference of the joint.

As for the postoperative treatment, we immobilize in the operating room with a orthopedic splint with the ankle in 20° of plantar flexion. After 2–3 weeks, we remove the skin sutures and

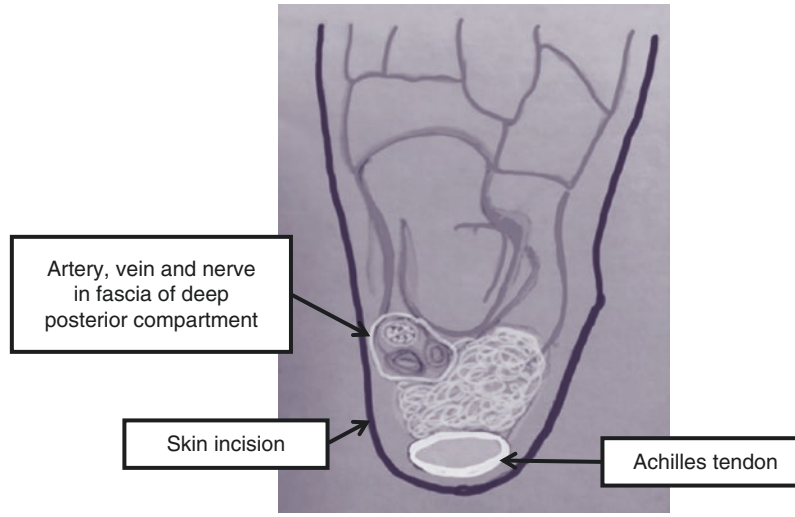

Fig. 17.3 Diagram of a coronal cut of ankle and Achilles tendon in its medial region. It shows the place where the posteromedial incision should be made for open tendon surgery, to avoid skin complications

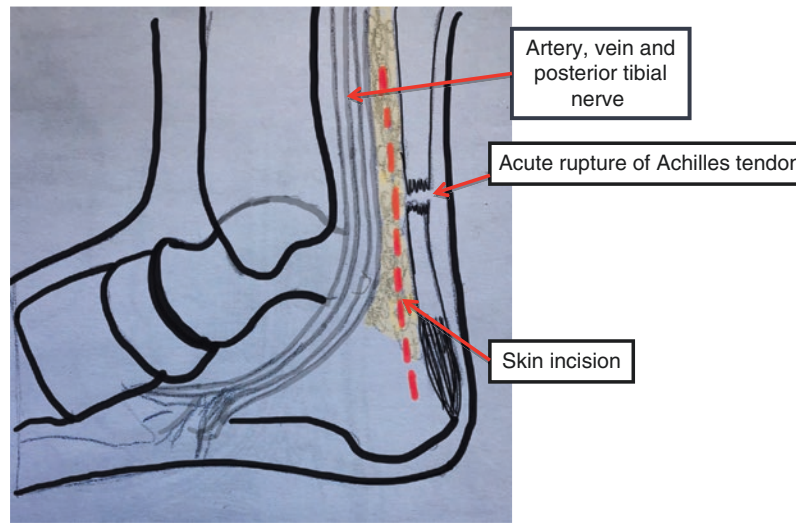

Fig. 17.4 Diagram of the lateral cut of the ankle and Achilles tendon, showing the posteromedial incision for open surgery of the Achilles tendon

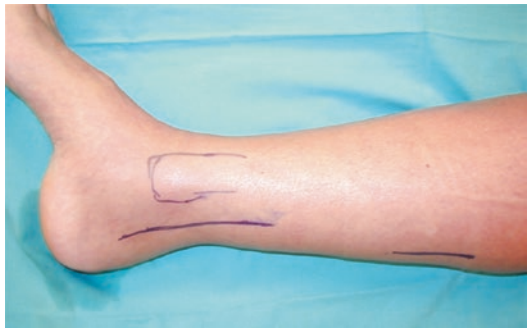

Fig. 17.5 Medial view of leg, in which the posteromedial incision for open Achilles tendon surgery is drawn in skin. It corresponds in depth to a safe area of pre-Achilles fat, which is less susceptible to skin complications. The most proximal medial incision to perform gastrocnemius lengthening and the tibial malleolus have also been drawn

place a non-articulated Walker orthopedic boot, but with three internal wedges so that the patient can begin early loading while maintaining the ankle in plantar flexion. From the second week, the patient is instructed to remove the boot 3 times a day to perform active dorsiflexion and plantar flexion without gravity. A wedge is removed every week; this way, up to 5 weeks. Then the patient will begin loading with the ankle in a neutral position and will be able to begin more intense and supervised rehabilitation.

17.4 Conclusion

There remains great controversy regarding the treatment of acute Achilles tendon rupture. Conservative treatment was only performed on patients where surgery was not indicated and had a high rate of ruptures; however, recent studies show good results even similar to surgical treatment, if early loading and rehabilitation of the Achilles tendon are performed. In spite of this, there is no consensus as to the time of immobilization, unloading, or type of exercises to be performed. In addition, the Department of Physical Medicine and Rehabilitation must be available to execute the rehabilitation protocols, which in many centers is difficult to coordinate. As for percutaneous or minimally invasive surgical treatment, it has shown similar results to open surgical treatment although with a lower rate of skin complications. However, in some of the recent studies and meta-analyses, nerve injuries related to the sural nerve are still present. Good functional results and patient satisfaction continue to be obtained with classic open surgical treatment. The Krackow-type suture or its modification (gift box technique) are the most used techniques and with very good levels of resistance in biomechanical studies. Open surgery offers the possibility of assessing the condition of the tendon and strengthening it if necessary. If we take care of the surgical technique and avoid incisions behind the Achilles tendon, we will minimize or eliminate the possibility of such skin complications.

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18 Biomarkers in Osteoarthritis: Their Role in Predicting the Progression of the Disease and Their Ability to Assess the Efficacy of Existing Treatment

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18.1 Introduction

Osteoarthritis (OA) is a very prevalent and debilitating condition, so it would be important to reduce its negative impact on the population. Biomarkers of OA could be of great help in this regard [1, 2]. This article reviews the role of biomarkers in predicting the progression of OA, in allowing differential diagnosis, and their ability to assess the efficacy of existing treatments for the disease.

18.2 The Role of Biomarkers in the Clarification of the Pathogenetic Mechanisms of OA

In 2019 Li et al. published a combined analysis of two types of microarray datasets [gene expression and (deoxyribonucleic acid) DNA methylation] to detect methylation-based key biomarkers to give a superior comprehension of molecular biological mechanisms of OA [3]. They attained two expression profiling datasets (GSE55235, GSE55457) and one DNA methylation profiling dataset (GSE63695) from the Gene Expression Omnibus. First, differentially expressed genes (DEGs) between patients with OA and controls were detected utilizing the Limma package in R(v3.4.4). Later, function enrichment analysis of DEGs was carried out utilizing a DAVID (*Database* for Annotation, Visualization and Integrated Discovery) database. For DNA methylation datasets, ChAMP methylation analysis package was utilized to detect differential methylation genes (DMGs). Eventually, a complete analysis of DEGs and DMGs was performed to detect genes that exhibited differential expression and methylation at the same time. Li et al. detected 112 DEGs and 2896 DMGs in individuals with OA compared with controls. Functional analysis of DEGs showed that inflammatory responses, immune responses, and positive regulation of apoptosis, tumor necrosis factor (TNF) signaling pathway, and osteoclast differentiation may be implicated in the pathogenesis of OA. Cross-analysis detected 26 genes that exhibited differential expression and methylation in OA. Among them, ADAMTS9 (a disintegrin and metalloproteinase with thrombospondin motifs 9 is an enzyme that in humans is encoded by the *ADAMTS9*), FKBP5 (a protein which in humans is encoded by the *FKBP5* gene which is a member of the immunophilin protein family, which play a role in immunoregulation and basic cellu-

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lar processes involving protein folding and trafficking), and PFKFF3 (a gene that encodes the 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3 enzyme in humans). This study detected different molecular features between individuals with OA and controls. This may give new proofs for explaining the pathogenetic mechanisms of OA.

In 2019 Ruan et al. investigated the relationship between serum interleukin-8 (IL-8) levels and a number of parameters in 180 patients with symptomatic knee OA [4]. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score and the Lequesne index were used. Magnetic Resonance Imaging (MRI) was used to measure structural abnormalities of the knee, as well as the infrapatellar fat pad (IPFP) signal intensity alternation. The degree of radiographic knee OA was evaluated using the Kellgren–Lawrence (K-L) classification. The enzyme-linked immunosorbent assay was used to measure serum IL-8 levels and cartilage and bone biomarkers. In multivariable analyses, serum levels of IL-8 were positively associated with increased knee symptoms (WOMAC weight-bearing pain, WOMAC physical dysfunction, and Lequesne index), IPFP signal intensity alteration and serum levels of N-telopeptide of type I collagen (NTXI), N-terminal procollagen III propeptide (PIIINP), matrix metalloproteinase (MMP3), and MMP13 in patients with clinical knee OA. Moreover, there were positive associations between IL-8 and WOMAC score, K-L grades, and IPFP signal intensity alteration in patients with radiographic OA. The findings of this study seem to indicate that IL-8 may have a role in knee OA.

18.3 The Role of Biomarkers in the Prediction of OA Occurrence and Detection of Early Development of OA

Zhang et al. attempted to identify new biomarkers in the synovial tissue of patients with rheumatoid arthritis (RA) and OA in order to make a differential diagnosis between the two diseases [5]. The genome-wide expression profiling datasets of synovial tissues from RA and OA groups, including GSE55235, GSE55457, and GSE55584 datasets, were retrieved and utilized to detect differentially expressed genes (DEGs; $P < 0.05$; false discovery rate <0.05 and Fold Change >2) between RA and OA using R software. Gene Ontology and Kyoto Encyclopedia of Genes and Genomes pathway enrichment analyses of DEGs were carried out to define molecular and biochemical pathways associated with the detected DEGs, and a protein–protein interaction (PPI) network of the DEGs was constructed utilizing Cytoscape software. Significant modules in the PPI network and candidate driver genes were screened using the Molecular Complex Detection Algorithm. Potential biomarkers were assessed by receiver operating characteristic and logistic regression analyses. Large numbers of DEGs were identified, including 273, 205, and 179 DEGs in the GSE55235, GSE55457, and GSE55584 datasets, apiece. Among them, 80 DEGs exhibited identical expression trends in all the three datasets, including 49 upregulated and 31 downregulated genes in individuals with RA. DEGs in individuals suffering from RA compared with individuals suffering from OA were mostly associated with the primary immunodeficiency pathway, including interleukin 7 receptor (IL7R) and signal transducer activator of transcription 1 (STAT1). The sensitivity of IL7R + STAT1 to distinguish RA from OA was 93.94% with a specificity of 80.77%. The results generated from analyses of the GSE36700 dataset were closely associated with results generated from analyses of GSE55235, GSE55457, and GSE55584 datasets, which further proved the dependability of the aforesaid results. The results of this study suggest that increased expression of IL7R and STAT1 in synovial tissue, as well as primary immunodeficiency, may be associated with the development of RA. These biomarkers can be used to clinically differentiate RA from OA.

Early detection of OA is crucial for Boeth et al. who assessed whether the molecular biomarkers of cartilage turnover were associated with a longitudinal change in knee cartilage thickness over a 2-year period in people at

increased risk of developing knee OA. A secondary objective was to assess whether previous knee injury or subjective patient-reported outcomes at baseline (BL) were associated with changes in joint cartilage. Nineteen volleyball players (mean age 46.5 ± 4.9 years, 47% male) with a 30-year history of regular high-impact training were analyzed. The serum biomarkers C-propeptide of type II procollagen (CPII), cartilage oligomeric matrix protein (COMP), collagenase-generated carboxy-terminal neoepitope of type II collagen (sC2C), cartilage intermediate layer protein 2 (CILP-2), and the urine biomarkers C-telopeptide of type II collagen (CTX-II) and collagenase-generated peptide(s) of type II collagen (C2C-HUSA) were evaluated at BL and at 2 year follow-up. Femorotibial cartilage thinning, thickening and absolute thickness change between BL and FU was assessed from MRI. Subjective clinical status at BL was assessed by the International Knee Documentation Committee (IKDC) Subjective Knee Form and the Short-Form 36 (SF-36) Physical Component Score. CILP-2 was significantly higher at the end of follow-up and was associated linearly with absolute change in cartilage thickness during the study period. The existence of a previous injury was predictive of the increase in absolute change in cartilage thickness. Measuring the change in the CILP-2 cartilage biomarker may be a valid and sensitive method of detecting the early development of knee OA, as CILP-2 appears to be related to cartilage thickness loss in certain individuals at increased risk of developing OA. Previous injury to the knee may also predict increased absolute cartilage thickness change [6].

18.4 The Role of Biomarkers in the Prediction of Radiographic Severity in Symptomatic OA

Bournazon et al. conducted a study to investigate the expression of vascular adhesion protein-1 (VAP-1) in the joint tissues and serum of patients with symptomatic knee OA, and to analyze whether VAP-1 levels could predict an increased risk of disease severity [7]. These authors evaluated baseline VAP-1 expression and soluble VAP-1 (sVAP-1) levels in synovial fluid and serum from patients with medial knee OA and healthy subjects (control group). The K-L radiographic classification score (0–4) was noted and the medial joint space width (JSW) was measured. The K-L 1/2 vs. K-L 3/4 scores defined early and advanced radiographic severity, respectively. Biochemical markers assessed in serum or synovial fluids included sVAP-1, interleukin 1 receptor antagonist (IL-1Ra), interleukin 6 (IL-6), soluble receptor for advanced glycation end-products (sRAGE), C-C motif chemokine ligand 2 (CCL2), C-C motif chemokine ligand 4 (CCL4), cluster of differentiation 163 (CD163), high-sensitivity C-reactive protein (hsCRP), and MMPs-1,-3,-9. Associations between biomarkers and radiographic severity (K-L 1/2 versus K-L 3/4) and pain level were evaluated. Elevated levels of sVAP-1 were found in OA synovial fluid and VAP-1 expression in synovium based on immunohistochemical, microarray, and real-time quantitative polymerase chain reaction (qRT-PCR) analyses. However, serum sVAP-1 levels in OA patients were lower than those in the control group and correlated inversely with markers of pain and inflammation (hsCRP and soluble RAGE). Serum sVAP-1 levels were also lower in patients with advanced OA (K-L 3/4) than in individuals with early OA (K-L 1/2). Local (synovial fluid) semicarbazide-sensitive amine oxidase (SSAO)/sVAP-1 levels were elevated in OA and correlated with radiographic severity. However, systemic (serum) levels of sVAP-1 were lower in patients with OA than in the control group and inversely correlated with markers of pain and inflammation. Serum sVAP-1 levels were higher in patients with early (K-L 1/2) OA than in patients with advanced (K-L 3/4) OA.

18.5 Biomarkers Associated with the Progression of OA

Chen et al. attempted to identify and investigate the role of biomarkers associated with long noncoding RNA (lncRNA) in knee OA progression

using lncRNA-associated competing endogenous RNA (ceRNA) integrated network analysis [8]. High quality microRNA (miRNA) and miRNA-mRNA expression profiles for patients with mild and severe knee OA were obtained from the Gene Expression Omnibus (GEO) database (GSE99662). A three-step computational method was used to construct the lncRNA-associated ceRNA interaction network in OA by integrating miRNA-lncRNA/mRNA interactions and lncRNA/mRNA expression profiles in patients with OA with mild and severe pain. A total of 1870 deregulated lncRNA–mRNA interactions were obtained in the lncRNA network associated with lncRNA in the OA, including 476 gain and 1394 loss interactions, covering 131 lncRNA and 1251 mRNA. Characterization of the small interfering RNA (siRNA)-associated ceRNA network in the OA indicated that siRNAs performed functions in the network. Further analysis of differential expression identified eight biomarkers of siRNA, which could distinguish between patients with mild pain and patients with severe pain. These siRNA-associated interactions showed significantly different co-expression patterns in samples from patients with mild pain. Analysis of the integrated siRNA network identified eight siRNA molecular biomarkers associated with the progression of knee OA [8].

Nelson et al. applied innovative automatic learning approaches to the phenotype of knee OA to define progression phenotypes that were potentially more sensitive to interventions [9]. They used publicly available data from the Foundation for the National Institutes of Health (FNIH) OA Biomarkers Consortium, where the WOMAC Osteoarthritis Index radiographic points (narrowing of the medial joint space from ≥0.7 mm), and pain progression (increase of ≥9 WOMAC points), were defined at 48 months as four mutually exclusive outcome groups (none, both, pain only, radiographic only), along with several covariates. They applied distance weighted discrimination (DWD), direction-projection-permutation (DiProPerm) testing, and clustering methods to focus on the contrast (z-scores) between those progressing by both criteria ("progressors") and those progressing by neither ("non-progressors"). Using all observations (597 individuals, 59% women, mean age 62 years and a body mass index (BMI) of 31 kg/m^2) and the 73 baseline variables available in the dataset, there was a clear separation between progressors and non-progressors ($z = 10.1$). Higher z-scores were observed for MRI-based variables than for demographic/clinical variables or biochemical markers. The reference variables that most contributed to non-progressors at 48 months were WOMAC pain, lateral meniscal extrusion, and N-terminal propeptide of collagen IIA (PIIANP), while those that contributed to progression were bone marrow lesions, osteophytes, medial meniscal extrusion, and urine CTX-II.

Gu et al. explored biomarkers and pathological processes of OA in subchondral bone samples [10]. The gene expression profile GSE51588 was downloaded from the Gene Expression Omnibus database. Fifty subchondral bone samples [lateral tibial knee (LT) and medial tibial (MT)] from 40 subjects with OA and 10 individuals without OA were analyzed. After data pre-processing, 5439 genes were obtained for the analysis of the weighted gene co-expression network. The highly correlated genes were divided into 19 modules. The yellow module was found to be highly correlated with OA ($r = 0.71$, $p = 1e-08$) and the brown module was most associated with differences between the LT and MT regions ($r = 0.77$, $p = 1e-10$). Gene ontology functional annotation and Kyoto Encyclopedia of Genes and Genomes pathway enrichment indicated that the yellow module was enriched in a variety of components including proteinaceous extracellular matrix and collagen trimers, involved in protein digestion and absorption, axon guidance, extracellular matrix (ECM)–receptor interaction, and the PI3K-Akt signaling pathway. In addition, the brown module suggested that the differences between the early LT and end MT stage of OA were associated with extracellular processes and lipid metabolism. Finally, 45 hub genes in the yellow module (COL24A1, COL5A2, COL3A1, MMP2, COL6A1, etc.) and 72 hub genes in the brown module (LIPE, LPL, LEP, SLC2A4, FABP4, ADH1B, ALDH4A1, ADIPOQ, etc.) were identified. Hub genes (genes with high cor-

relation in candidate modules) were validated using samples from cartilage (GSE57218). In summary, 45 hub genes and 72 hub genes in two modules were associated with OA. These hub genes could provide new biomarkers and drug targets in OA.

Henrotin et al. tried to identify if biochemical markers s-Coll2-1 and s-Coll2-1NO2 were associated with knee OA phenotypes, focusing on pain, function as well as structural characteristics evaluated by MRI in diverse knee compartments, and to evaluate their capacity to anticipate knee OA aggravation [11]. 116 patients with knee OA were followed during 1 year, variables including pain, function, and MRI evaluation (PRODIGE study, NCT02070224). Type II collagen-specific biomarker Coll2-1 and its nitrated form Coll2-1NO2 were directly determined in serum utilizing immunoassays at baseline and after 3, 6, and 12 months follow-up. Coll2-1 is a nine amino acid sequence (HRGYPGLDG) specific of type II collagen which is released during cartilage degradation. This peptide is located in the triple helicoidal part of type II collagen molecule. Coll2-1 and Coll2-1NO2 are biomarkers of type II collagen denaturation. In this study sColl2-1 and sColl2-1NO2 were associated with some baseline knee characteristics quantified with Whole-Organ Magnetic Resonance Imaging Score (WORMS). S-Coll2-1 was significantly correlated with bursitis (r¼0.29, $P < 0.01$), bone attrition (r¼0.25, P¼0.01), cysts (r¼0.24, P¼0.02), and cartilage (r¼0.23, P¼0.03) WORMS sub-scores for the whole joint as well as with the medial femorotibial joint sum score (r¼0.26, P¼0.01) and medial femorotibial joint cartilage (r¼0.23, P¼0.02). s-Coll2-1NO2 was correlated with WORMS total score (r¼0.23, P¼0.02), WORMS scores in the patellofemoral (r¼0.23, P¼0.02) and medial femorotibial compartments (r¼0.21, P¼0.03), and with osteophytes scores (r¼0.27, $P < 0.01$). Baseline s-Coll2-1NO2 was higher in patients with a pain aggravation (426.4 pg/mL, 278.04–566.95) as compared to non-progressors (306.84 pg/mL, 200.37–427.84) over 1 year (AUC¼0.655, P¼0.015). Cartilage biomarkers s-Coll2-1 and s-Coll2-1NO2 were associated with various knee OA characteristics quantified with WORMS scoring system on MRI. Serum values of Coll2-1NO2 were also associated with an aggravation of target knee pain over 1 year. Coll2-1 and Coll2-1NO2, in association with other structural characteristics, pain, and function, could help at detecting OA phenotypes and patients at risk of OA aggravation.

18.6 OA-Related SF Biomarkers Are Specifically Linked to Indicators of Activated Macrophages and Neutrophils: Therapeutic Targeting of a Subset of Individuals at High Risk for OA Progression

Haraden et al. conducted a study to identify a synovial fluid (SF) biomarker profile characteristic of individuals with an endotype of inflammatory OA [12]. A total of 48 knees (of 25 participants) were characterized for an extensive array of SF biomarkers quantified by Rules Based Medicine using the high-sensitivity multiplex immunoassay, Myriad Human Inflammation MAP® 1.0, which included 47 different cytokines, chemokines, and growth factors related to inflammation.

Multivariable regression with generalized estimating equations (GEE) and false discovery rate (FDR) correction was used to assess associations of SF RBM biomarkers with etarfolatide imaging scores reflecting synovial inflammation; radiographic knee OA severity (based on K-L) grade, joint space narrowing, and osteophyte scores); knee joint symptoms; and synovial fluid biomarkers associated with activated macrophages and knee OA progression including cluster of differentiation (CD)14 and CD163 (shed by activated macrophages) and elastase (shed by activated neutrophils). A subset of six SF biomarkers was associated with synovial inflammation in OA, as well as radiographic and symptomatic severity. These six OA-related SF biomarkers were specifically linked to macrophage and neutrophil indicators that were acti-

vated. This study demonstrated an endotype of inflammatory OA in the knee that could be used for therapeutic selection of patients at high risk of progression.

Sofat et al. evaluated the relationship between clinical pain measures and evoked pain in relation to structural damage and biochemical biomarkers in knee OA [13]. These authors conducted a cross-sectional study in patients with knee OA to compare it with healthy controls. They analyzed 130 participants divided into three groups: 78 with advanced OA requiring total knee replacement, 42 with mild OA with standard treatment, 6 controls without OA (n = 6), and four drop-outs. Pain intensity was measured with the OA Index (WOMAC_P) and the Visual Analog Scale (VAS). Pain sensitivity was assessed by pain pressure thresholds (PPTs). MRI evaluated joint damage using the MRI Knee OA Score (MOAKS). Overall MOAKS scores were created for bone marrow injuries (BMLs), cartilage degradation (CD), and effusion/Hoffa synovitis (tSyn). CTX-II was determined by ELISA. The advanced OA group had a mean age of 68.9 years and the mild group 63.1. The advanced OA group had higher levels of pain, with a mean WOMAC_P of 58.8 compared to a mean 40.6 for the mild OA group. All subjects with OA had pain sensitization by PPT compared to controls. WOMAC_P correlated with the total number of cartilage damaged regions (nCD) and the total number of bone marrow lesions (BMLs)—(nBML) using body mass index (BMI), age and hospital anxiety and depression scale (HADS) as covariates. CTX-II levels were correlated with total synovitis score (tSyn), nBML, number of osteophytes, and number of cartilage damage (nCD), using BMI and age as covariates. A multivariate analysis indicated that BMI and HADS were the most significant predictors of pain scores. People with mild and advanced OA show characteristics of pain sensitivity. It was noted that increased joint damage detected by MRI was associated with higher levels of CTX-II, suggesting that increasing disease severity can be evaluated with MRI and CTX-II biomarkers in order to assess OA progression.

18.7 The Role of Biomarkers to Differentiate Between OA Patients and Other Problems

According to Lynch et al., early recognition and treatment of patients with hip injuries, such as femoroacetabular impingement (FAI) and early OA of the hip, could prevent significant morbidity in the hip [14]. The identification of reliable biomarkers could help to make decisions efficiently and effectively. In their study (systematic review and meta-analysis) they attempted to determine the biomarkers associated with FAI and identify the serum, synovial, and urinary analyses of clinical utility in predicting or identifying hip OA. Lynch et al. identified 1747 patients with a mean age of 37.5 ± 4.5 years (76.4% women). Forty-three biomarkers were evaluated. Although general proinflammatory cytokines IL-1 and TNF-α exhibited inconsistent trends in arthritic hips, IL-6 demonstrated a consistent increase (+84.8). A significant difference in fibronectin-aggrecan complex (FAC) levels was found in patients with OA compared to individuals in the control group (0.08 vs. 1.15 μg/mL, respectively). It was the only specific analysis that showed a significant difference between individuals who had OA and those who did not. In the setting of FAI, cartilage oligomeric matrix protein (COMP) was significantly increased in athletes after adjusting for concurrent knee and hip OA. A statistically significant difference was observed in the hips with positive FAI (9.0) compared to the control group (8.4). Other biomarkers, such as CXCL3, which showed statistically significant differences compared to controls, did not control for underlying factors such as age and concomitant lesions. Given their ability to differentiate between controls and patients with hip injuries, COMP and FAC were specific biomarkers with potential utility in the diagnosis and management of FAI and hip OA. However, further research is needed to identify their ability to determine disease severity, predict response to treatment, and establish an association with long-term risk of OA.

Hao et al. designed a study (systematic review and meta-analysis) to examine the diagnostic

performance of COMP, CTX-II, and MMP-3 as biomarkers of knee and hip OA [15]. Moderate performance of the COMP was found to distinguish between patients with knee or hip OA and controls. The CTX-II showed a moderate standardized mean difference (SMD) of 0.48 in the detection of knee OA and a large SMD of 0.76 in the diagnosis of hip OA. A small SMD of 0.32 was found for MMP-3 performance and the results did not reach statistical significance. The progression study revealed the potential efficacy of serum COMP in predicting the progression of OA. Subgroup analysis showed that serum COMP and urinary CTX-II worked better in men than in women. Study size and diagnostic criteria did not significantly influence the combined SMD, but could be the source of heterogeneity between studies. Serum COMP and urinary CTX-II can distinguish between patients with knee or hip OA and control subjects.

The results of a study by Zahn et al. suggest that increased expression of IL7R and STAT1 in synovial tissue, as well as primary immunodeficiency, may be associated with the development of RA [5]. The newly identified biomarkers can be used to predict disease emergence and clinically differentiate RA from OA.

In one study, Zhang et al. conducted an integrated analysis of the network and pathways ~~to~~ of the biological function of the genes associated with OA in order to obtain valuable information for further study of the etiology and pathogenesis of OA [16]. A total of 2548 genes were examined. An OA-specific protein–protein interaction (PPI) network was constructed by cytocluster based on the Molecular Complex Detection Algorithm (MCODE) to screen its candidate biomarkers. Quantitative real-time polymerase chain reaction was utilized to confirm the expression levels and to validate the results of MCODE cluster analysis by six genes. The pathway networks suggested that ECM organization, collagen degradation, and collagen formation showed important associations with OA. In top two PPI clusters, 61 of the OA-associated genes were included in the OA-specific PPI network, which also included 23 candidate genes that are likely to be highly associated with OA based on MCODE clusters. Analysis of mRNA showed that the expression levels of COL9A1, COL9A2, ITGA3, COL9A3, ITGA2, and LAMA1 in the peripheral blood mononuclear cells of OA patients were significantly lower than those of the normal controls ($p < 0.005$). This study showed that the functional destruction of collagen in cartilage can be a major contributor to OA. Quantitative detection of collagen synthesis can be of great help for early identification and prediction of OA. Maintenance of collagen quality and quantity may be a potential target for clinical treatment of OA in future practice.

18.8 Associations Between Serum Muscle Biomarkers and Sarcopenia in OA

According to Kurita et al., the reduction of muscle markers, such as creatinine phosphokinase (CPK), in rheumatic diseases and their association with reduced muscle mass may be clinically important in OA [17]. Considering the complexity of secondary sarcopenia, it is of clinical importance to clarify the association between muscle markers and sarcopenia and to unravel the involvement of OA-related conditions. The association between serum muscle biomarkers and sarcopenia has been investigated among patients with OA, taking into account the presence of pain and inflammation. Overall, 1425 patients with knee and hip OA scheduled for joint replacement surgery were included in a single-center cross-sectional study from Screening for People Suffering Sarcopenia in Orthopedic cohort of Kobe study. Primary outcome was sarcopenia defined by two criteria (the Asian Working Group for Sarcopenia and the European Working Group on Sarcopenia in Older People). Pain and inflammation were measured using the numeric rating scale and serum C-reactive protein (CRP) levels, respectively. Associations between the biomarkers (serum CK, aspartate aminotransferase, alanine aminotransferase) and sarcopenia were examined using logistic regression models. Sarcopenia according to the criteria of the Asian Working Group for Sarcopenia was

present in 4.0% of patients. In the adjusted analyses, sarcopenia was negatively associated with higher serum CK levels, but not with serum aspartate aminotransferase or alanine aminotransferase levels independent of pain score and serum CRP. Neither the pain score nor the serum CRP level was associated with sarcopenia. Similar results were found when the criteria of the European Working Group on Sarcopenia in Older People were used. Serum CPK was associated with sarcopenia, suggesting its potential usefulness in detecting sarcopenia in OA regardless of pain or inflammation.

18.9 Biomarker Differences Between Genders

According to Bihlet et al., excessive cartilage degradation is a known feature of OA [18]. Biochemical markers, such as uCTX-II, have been shown to be associated with disease severity although the tissue origin of CTX-II has been discussed. This analysis investigates the association between knees with OA at different radiographic stages and pain categories with uCTX-II levels and biomarkers of bone resorption and formation. Baseline data from two randomized clinical trials (NCT00486434 and NCT00704847) in patients with radiographic OA and knee pain were analyzed post hoc. A subgroup was analyzed with available urine samples and evaluable radiographs for both knees (N = 1241). CTX-I urine, CTX-II urine, and serum osteocalcin were analyzed for associations with combined K-L, gender and pain scores for both knees to assess the contribution of the joints at different stages. Pain, BMI, age, gender, and KL grade were significantly associated with uCTX-II. The association between pain and CTX-II appeared to be driven by pain due to weight. The level of uCTX-II increased with increasing radiographic severity of each knee. CTX-I, bone marker, and osteocalcin levels were significantly associated with BMI and gender, but neither was associated with radiographic severity. Biomarker levels among male or female groups of identical KL scores were found to be higher in women than in men in some but not all KL score groups. These results indicated that levels of uCTX-II were independently associated with radiographic severity of OA and pain intensity. CTX-II was associated with weight-bearing pain, but not with non-weight-bearing pain, regardless of co-variants. Bilateral OA knee joints appear to contribute to uCTX-II levels in an incremental manner according to radiographic severity of single joints. This study suggested that differences in biomarkers between genders should be taken into account when evaluating these markers in the context of structural features of OA.

18.10 Impact of Exercise on Molecular Biomarkers Related to Cartilage and Inflammation

Bricca et al. investigated the impact of exercise therapy on molecular biomarkers related to cartilage and inflammation in individuals at risk for knee OA, or with established knee OA, by conducting a systematic review of randomized controlled trials (RCTs) [19]. Twelve RCTs involving 57 study comparisons at 4–24 weeks following an exercise therapy intervention were included. Exercise therapy decreased molecular biomarkers in 17 study comparisons (30%), had no effect in 36 (63%), and increased molecular biomarkers in 4 study comparisons (7%). Meta-analyses of 9 biomarkers showed that exercise therapy was associated with nonsignificant reductions of the CRP level, C-terminal cross-linking telopeptide of type II collagen, TNF, soluble TNF receptors 1 and 2, C2C neoepitope of type II collagen, and cartilage oligomeric matrix protein, compared to non-exercising control groups, and exercise therapy had no effect on IL-6 and soluble IL-6 receptor. Exercise therapy is not harmful because it does not increase the concentration of molecular biomarkers related to cartilage turnover and inflammation, which are involved in the progression of OA. The overall quality of evi-

dence was reduced to low due to the limited number of RCTs available.

Bender et al. evaluated possible biomarkers of OA in the hand and attempted to identify an optimal time point for venous blood sampling, and to correlate biomarker levels with radiological and clinical scores [20]. Four female cohorts were investigated. One with a more Heberden-accentuated OA and one with a more Bouchard-accentuated hand OA, and two symptom-free control groups aged 20–30 or 50–75 years. A Heberden node describes a bony swelling of the distal interphalangeal finger joint. It is a sign of osteoarthritis, a degenerative joint disease. A Bouchard node is a similar swelling affecting the proximal interphalangeal finger joint. Venous blood samples were taken before and at eight time points after mechanical exercise of the OA hand. X-rays of the OA hands were evaluated using the K-L classification and the Kallman classification. Participants were assessed clinically using the AUSCAN™ Index, the Visual Analog Scale (VAS), and the Health Assessment Questionnaire (HAQ). Serum levels of seven biomarkers were measured by ELISA. The concentrations of CPII, COMP, IL-15, sVCAM-1, NGAL, and PIIANP were significantly increased within 15 min after exercise. PIIANP was markedly elevated in the Heberden-accentuated OA group as compared to both control groups, but did not correlate with any radiological or clinical score. Analysis of the probabilistic index further revealed that CPII can distinguish between Bouchard's OA and premenopausal controls, whereas COMP can discriminate between Bouchard's and Heberden's OA. This study showed that even previously undetectable biomarkers can be quantified in serum after mechanical exercise. However, future larger studies are needed to determine the specificity and sensitivity of these markers and their ability to diagnose pre-radiological OA.

Table 18.1 shows the most important data from the literature on the role of biomarkers in osteoarthritis.

Table 18.1 Most important data from the literature on the current role of biomarkers in osteoarthritis

Functional analysis of DEGs (differentially expressed genes) has shown that inflammatory responses, immune responses, and positive regulation of apoptosis, tumor necrosis factor (TNF) signaling pathway, and osteoclast differentiation may be implicated in the pathogenesis of osteoarthritis
Serum levels of interleukin (IL-8) may have a role in knee osteoarthritis
Augmented expression of interleukin 7 receptor (IL7R) and signal transducer activator of transcription 1 (STAT1) in synovial tissue, as well as primary immunodeficiency, may be associated with the development of rheumatoid arthritis. These biomarkers can be utilized to clinically differentiate rheumatoid arthritis from osteoarthritis
Measuring the change in the cartilage intermediate layer protein 2 (CILP-2) may be a valid and sensitive method of detecting the early development of knee osteoarthritis, as CILP-2 appears to be related to cartilage thickness loss in certain people at increased risk of developing osteoarthritis
Serum soluble vascular adhesion protein-1 (sVAP-1) levels in osteoarthritis patients are lower than those in healthy people and correlates inversely with markers of pain and inflammation [hsCRP (high sensitivity C-reactive protein) and soluble RAGE (soluble receptor for advanced glycation end-products)]. Serum sVAP-1 levels are also lower in patients with advanced osteoarthritis (Kellgren–Lawrence 3/4) than in patients with early osteoarthritis (Kellgren–Lawrence 1/2). Local (synovial fluid) semicarbazide-sensitive amine oxidase (SSAO)/sVAP-1 levels are elevated in osteoarthritis and correlate with radiographic severity
Analysis of the integrated small interfering RNA (siRNA) network has identified eight siRNA molecular biomarkers associated with the progression of knee osteoarthritis
Variables that most contribute to non-progression of osteoarthritis of the knee at 48 months are WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) pain, lateral meniscal extrusion, and N-terminal pro-peptide of collagen IIA (PIIANP), while those that contribute to progression are bone marrow lesions, osteophytes, medial meniscal extrusion and urine C-terminal crosslinked telopeptide type II collagen (CTX-II)
45 hub genes (genes with high correlation in candidate modules) and 72 hub genes in two modules are associated with osteoarthritis. These hub genes could provide new biomarkers and drug targets in osteoarthritis

(continued)

Table 18.1 (continued)

Type II collagen-specific biomarker Coll2-1 and its nitrated form Coll2-1NO2 are associated with various knee osteoarthritis characteristics quantified with WORMS (Whole-Organ Magnetic Resonance Imaging Score) scoring system on magnetic resonance imaging (MRI). Serum values of Coll2-1NO2 are also associated with an aggravation of target knee pain over 1 year. Coll2-1 and Coll2-1NO2, in association with other structural characteristics, pain and function, could help at detecting osteoarthritis phenotypes and patients at risk of osteoarthritis aggravation
A subset of six synovial fluid biomarkers is associated with synovial inflammation in osteoarthritis, as well as radiographic and symptomatic severity. These six osteoarthritis-related synovial fluid biomarkers are specifically linked to macrophage and neutrophil indicators that are activated. There is an endotype of inflammatory osteoarthritis in the knee that could be used for therapeutic selection of patients at high risk of progression
Augmented joint damage detected by MRI is associated with higher levels of C-terminal crosslinked telopeptide type II collagen (CTX-II), suggesting that increasing disease severity can be assessed with MRI and CTX-II biomarkers in order to evaluate osteoarthritis progression
Given their ability to differentiate between controls and patients with hip injuries, cartilage oligomeric matrix protein (COMP) and fibronectin-aggrecan complex (FAC) are specific biomarkers with potential utility in the diagnosis and management of femoroacetabular impingement (FAI) and hip osteoarthritis
Serum COMP and urinary CTX-II can distinguish between patients with knee or hip osteoarthritis and control individuals. Serum COMP is effective in predicting the progression of osteoarthritis
Augmented expression of IL7R and STAT1 in synovial tissue, as well as primary immunodeficiency, may be associated with the development of rheumatoid arthritis
The functional destruction of collagen in cartilage can be a major contributor to osteoarthritis. Quantitative detection of collagen synthesis can be of great help for early identification and prediction of osteoarthritis. Maintenance of collagen quality and quantity may be a potential target for clinical treatment of osteoarthritis in future practice
Serum creatinine phosphokinase (CPK) is associated with sarcopenia, suggesting its potential usefulness in detecting sarcopenia in osteoarthritis regardless of pain or inflammation
Differences in biomarkers between genders should be taken into account when assessing these markers in the context of structural features of osteoarthritis
CPII (C-propeptide of type II collagen) can distinguish between Bouchard's osteoarthritis and premenopausal controls, whereas COMP can discriminate between Bouchard's and Heberden's osteoarthritis. Besides, even previously undetectable biomarkers can be quantified in serum after mechanical exercise

18.11 Conclusions

IL-8 appears to have a role in knee OA, as serum IL-8 levels are positively associated with increased knee symptoms, IPFP signal intensity alteration and serum levels of NTXI), PIIINP, MMP-3, and MMP-13 in patients with symptomatic knee OA. Moreover, there are positive associations between IL-8 and WOMAC score, K-L grades, and IPFP signal intensity alteration in patients with radiographic OA.

Since the cartilage biomarker CILP-2 appears to be related to cartilage thickness loss in certain individuals at increased risk of developing such disease, measuring its changes may be useful in detecting the early development of knee OA. Previous injury to the knee may also predict increased absolute cartilage thickness change. Local (synovial fluid) SSAO)/sVAP-1 levels are elevated in OA and correlate with radiographic severity. However, systemic (serum) levels of sVAP-1 are lower in patients with OA than in control patients and are inversely correlated with markers of pain and inflammation. Serum sVAP-1 levels are higher in patients with early OA (KL1/2) than in patients with advanced OA (KL3/4). The major factors contributing to non-progression of OA at 48 months are pain, WOMAC, lateral meniscal extrusion, and PIIANP serum, while those contributing to OA progression are bone marrow lesions, osteophytes, medial meniscal extrusion, and CTX-II urine. Given their ability to differentiate between controls and patients with hip injuries, COMP and FAC are potentially useful biomarkers in the diagnosis and management of FAI and OA of the hip. Serum COMP and urinary CTX-II can distinguish between patients with knee or hip OA and control subjects. In addition, serum COMP is effective in predicting the progression of OA.

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