Decision making in articular fractures

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Objectives

▸ Understand the healing mechanisms of articular cartilage and how they can be affected by treatment
▸ Understand the importance of anatomical reduction, rigid fixation and early movement for treatment of articular fractures
▸ Be familiar with the techniques and implants used for the treatment of intra-articular fractures

Function of articular cartilage

▸ Distribute forces evenly
▸ Provide a frictionless surface to the joint
▸ Shock absorber

I.A Fractures – Advocated conservative treatment

▸ Sir John Charnley – closed treatment of fractures
▸ Neer et al – 1967 JBJS – 49
▸ Stewart et al – 1966 JBJS – 48A
▸ Non-availability of proper implants and proper understanding of cartilage healing
▸ Led this great stalwarts to make this statement 50 years ago

Credit of Understanding Intra articular Fractures – AO Group

▸ Muller et al
▸ Mitchell & Sheppard
▸ Salter et al
▸ Schatzkar et al
▸ Anatomical reduction
▸ Absolute stability is necessary for healing of articular cartilage

Articular Cartilage is an aneural structure with no blood or lymphatic supply and depends on diffusion from surrounding tissues for nutrition.

The cartilage matrix has got hypoxic environment and depends on anaerobic glycolysis and mainly consists of type II collagen and proteoglycans important for the joint. So it confers to poor reparative potential.
Relationship between Articular Cartilage injury and osteoarthritis is a complex phenomenon

Articular Cartilage healing leads to formations of fibrocartilage, however it does not restore the structural and mechanical properties of normal cartilage

Larger the defect, larger is the alteration of the mechanical properties and thereby the larger risk of progression of osteoarthritis

Effect of step off defects and development of post Traumatic Osteoarthritis

- Depends on thickness of articular cartilage which varies from joint to joint
  - Ankle – 1.0 – 1.62 m
  - Knee – 1.69 – 2.55 m
  - Patella – 1.76 – 2.59 m
- Remodelling depends on the defects – if it exceeds the thickness – remodelling does not occur fully.
  - Usually, less than 2 mm step off is acceptable
- Extra articular deformities also affects by virtue of altered mechanical axis and eccentric joint loading.
- Management of soft tissue is also vital for the final outcome in I.A Fractures.

Joint immobilization increases Joint Pressure and this increases:

- Loss of nutrition resulting in Chondrocyte death
- Liberates several enzymes like proteases resulting in Articular surface degeneration whereas motion promotes healing of full thickness articular cartilage with hyaline or cartilage like material

Nutrition of articular cartilage

- Nutrition comes from synovial fluid
- Flow of synovial fluid requires motion and load

Therefore any treatment designed to restore normal joint function should include:
- early joint motion
- restricted weight bearing

Articular cartilage response to trauma

- Very sensitive to injury
- Poor healing potential
- In non treated injuries, articular cartilage heals with a mixture of fibrous tissue and fibro cartilage

Response of articular cartilage to trauma

Anatomical reduction
  +
Interfragmentary compression
  +
Early mobilisation
  ↓

Healing with hyaline cartilage

Clinical/experimental evidence 1

In articular fractures: (Schatzker 1987)

- Immobilization results in stiffness.
- Immobilization after ORIF will lead to much greater stiffness.
- Metaphyseal and diaphyseal displacements should be reduced to prevent joint overload

PRINCIPLES

1. ANATOMIC REDUCTION
2. STABLE FIXATION
3. EARLY RANGE OF MOTION
Pauwels proposed that anatomic restoration of joint surface and mechanical axis are necessary for successful outcome.

Articular cartilage defects usually heal with fibrocartilage with inferior mechanical properties and durability.

Mitchell and Shephard demonstrated experimentally that anatomical restoration of joint surface and interfragmentary compression fixation followed by continuous motion can lead to true hyaline cartilage repair.

Clinical/experimental evidence 2 (Schatzker 1987)

In articular fractures:
- Anatomical reduction and stable fixation of articular fragments is required to restore joint congruency
- Major defects do not fill with fibrocartilage and the resulting instability is permanent

Clinical/experimental evidence 3 (Schatzker 1987)

In articular fractures:
- Depressed osteochondral fragments are usually impacted and will not reduce by closed means
- Metaphyseal defects must be filled with bone graft to prevent redisplacement

Treatment of articular cartilage
- Anatomic reduction of fragments
  No step off, no depression, no gaps
- Stable internal fixation (absolute stability)
  Can withstand early mobilization
- Early motion of joint
  For healing with hyaline cartilage
  Prevent joint stiffness

Outcome after articular fractures

The results of treatment of articular fractures depend on many factors:
- Trauma energy
- Residual malalignment
- Ligamentary instability
- Meniscus preservation in the knee
- Step-offs in articular cartilage

Principles of treatment
- Understand the injury
- Preoperative planning
- Timing
- Surgical approach
- Articular reduction
- Buttress of the metaphysis
- Postoperative care
- Understand the injury
- Evaluation of soft tissue
- Indirect injury: less soft tissue damage
Timing is Vital

- I.A Fractures are also complex soft tissue injuries – except in elderly osteoporotic patients
- Wait – Wrinkle sign to appear
  - Till then bridging ext fixatures
  - Indirect reduction techniques
  - Biological fixations to be undertaken

Principles of treatment

Soft tissue is the most important factor in determining the type and time of management and stabilization

- Adequate imaging
  - X-ray AP, La, Oblique and traction
  - CT
  - MRI

Imaging in Intra Articular Fractures

- X-ray
  - AP & Lat. Oblique & stress views
  - CT – Useful in delineating fracture configuration

specially complex fractures – acetabulum, distal humerus and prox and distal tibial fractures. Articular gap and step offs can also be estimated.

TRACTION VIEW

Adequate imaging
- X-ray AP, Lat, Oblique and traction
- CT
- MRI

TRACTION VIEW—evaluation of the fracture using CT

With 3D and Axial CT

- Surgical Plan changed – 64% of cases
- Additional information – 82%

Tornetta Clin. Ortho 323:273.6

AO CLASSIFICATION

Partially articular B1, B2 and B3

C1- articular simple, metaphtyal simple
C2- articular simple, metaphtyal complex
C3- articular complex
Principles of treatment

Timing

➤ Primary:
  • Little edema
  • Good skin
  • Recent trauma

DO NOT OPERATE IF THERE IS TOO MUCH SWELLING

Surgical principles in Intra Articular Fractures

➤ Atraumatic Surgical approach
➤ Minimally invasive or open
➤ All articular fragments should be reduced anatomically
➤ Ligamentotaxis will work only when fragments are attached to ligaments
➤ Depressed fragments should be elevated and supported by graft
➤ Anatomical plates have made things much easier.

Principles of treatment

➤ Timing
➤ Primary deferred:
  • Traction or external fixator
  • ORIF 1–2 weeks later

In 2 sessions:

Assembling of the articular surface + transarticular external fixator

FIXATION

➤ Lag screw achieves compression and provides stable fixation and then a buttress plate can be put
➤ If multiple small fragments are present they are reduced and held together with fully threaded position screws.
➤ Care must be taken not to over compress fragments
➤ Recently techniques are described in which multiple screws are placed in proximity of subchondral surface to support fracture fragments—rafting technique

Types of fixation

➤ Minimal osteosynthesis:
  • K-wires, ss wire
  • cannulated screws
  • Buttress plate
  • Hybrid external fixator
  • Transarticular external fixator

Post operative Rehabilitation

➤ Is most vital
  • Salter RB—J. Rhemat-31—2004
  • Salter RB—Hand clinic 10 (2)
  • Active assisted exercises from Day 1 and CPM. However CPM does not prevent muscle atrophy.
Postoperative care:

- Pain-free active mobilization
- Isometrics in day 1
- Physiotherapist

Limited weight bearing (15–20 K)

32-year-old male, 41-B3 fracture

Emerging technologies in the treatment of Intra articular fractures

- \( \text{TI – rho MRI mopping} \) – this measures relaxation times in cartilage can assess specific components of articular cartilage biochemistry and ultra structures
- More specific than conventional MRI – in cartilage degradation
- Virtual operative planning including implants – preoperatively with electronic templating
- Navigation – CT based
  - Fluoroscopy based

» Nano technology are making newer in roads in the management of intra articular fractures

Summary

» Articular cartilage is avascular
» Poor healing capacity
» Adequate pre op planning
» Soft tissue condition determines the timing and type of fixation

» REDUCTION? DIRECT ANATOMIC
» STABILITY? ABSOLUTE
» POST OP CARE? EARLY MOBILIZATION

TAKING CARE OF THE SOFT TISSUE

Conclusion

To Conclude

» Anatomical reduction and absolute stability are the vital pillars for optimum healing of articular fractures
» Immobilization of I.A Fractures leads to stiffness
» Immobilization after fixation of I.A Fractures lead to more stiffness
» You cannot reduce depressed, impacted articular fragments by close reduction
» Big articular fragments do not fill by fibrocartilage
» Any metaphyseal or diaphyseal fragments should be reduced, bone grafting if necessary
» Always restore joint congruity and axial and rotational alignment
» Early motion and stable fixations are the key for the success in Intra Articular Fractures
Decision making in shattered diaphysial fracture of long bones

**Author:** Dr D D Tanna.

It is a definite vague science. As individual series by any institute is always very small. My approach simple fracture take a length of opposite side and paste it on viewing box. keep whole extremity sterile, as u may need to span from knee to hip or knee to ankle. Aim of treatment is reposition the extremity in normal length, normal axis, normal rotation. I feel shortening of limb to get quick bone healing is not desirable in simple fractures, which may be ok for bad compound fractures. This limb is going to take long time for healing and may need bone grafting and multiple procedures. And hence keep patient informed about this. But assure him that he will be ok and there is no short cut to this treatment.

**Planning Choice of implant**

Nailing is the primary choice. Long plate is also required often. So keep nail and longest plates, mainly blade plates of long length should be available if fracture extends till proximal end of femur.

Most of these Fractures need cephalo condylar nails with neck screws and additional upper end femur screw, and distally multidirectional. Multi screw construct to achieve stability. Nail should be reamed in intact bones avoiding shattered bones where reamer is pushed without motor running, till distal end and then reamed.

longest nail, engaging the subchondral bone of the lower end should be used. no dynamisation, and most often, it will need bone grafting after about 6 wks of surgery, may need additional allo graft often. I would not do bone grafting primarily. Or even not try to turn 180 degree turned fragment primarily, which can be done at about 6 wks while bone grafting.

Plate if it is used, it should be spanning plate without opening the fragment unless large fragment which can be lagged, should be lagged, before bridge plating is done. I feel this bridge plating needs more screws in the intact fragments to improve the rigidity of construct, due to spanning of the long segment still it will remain in a micro motion mode. In spite of more screws in intact ends of the bone.

Post op non wt bearing, toe touching should be practiced for a long time till early sings of healing appear.

Implants should not be removed at least till 2/3 yrs. after healing.

Compound fracture is a different ball game. This will need multiple debridement, ex fix, segment transport and secondary fixation etc. In this short time I feel, I will not touch on this aspect in order to discuss non compound but complex fractures in more detail.

Floating Shoulder Injuries

**Author:** Dr Nirmal Chandra Mohapatra.

**Introduction:** Shoulder is frequently defined as an ipsilateral fracture of the clavicle and scapular neck, but the definition continues to evolve with our growing understanding of the role of coracoclavicular and coracoacromial ligaments in maintaining stability of the shoulder girdle. Current studies suggest that ligament disruption associated with a scapular neck fracture can contribute to the functional equivalent of this injury pattern, with or without an associated clavicle fracture.

Floating shoulder is a complex injury & requires through evaluation & planning for a satisfactory outcome. This is because of several factors. First it is difficult to precisely define the injury pattern to bone & soft tissues around shoulder. Secondly there is no definite evidence based
publication for treatment protocol for management, the studies are erratic or very scant in numbers. Thirdly, satisfactory results have been achieved with both nonsurgical and surgical treatment strategies & finally, assessing outcome can be difficult given the compensatory mechanisms for upper extremity function.

The overall goal of treatment is to restore function of the shoulder and avoid morbidity. In general, effective management of a floating shoulder requires an understanding of its pathoanatomy and biomechanics as well as an individualized approach based on surgeon experience.

**Surgical Pathoanatomy:** Functionally, the shoulder girdle complex suspends the upper extremity from the thorax. This complex has been referred to as the superior suspensory shoulder complex (SSSC) by Goss. The SSSC consists of osseous and soft tissue structures that exist between two struts. The lateral end of the clavicle acts as the superior strut, while the lateral scapular body and spine serves as the inferior strut. The components of the SSSC create a ring that includes the acromion, coracoid, distal clavicle, glenoid, coracoclavicular ligaments and the acromioclavicular joint. Though not originally included coracoacromial ligament has been found to be an important stabiliser of the scapular neck & should be included. The complex is responsible for maintaining a stable relationship between the axial skeleton and the upper extremity. A single disruption in the ring of the SSSC is a stable injury. Disruption in two or more places, however, results in instability & may require surgery.

The primary pathology in all injury patterns for which the term floating shoulder has been used is a scapular neck fracture. The associated injury that imparts instability to this fracture may be purely ligamentous, purely osseous, or a combination of both. The combination of the scapular neck fracture with one of these associated injuries defines a floating shoulder.

This, in turn, often leads to adverse long-term functional consequences, including delayed union, non-union, and malunion; subacromial impingement; decreased strength and muscle-fatigue discomfort due to altered shoulder mechanics; neurovascular compromise & Brachial Plexopathy due to a drooping shoulder; and glenohumeral degenerative joint disease.

**Evaluation**

**Clinical evaluation:** Floating shoulder injury is a severe injury & is frequently associated with other systemic injury to lungs, chest, head & neck. So the initial evaluation of the patient should be according to ATLS protocol. Associated injuries should be identified & treated promptly. These may include head injury, fracture ribs, haemothorax, cervical spine injuries & injury to the neurovascular structures. A thorough well-documented neurovascular examination is required to establish a baseline of function as well as determine which evaluations and tests are necessary to guide further treatment. Inspection for gross deformity like drooping shoulder, abrasions over the shoulder should be observed. And palpation for crepitus and tenderness facilitate accurate localization of the injury site. Sternoclavicular, acromioclavicular, and glenohumeral joints must be assessed for dislocation. Both passive and active ranges of motion of the shoulder (glenohumeral and scapulothoracic), muscular strength, status of the rotator cuff, and competency of ligaments are necessary tests in the acute phase of injury.

**Radiological evaluation:** A standard chest radiograph should be obtained to evaluate for pneumothorax, haemothorax & fracture ribs and a trauma lateral
cervical spine radiograph should be obtained to assess the patient for associated spinal fractures. A shoulder trauma series (anteroposterior in the plane of the scapula, scapular lateral Y view, and axillary lateral views) are required to establish the type of injury. Important factors to assess on radiographs include the amount of clavicular displacement, glenoid medialization and angulations, intraarticular involvement, and the extent of comminution. More than 5mm displacement of glenoid, 10 mm of clavicular displacement are indicative of instability. Medialization of glenoid of more than 30mm is indicative of severe instability. The angular displacement of the glenoidal neck can be measured by the Glenopolar Angle (GPA) & the Inclination Angle on Plane Xray.

Glenopolar Angle: The GPA is the angle formed by a line connecting the most cranial with the most caudal point of the glenoid cavity. The GPA provides a value for the obliquity of the glenoid articular surface in relation to the scapular body. A normal GPA may be in the range of 30° to 45°. GPA of <30° as an indirect sign of associated ruptured ligaments (labler et al) &GPA of <20° as indicative of severe glenoid rotational malalignment (Romero et al).

Inclination Angle: This angle is formed by two lines, one drawn perpendicular to the line connecting the most cranial with the most caudal point of the glenoid cavity and the other drawn perpendicular to the tangent along the medial border of the scapula. Using this angle, caudal dislocation of the glenoid is arbitrarily defined as inferior glenoid displacement <or equal to 20°.

CT: CT with three-dimensional reconstructions is frequently used to assess the patient suspected of having a floating shoulder. The 3D CT can be rotated to the optimal AP plane and to the lateral plane (ie, scapula Y) for more accurate measurement of displacement and angular deformity, identification of fracture fragments &intraarticular fractures.

MRI: the displacement of fracture fragments can give an indirect indication of soft tissue injury though its difficult to evaluate both radiologically & clinically. Here in selected cases MRI can be used to evaluate the status of the ligamentous complex of SSSC.

Treatment
Definitive treatment of floating shoulder injuries continues to be controversial. Traditionally these injuries have been treated conservatively. With increasing understanding of the Pathoanatomy & biomechanic more & more surgically treated cases are being reported. Although definitive algorithm for management based on scientific evidence is not possible at this time; however review of the literature does provide a good insight into key elements to consider in deciding how to treat the patient with a floating shoulder.

Non surgical Treatment: The advantages of nonsurgical management are its noninvasive nature and low morbidity. Treatment is symptomatic. Short-term immobilization in a sling and swathe bandage is provided for comfort. Early progressive range-of-motion exercises and use of the shoulder out of the sling within clearly defined limits are begun as pain subsides. Progressive use of the upper extremity is encouraged. Range-of-motion exercises continue until full shoulder strengthening exercises are added. It can be anticipated that full functional recovery will take several months.

Surgical treatment: surgery is gaining popularity because internal fixation can restore rapid stability & helps in rehabilitation. As the potential for future complications because of gleno humeral & scapulothoracic functional imbalance some type of internal fixation of clavicle, Scapula of both may be essential to minimise long term complications. The indications of surgery are double disruptions of the SSSC, GPA <20 degree, medial displacement of 30 mm which suggest gross instability of the fracture.

Some surgeons believe there are two groups of patients.
In one group patients with minimal displacement of the scapular neck fracture and intact coracoclavicular ligaments can be stabilized by internal fixation of the clavicle alone. The other group needs internal fixation of both clavicle & the neck of scapula as they have significant displacement of Glenoid & double disruption of SSSC. Here unless both are fixed there is risk of malunion which may affect rotator cuff function.

### Treatment algorithm/take home message

1. **Minimally displaced, Associated co morbidities & High priority injuries**
   - Conservative care
   - Weekly radiographs to check for union & stability of fracture
   - Relative indication &
     - Medicareation <20mm
     - Glenopolar angle < 20mm
     - Clavicle # displacement > 10mm
     - Glenoid displacement < 5mm

2. **Severe Displacement & young person with high physical demand**
   - CT with 3D reconstruction to accurately identify the fracture, MRI to identify the ligament injuries
   - Surgical management

3. **Trauma series X-ray to visualise scapula & clavicle**
   - Surgical management
   - Delayed surgical management

### References:

Acute knee dislocation is a serious injury resulting from high energy trauma to the knee joint. This injury can be a limb threatening injury and can be the cause of a serious long term morbidity to the affected limb. The injury was first described by Sir Asteley Cooper in 1825. It constitutes 0.02 to 0.2 % of all the orthopaedic injuries. It is mainly seen in young patients. Males are affected 4 times more commonly than females. Poly trauma patients have associated knee dislocations in 14 to 44% cases.

About 50% of knee dislocations are reported to result from road traffic accidents (high velocity injuries), 40% from sports injuries (low energy injuries usually in contact sports) and 10% from spontaneous falls caused by very low energy injury.

5% of the knee dislocations can affect bilateral knees. True incidence is under reported due to spontaneous reductions of the dislocated knee at the time of accident. It is likely to be missed in patients with morbid obesity and in polytrauma patients.

Of the four major ligaments of the knee - anterior cruciate ligament (ACL), posterior cruciate ligament (PCL), medial collateral ligament (MCL) and lateral collateral ligament (LCL) + Popliteofibular ligament complex, to label it as a dislocation of the knee, it requires injury to at least two ligaments. The commonest injury profile includes three or more ligament injury the common being ACL injury + PCL injury + another ligament (medial or lateral). The spectrum of injuries ranges from only two ligament injury to all the four ligament injury with different permutation and combinations and as the energy involved in the injury is increased, the spectrum becomes more and more extensive involvement. Majority of the knee dislocations are involved while 5-15% of the patients have open injuries.

Depending on the displacement of the tibia in relation to femur, the dislocation is labeled as:

- a) anterior dislocation which usually results from hyperextension
- b) posterior dislocation which usually results from posterior impact in a semiflexed knee or a dash board injury
- c) Medial dislocation resulting from varus impact
- d) Lateral dislocation resulting from a valgus impact
- e) Rotatory dislocations include anteromedial, posteromedial, anterolateral and posterolateral

About 50% of the anterior and posterior dislocations are associated with vascular injury. Medial and lateral dislocatins are more commonly associated with tibial plateau fractures and have a high risk of getting missed on clinical examination because of their subtle clinical signs.

For better documentation, the classification of Schenck is produced as under:

**High Index of Suspicion:**

To avoid missing a dislocated knee one should have a high index of suspicion. If the following deformities/signs are present, one should always rule out a dislocation of the knee joint:

- i) Hyperextension at the knee joint
- ii) Ecchymosis in the popliteal fossa
- iii) Vascular insufficiency of the toes
- iv) Peronealnerver injury
- v) Morbidly obese patients with history of fall and injury to knee

On clinical examination, if the skin is puckered around the knee, it is a sign of rotatory element in the dislocation resulting in button holing of the one of the bony end and usually the dislocation in such cases is irreducible.
Initial Management

All the patients of knee dislocation should be admitted in the emergency department for careful serial neurovascular examination (usually every 2-3 hourly) for at least 48 hours. If at the time of presentation in the emergency the knee is still unreduced, one should reduce the dislocation and examine for the neurovascular function before as well as after the reduction.

One should look for the usual signs of avascularity in all the cases before and after the reduction. Other sign of high suspicion of the vascular injury is an expanding hematoma in the popliteal fossa. Even if the pulses are present in the foot, one should compare the volume of pulses with the normal side foot to rule out partial blockage of the lumen of the artery due to intimal damage. It is recommended that, if possible ankle brachial index should be measured in all cases which is a non invasive supplement to clinical examination and has been reported to have a 100% predictive value for patients having vascular injury if the ABPI <0.9%. Some centers routinely recommend angiography in all cases of dislocated knees. However, being an invasive procedure we do not recommend this as a routine in our center.

The other investigations being recommended nowadays include CT and MR angiography.

Apart from vascular injury, the other important immediate complication of the Acute Knee Dislocation is common peroneal nerve injury which is seen in 10-40% of the cases. It is usually an axonotemesis type of injury.

If the knee is reduced at the time of presentation to the emergency, a gentle clinical examination is performed to assess the integrity of the four major ligaments of knee. It is important to be gentle during the examination to avoid iatrogenic neurovascular injury in a grossly unstable knee.

Investigations (Imaging):

Usual imaging modalities are the following ones:

- Plain X-ray
- MRI
- CT scan (If Plain X ray shows/ has a suspicion of fracture)
- Avulsions (better detail)
- Associated fractures (distal femur, proximal tibia)

While the plain X ray can show lesions like a Segond fracture, frank dislocation/subluxation, asymmetrical joint space, avulsions of ACL and fibula, MRI is very useful to know the condition of menisci, articular cartilage, ligaments, and various tendons like iliotibial tract, biceps, popliteus etc. However, MRI should not be blindly trusted because it can over or underdiagnose the injury. The report of MRI should always be read in conjunction with the clinical examination and the examination under anesthesia (EUA); the EUA should be a routine after any surgery on femur and/ or tibia for other injuries and before the limb is draped and prepped for surgery of any ligament. If need be, especially in morbidly obese patients, the EUA may be combined with stress fluoroscopy.

While doing MRI, if there is suspicion of vascular injury, MR angiography may be combined as a single procedure.

Classification

According to Positional Classification (Kennedy), the dislocation may be classified as anterior (40%), posterior (33%), lateral (18%), medial (4%) and rotational (5%). The problems with the positional classification is that in case of spontaneous reductions, it is not possible to classify and it does not provide any information about the ligaments. However, it is useful to decide the maneuver of closed reduction.
The other classification is anatomical classification which is classified on the basis of MRI and the associated neurovascular injury. The classification is as follows:

<table>
<thead>
<tr>
<th>Classification</th>
<th>Associated ligament injury</th>
</tr>
</thead>
<tbody>
<tr>
<td>KD-I</td>
<td>Single cruciate only: ACL or PCL</td>
</tr>
<tr>
<td>KD-II</td>
<td>Bicruciate disruption only: ACL and PCL</td>
</tr>
<tr>
<td>KD-III</td>
<td>Bicruciate and posteromedial or posterolateral disruption: (ACL and PCL) + (MCL or LCL/PLC)</td>
</tr>
<tr>
<td>KD-IV</td>
<td>Bicruciate + posteromedial and posterolateral disruption (ACL and PCL) + (MCL and LCL/PLC)</td>
</tr>
<tr>
<td>KD-V</td>
<td>Dislocation with associated fracture</td>
</tr>
</tbody>
</table>

To this classification letter 'C' is added for associated vascular injury and letter 'N' is added for associated nerve injury.

**Treatment**

Non surgical treatment is not recommended nowadays due to poor outcome reported unanimously by majority of the centers. Hence surgery is recommended in all the cases.

Goals of treatment include:

- Painless and stable knee
- Full ROM
- Normal Function

In the emergency, after the closed reduction, the knee is assessed for stability. If the knee is grossly stable, a long knee brace is given, while it is grossly unstable an external fixator is recommended.

Casts are usually discouraged because they can hinder in the assessment of vascularity of the limb.

After the closed reduction:

**Situation 1: ISCHEMIC LIMB after REDUCTION**

**EMERGENCY EXPLORATION**

- On table Arteriogram can be done
- Circulation has to be restored in 6-8 hrs

**Scenario 2: ABNORMAL VASCULAR EXAM – perfused LIMB**

**URGENT ARTERIAL STUDY**

- CT-Angiogram
- Angiography

**Scenario 3: NORMAL VASCULAR EXAM (No planned surgery)**

- Serial examination q 2-4 hrs for 48 hrs if can reliably be performed
- If NOT, order arterial study to r/o vascular injury
- MR Angio may be preferred as it will also show injured structures

**Scenario 4: NORMAL VASCULAR EXAM – Planned Extremity Surgery**

- Serial examination q 2-4 hrs for 48 hrs if can reliably be performed
- MR Angio for both to r/o vascular injury and operative planning

**Type of Surgery for knee dislocation:**

As Emergency: Apart from vascular repair, an emergency surgery may be required to reduce a dislocation which is not amenable to open reduction. The typical sign—“Dimple sign” caused by puckering of anteromedial skin due to buttonholed medial fem condyle through capsule, MCL, retinaculum, vastusmedialis should alert the surgeon about the possible need of open reduction.
After closed reduction, if the knee is grossly unstable, it is recommended to apply an external fixator after reduction of the knee for 6-8 weeks if the patient is not a candidate for ligament reconstruction due to medical reasons. Otherwise, the external fixator is continued till the definitive surgery is done in the next few days; in such cases the placement of the pins of the fixator should be such that they do not interfere with the incisions of the definitive surgery. External fixator is also required usually after vascular repair.

Whether conservative or operative treatment after closed reduction:

Grade I or Grade II injuries are usually treated nonoperatively initially till the knee is cold and then definitive ligament reconstruction is taken at a later time. However, for grade III and above injuries, it is recommended that the surgery should be undertaken early.

Indications of emergent surgery (within 4-6 hours)

- Associated vascular injury
- Irreducible dislocation
- Open injury
- Compartment syndrome

If time to revascularization is greater than 6 to 8 hours, then amputation rates are as high 86%.

During the emergency surgery, it is recommended to do simple ligament repairs and delay formal reconstruction for 1-3 weeks to allow soft tissue healing. Usually, within one week the repair of the medial and lateral ligaments and fixation of associated fractures, if any, should be performed. After 2 weeks, it is usually not possible to identify the torn ligaments and at that time, reconstruction is the best option.

Complications of Knee Dislocation:

1. STIFFNESS: This is the most concerning problem after a knee dislocation and starting of early ROM exercises is crucial to prevent this. Stiffness occurs with both nonoperative & operative treatment. The risk factors include high velocity trauma to knee, multiple injured patient, head injury. This is very difficult to treat. One should try early manipulation under anesthesia (at 6 weeks) if no progress is visible in ROM with aggressive physiotherapy.

2. Instability/Residual Laxity: It is more common with nonoperative treatment. It is also common after failed surgery for reconstruction of various ligaments. It is relatively easier to treat than stiffness.

3. Compartment syndrome: One should have a high index of suspicion for compartment syndrome after the injury as well as after the surgery because the rupture of the knee capsule results into leakage of fluid of arthroscopy into the compartments of the leg. The management is on the standard lines of management of compartment syndrome.

4. Iatrogenic vascular /nerve injury: Early exploration should be done.

5. Osteoarthritis: Upto 50% of patients of knee dislocation get early osteoarthrosis in the long term.

Conclusion: Early Reconstruction with modern Arthroscopic techniques results in a better outcome. Return to preinjury level is uncommon. Various studies show that approximately 40% get nearly normal function, 40% get abnormal with normal ADL, while 20% have severely abnormal function.

The take home message is:

- Do not MISS Vascular Injury
- Evaluate the severity of injury
- ALL unstable knees are NOT the same
- EUA is key in decision making for treatment
- PLAN, PLAN, PLAN before surgery
- Stiffness is major problem
- Return to Previous Activity Level is UNCOMMON
Femoro-Acetabular Impingement (FAI)

Introduction

The evolution of hip arthroscopy started in early 80’s in Europe & North America. In next two decades it gradually progressed, where the pioneers kept on exploring and pushing the limits despite all opposition and criticism. With their perseverance they helped in shaping and establishing hip arthroscopy into a well-accepted specialist procedure. Since the turn of this century there has been rapid progression and a significant increase in the popularity of the technique. This progress was particularly due to enhanced technical skills, improved instrumentation, the development of specialist distraction systems and a better understanding of the patho-physiology of the hip joint. Various traumatic and atraumatic intra and extra-articular condition are amenable for the treatment using this minimally invasive procedure. This can be supplemented with a short rehabilitation program to provide with desired outcome in the younger age group of patients. The role of this procedure continues to evolve. It is now being performed for several indications that would change the management of early degenerative changes within the hip joint. This would invariably alter the outcomes of the degenerative joint disease of the hip joint.

Femoroacetabular impingement (FAI) is one such condition that is increasingly recognised as a disorder that can lead to progressive articular chondral and labral injury. It can then gradually progress to wide spread osteoarthritic changes within the joint.

Etiopathology & Classification of FAI

It has been suggested that aberrant morphological features in certain hips leads to an abnormal contact between the proximal femur and the acetabular rim occurring during the terminal flexion phase of the range of movement. These repeated impacts lead to sheering stresses that leads to progressive acetabular labral and adjoining articular cartilage lesions.

The anomalous morphological features can distinctively present around the hip joint and are classified depending on their anatomical location. The first is the ‘Cam lesion’, occurring in young adult athletic males. The head of the femur is morphologically oblong or has lost the spherical feature. This change in the morphology causes a reduction of the femoral head-neck offset, which in turn predisposes the head to abut against the corresponding region of acetabulum in various degrees of flexion. The repeated impingement results in abnormal sheering forces being produced at the chondro-labral junction on flexion leading to an outside-in abrasion of the acetabular cartilage and/or its avulsion from the labrum and the subchondral bone.

The second type is pincer lesion which is usually found in middle-aged women who are physically active. In this group of patients the lesion is on the acetabular side. This occurs because of a linear contact between the femoral head–neck junction and the acetabular rim. The repeated impingement results in a general (coxaprofunda) or localised overcoverage (retroversion) of the anterior acetabular wall. This largely impacts the labrum which progressively leads to intra-substance degeneration, ganglion formation, fraying and tearing. Sometimes the degenerative process leads to intra-mural ossification which results in worsening of the over-coverage. The persistent abutment which is often anterior, results in chronic levering of the head in this region of acetabulum and can consequentially lead to chondral injury in the postero-inferior aspect of the acetabulum. It have been suggested that these chondral lesions are limited to a small area and therefore benign.
The third type of impingement is mixed and essentially has a component of both, the cam and the pincer lesions. This is most commonly seen in the patients presenting with on-going / longstanding impingement problems.

**Clinical Finding and Investigation**

The presentation in the outpatient clinic is classically a young athletic adult with a history of pain in groin that is worsened by athletic activities or prolonged walking and is also evident after prolonged periods of sitting pain on deep flexion. It is rare for these patients to present acutely; their symptoms usually have been present for some time and would have been gradually worsening over a period of few months.

It is essential to thoroughly examine these patients to reach a conclusive working diagnosis. The most constant finding on examination is restriction of internal rotation. They also demonstrate a positive impingement test which can be elicited by passive flexion of the hip up to 90° followed by adduction and internal rotation. It is important to exclude conditions like inguinal hernias and radiation symptoms from the lower back.

Once the clinical examination is highly suggestive of soft tissue or FAI lesions, further investigations are necessary to establish the diagnosis. An optimal plain radiograph of the pelvis in the antero-posterior (AP) and the lateral plane, and a weight-bearing view of the AP radiograph are preferred. The AP radiograph may demonstrate the loss of the spherical anatomy of the femoral head and a pistol-grip type of deformity of the proximal femur. On the acetabular side, there may be acoxavara, coxaprofunda and/or various degree of dysplasia. The lateral radiographs are very helpful in demonstrating the bony 'bump'on the anterolateral head-neck junction and a reduced femoral head-neck offset. Magnetic resonance arthrography is essential to assess the sphericity of the femoral head; further it is very sensitive in revealing the subtle and advanced changes in the articular cartilage and the acetabular labrum.

**Surgical treatment & Post-operative management**

Once the diagnosis is established there is limited role for conservative management of the patient. The definitive treatment is surgical. This can be done through 1) an open procedure that requires dislocation of the joint or 2) can be performed using minimal invasive techniques. There is a raging debate to which procedure provides better results and long term benefits to the patients. This is a contentious issue, as proponents of both groups have substantial evidence to support their cases.

Minimally invasive techniques for the management of various soft tissue conditions and FAI through hip arthroscopy are being increasingly practiced. Ever enhancing technical skills, improved instrumentation, the development of specialist distraction systems and a better understanding of the biomechanical concepts of the hip joint has helped in the evolution of these treatment modalities. Hip arthroscopy can be performed both in the supine or the lateral position. The supine position, on the other hand, was popularised by Byrd and offers the advantage of the use of a standard fracture table, the ease and simplicity of patient positioning, thereby circumventing the need for highly specialised distraction devices. It also offers familiar joint orientation and optimal access for the placement of the direct anterior portal.

The lateral position was originally described by Glick, this offers the advantage of providing reproducible bony landmarks for orientation. It also allows peritrochanteric approaches to be undertaken with ease and facilitates access and instrumentation of most areas within the hip joint. It has gained widespread acceptance by hip arthroscopists and is also the preferred position in our practice.

However, during the presentation, we will discuss the details of our technique which is performed in the lateral position. We will further elaborate our rehabilitation regime and details to avoid the associated complications.
Shoulder instability

Authors: Dr. Ashish Babhulkar.

INTRODUCTION

Historical aspects & Terminology

Over centuries now, the treatment of shoulder dislocation, has undergone a paradigm shift. It is only in recent years that common consensus seems to have been achieved over the “essential lesion” and the surgery to repair it. Within Orthopaedic literature, it was widely assumed, that if a particular problem had ten to twelve different surgeries to address on common problem, then the jury was out on the “correct” treatment. Thus we passed through a phase where it was common for one patient to be recommended for Bristow repair, Hybinette procedure, Putti-Platt surgery, Nicola procedure, Weber osteotomy etc etc. Most of these procedures were successful but the aim of surgery was to eliminate dislocation, which was achieved with a fair amount of certainty. Finally the exact pathology in the form of Broca-Perthes-Banlart lesion was described. The success of treating athletes for shoulder dislocation along with restoration of movement, strength and stability was a huge landmark. This success was then applied to the common patient and the goal posts shifted. On a different wavelength, episodes of recurrent subluxation have also been recognized to be as damaging as formal dislocations. Hence the modern term of “Anterior Instability” rather than dislocation. Henceforth in this article the term “Instability” would be used to address the problem of dislocation.

Clinical Anatomy & Factors related to stability

The labrum enhances the depth of the shallow glenoid
by close to 50% (Howell, Clin. Orthop 1989) and provides a secure site for insertion for the Gleno-humeral ligaments. Studies have also shown free nerve endings within the labrum that provide proprioceptive support for shoulder joint. The superior, middle and inferior glenohumeral ligament offer static restraint in typical positions of abduction. By far the most important and “essential” structure for maintaining stability is the Inferior Gleno-humeral Ligament complex, which along with the inferior labrum provides anterior restraint in the common Abducti on external rotation position.

The rotator cuff tendons provide dynamic support for stability; especially the subscapularis reflex contraction when the humerus commences its glide over the anterior glenoid margin in the abducted externally rotated position. Innate reflexes, ligament laxity are other co-morbidity factors affecting the stability of the Gleno-humeral joint. The position of the scapula vis-à-vis the humeral head influences the stability by influencing the glenoid version.

Similarly any glenoid defect especially at the anterior margin will simply encourage the humeral head to trespass anteriorly in the subcoracoid position. Lazarus (JBJS 78A 1996) assessed that a chondral defect in the glenoid can reduce its depth by 80% and adversely affect the stability ration by 65%. Fortunately reconstruction of the anatomy has shown to restore these values to normal.

Obrien (J Sho Elbow Surg 1995) has demonstrated in his biomechanical study, by serial isolated and combined sections of the Inferior glenohumeral ligament complex, its contribution to stability in abduction.

PATHOLOGY

In the event of an anterior dislocation of the shoulder, not only is the anterior labrum damaged, but a variety of adjacent structures are also at risk. It is well known now that the anterior capsule undergoes plastic deformation to a variable extent and also needs to be addressed at the time of surgery in the form of a plication. The Hill-Sachs lesion may be the only sign of recurrent subluxation episodes whereas some times the very first dislocation may result in an impressive Hill-Sachs lesion postero-laterally. Anterior or inferior margin of the glenoid may be fractured and negligence to address this is the most common reason for failure in arthroscopic Bankart repair. Instead of glenoid margin fracture, there may be anterior glenoid bone loss (inverted pear shaped Glenoid). This will be tackled in more detail in chapter on Investigations. Patients of anterior instability above the age of 40 have a very low risk of recurrence. However they have at least a 40% prevalence of rotator cuff tears due to the inherent degeneration of the rotator cuff (Arahi et al). This increases to a incredible 65% in those above 60 years of age and suffered a dislocation. Collateral damage in the form of nerve compression is
quite common and unrecognized mild neuropraxia of the axillary nerve is quite common. Rarely one single episode of dislocation may lead to monoparesis or even monoplegia, especially in patients with ligament laxity. SLAP (Superior Labrum anterior to posterior) tears and posterior labral tears are also known to be associated with instability and would need to be addressed at the same time.

**RADIOLOGY**

Radiographs are mandatory (Edwards et al) in two perpendicular planes. Ideally a “True” AP radiograph, Stryker notch view and an axial radiograph are adequate. The size and extent of Hill-Sachs lesion is best noticed on Stryker view. The presence of glenoid defect and of course degenerative changes from repeated dislocations are few obvious findings on axial. Glenoid lesions were also noted amongst recurrent subluxators (Edwards et al) who never experienced a dislocation. The role of MRI is to merely confirm the clinical impression. Axial images will show Bankart lesion along with extent of Hill Sachs. In the elderly dislocator MRI will be of great help to rule out a rotator cuff tear and that I believe is the biggest advantage of an MRI. Otherwise an MRI has no advantage to offer over basic radiology. The role of CT scan has largely been underplayed. In fact if at all imaging is required I would prefer a multi slice CT to an MRI. An ordinary CT scan is unlikely to reveal the extent of the inverted pear shaped glenoid. It is important to have a Multi slice CT scan and request the radiologist to subtract the head of humerus and reconstruct the glenoid in the sagittal plane. Whenever in doubt such a CT scan is best asked for. The MRI is predictably inferior to pick up anterior glenoid bone loss. Arthroscopic assessment may also underplay the extent of loss unless viewed from the antero-superior portal to look down on the glenoid & measure from the bare spot.

**LOGIC OF BANKART REPAIR**

The goal of Bankart repair is restoration of normal anatomy. Surgery involves selective correction of the essential abnormality without over tightening of any anterior structure. This is conducive to achievement of full range of movement. Modern Bankart repair has a number of modifications. The anterior capsule that has undergone deformation is also addressed and a superior to inferior (pants over vest) plication is performed rather than a medial to lateral plication (Double breast).

In the initial days of arthroscopic Bankart repair the anchors were inserted on the face of the glenoid and this did not restore the normal anatomical volume nor did it provide the ideal “Chock Block” (example shown in above figure) effect of the modern Bankart repair. The emphasis is also on aggressive physiotherapy to help achieve a full range of movement along with a strong and stable shoulder. Immobilisation on would only be a counter to this philosophy and the arm sling is only used as a reminder that surgery has been performed on a particular shoulder. In the initial days of arthroscopic repairs the failure rate was fairly steep at about 40% as compared to over 90% with open Bankart repair. With the better understanding of shoulder biomechanics and arthroscopic techniques nearly all present day literature reveals an impressive over 90% success rate with arthroscopic Bankart repair. The basic advantage of arthroscopic Bankart repair over its open cousin is the success in picking up allied conditions such as a SLAP tear and rotator cuff tears that can be associated. There is no trauma to the healthy subscapularis and the risk of stiffness is much lesser. However there is a steep learning curve that has to be met and the surgery does get a tad expensive. Hospital stay is curtailed significantly and it is appealing to athletes and sportsmen to undergo arthroscopic repair.

**TRADITIONAL SURGERIES**

It would be inappropriate to finish without scientifically explaining the reasons behind condemning Putti-Platt procedure to history. All the anterior tightening procedures worked on the premise of preventing
external rotation and thus stopping dislocation. This would be akin to creating another defect away from the “essential Lesion”. The site of the Bankart lesion does not at all correspond to the site of subscapularis that is double breasted. Most importantly there is a given arc of rotation anteriorly and posteriorly across the Glenohumeral joint. If this is disturbed (read shortened) eccentrically on one side it will inevitably push the head of the humerus posteriorly and draw the head of the humerus towards the glenoid initiating arthritic changes on both sides of the shoulder joint. This has been well established in a number of articles across orthopaedic literature. The risk of developing secondary osteoarthritis after Putti-Platt surgery is well documented to occur after a few years of surgery.

I have not discussed Glenoid bone loss & the role of Latarjet as it is beyond the scope of this article. Managing glenoid bone loss is an article by itself but I have covered the techniques to diagnose the same in the investigations paragraph.

**Few relevant references related to the topic can be perused**


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**Painful hip following total hip replacement**

**Authors:** Dr P Suryanarayana.

Total hip replacement is one of the most successful procedures and is primarily done to relieve pain and restore function. Painful hip following Total hip arthroplasty can be a cause of concern. Some studies have reported painful hip following a THR in up to 25% of the patients. Though most of the times it’s a mild pain, it can be disabling to an extent that it requires careful evaluation. Careful clinical assessment plays a vital role in assessing this pain and it guides the further course of evaluation.

Primary hip pathology should always be reconsidered in patients presenting with hip pain unchanged since the surgery. Lumbar spine pathology, knee pathology and metabolic conditions can mimic a hip pathology and could often be the source of persisting pain.

Pain in the first one month following a THR requires detailed clinical evaluation of the intra operative and post operative course of events. Any untoward events in the intra operative period should be looked for. Infection should always be considered in the evaluation of a patient with hip pain. It can even present in the early phase of THR. Patients typically present with a continuous pain not relieved with rest and an unwell feeling. They might also have night pain which is often disabling. WBC, ESR and CRP have limited role in the early post op evaluation of sepsis. Cases with high clinical suspicion are subjected to aspiration of the hip. Ultrasound of the hip is a useful tool to detect fluid collection in the hip and it also helps in aspiration of suspected hips. Undetected iatrogenic acetabular fractures, especially following non cemented press fit sockets has been reported to be a cause of acute pain in the post operative period. Also subtle subluxation of the hip can present as a source of hip pain and a feel of some give way in the early post operative period. Patients often complain of pain and clicks seen in certain particular positions of the limb. Component malalignment is often the cause for these.

Presence of normal gait and negative Trendelenburg test rule out sources of pain directly related to the actual hip surgery. Extrinsic sources of hip pain like trochanteric bursitis, muscle tendinopathies (adductor, iliopsoas) can
present as a painful hip in the intermediate phase following a THR. High offset is the most common cause of trochanteric bursitis which often results in pain over the trochanter. Iliopsoas tendinitis causes a nagging groin pain. The culprit often being irritation of the psoas tendon by large jumbo cups especially following revisions. Most of these extrinsic conditions are often diagnosed by direct palpation and resistive muscle testing. Component malposition can sometimes be difficult to detect on plain x rays. However if there is a suspicion of issues of component alignment, further evaluation with CT scans is required to get the true picture of the degree of component malposition. Thigh pains a concern in patients with large diameter fully coated distal fixation straight stems. implant loosening, component wear often presents late in the course of total hip arthroplasty. In aseptic loosening pain is typically present on standing and walking and this pain in relieved by rest. Loosening is often evident on plain radiographs. Evaluation of serial radiographs plays a key role in evaluating an aseptic loosening. Infection should be considered in all the cases of loosening until proven otherwise. Infection can lead to a painful hip at any time during the course of THR. Psychological cause as a source of pain also needs to be considered, however all the possible pathological entities have been ruled out before coming to a conclusion.

Osteolysis in total hip replacement

**Authors:** Dr J A Pachore

**Definition:**

Osteolysis is new disease created by particles mainly polyethylene. The other particle responsible are metal and cement particles.

In 1994 (NIH) statement and its year 2000 update both emphasized role of UHMWPE wear debris major cause of osteolysis. Adaptive immune response to implant material including specific patient response, cannot be ignored in the biological cascade leading to osteolysis. Willert and Semiliton extensively studied biopsy from Periprosthetic tissues. They found these tissue contained sheds of macrophages laden with various types of particulate wear debris in a fibrous stroma, intermingled with multi nucleated giant cells encapsulating large debris. Willert hypothesis wear debris generated at the articular surface is clear from joint space by macrophage phagocytosis and transport is via lymphatic system. If wear debris amount exceed then debris is retained in local tissue. This stimulate Periprosthetic granuloma.

Initial observation was of Wellert in cemented hip arthroplasty but similar observation were reported in Uncemented hip replacement. Schmalzried et al point out theory of effective joint space.

**Pathophysiology:**

Natural history of osteolysis in cemented socket is progressive liner osteolysis leading to eventual loosening. In uncemented socket inspite of extensive osteolysis socket remains well fixed and stable. Joint fluid debris flows according to pressure gradient and follows the path of least resistance. In cemented socket there is fibrous tissue at bone consent interface which resist this flow and does not allow this to go into subchondral bone. Hence in cemented socket there is liner osteolysis. In cementless socket subchondral bone is expressed and has direct access to in this area leading to balloon type of osteolysis. The area which has spot welding are spared. The area of least resistance without spot welding shared osteolysis. Zone two and three are more common area as subchondral bone is more cancellous.
Fibrous tissue membrane which is produced by particles secretes variety of mediators, enzymes, prostaglandins, pro inflammatory cytokines such as interleukins (IL 1 Alpha, IL 1 Beta and IL 6), tumor necrosis factor alpha (TNF Alpha) and growth factors such as platelet derived growth factor PDGF. Main source of particles burden is 70-95% from the articulating surfaces. The other source are back side wear particles. The size of particles are 0.1 to 2 microns. Febrils inter contacting the spheroids and forming layer aggregates are also present. The back side particles are larger size. The other source is metallic particles from femoral head, screw holes and screws. These particles are harder and responsible for third body wear. Periprosthetic tissue contains many types and sizes of particulate debris but does not confirm which type of debris particles are involve in initiating the granulomatous reaction.

New cross link poly XLPE has decrease wear in lab as well as clinically particles are small size 0.2u. There is absence of febrils. The inflammatory response is much higher with these particles.

Wear debris effect on oseoblasts.

a) Osteoclast differentiation and activation are stimulated by particles through release of IL 1, IL 6, TNF alpha and other inflammatory mediators.

b) Same mediators repress osteoblast junction and synthesis of matrix.

c) Fibroblast activity is stimulated.

Cytokine play critical role in bone resorption. Identification of three osteoclast regulators- RANL, RANKL, OPG their association with bone resportion has focused the attention of TNF alpha as cytokine. There is need to find out primary mediator which stimulate the cytokines. Thinking is to block the primary mediator to stop the initiation of inflammatory cascade. Although the understanding of pathophysiology of osteolysis has increased it treatment and prevention remains challenging.

Diagnosis:

Patient do not present with symptoms until considerable bone loss occurs around socket. Silent osteolysis has reported as high as 48% on CT scan (Stulberg SD et al JBJS 2002 : 84A 116-122) It is often reported that discrepancy occur between the lesion seen radiographically and intraoperatively. There is total underestimation radilogically when seen intraoperatively. Best radiograph reported to see osteolysis AP 45degree iliac oblique and 60 degree obturator oblique view. (Southwell et al JBJS 1999:81B 289-295) Additional of 45 degree obturator view add to great value to see osteolysis.

CT scan gives precise information on location of lesion site of lesion and identification of pelvic discontinuity. It helps in planning revision surgery. Puri et al has given good protocol for CT scan which consist 140 kev, no impage enhancement, pitch of 1 or less small field of view as possible bone algorithm and overlapping images. (Puri et al JBJS 2002,84A: 609-614).

Treatment of Femoral osteolysis:

Type 1: Well fixed implant, metaphyseal lesion, extensive coated stem, enough area for growth.

Treatment: New polyethylene and debridment and grafting for metaphyseal lesion but diaphyseal lesions are not advisable for grafting due to risk of periprosthesic fracture.

Type 2: Well fixed implant, metaphyseal and diaphyseal lesion, no enough area for bone in growth.

Treatment option: New polyethylene and revise the stem.

Type 3: Loose implant with severe osteolysis.

Treatment option: New polyethylene and revise the stem.
Surgical treatment for trochanteric fracture with osteolysis. Remove the particulate debris generator which means put the new polyethylene liner. If the trochanteric bone quality is good fixation with bone grafting to heal the trochanter is ideal treatment. If bone is poor with good soft tissue attachment it should be left after putting the new polyethylene liner.

Treatment of Pelvic Osteolysis

Indication for treatment of osteolysis in cemented socket is defined clearly than uncemented. Patient with cemented socket present with pain with liner osteolysis and loosening which needs revision. In uncemented socket patient are asymptomatic inspite of extensive osteolysis. When socket is loose it may signify major structural compromise leading to pelvic discontinuity or column deficiency (Hozack et al J arthroplasty 1996 :11: 769-772).

Most agree for revision if there is

- progressive osteolysis 3 to 6 month followups.
- eccentric PE wear
- complete penetration of head.

Treatment option: initial it was advocated to removal of well fixed implant and revision of acetabulum with complete debridement of osteolytic lesion. This may cause severe damage to pelvic bone may lead to pelvic discontinuity. New treatment strategy which was proposed by Rabash et al for uncemented pelvic osteolysis.

Classification: Type I stable - which includes

- cup is not mal positioned.
- locking mechanism is intact.
- metal shell is damaged.
- new conventional liner is of adequate thickness.
- implant is good track record.
- implant is modular.

Treatment option includes Retain shell+ exchange liner + graft.

Type 2 stable - Well fixed implant but does not meet criteria of type 1.

Treatment option includes Revise acetabular component + graft.

Type 3 Unstable - Total loose implant.

Treatment option includes Revise component + graft.

Today there is enough evidence of well fixed socket with liner exchanges with or without grafting. Few studies


There has been few reports regarding cementing the liner in well fixed shell which is indicated in failed locking mechanism Bonnar et al JBJS 2002: 84A :1100-1110.

Surgical technique for revising acetabular component.

Surgical approach should allow wide exposure. The approach may be dictated by previous incision. Exposure is difficult due to previous scarring with retain femoral implant. 360 degree exposure the socket is required before polyliner is pulled out. If previous implant record is present it becomes easy to use proper instrumentation.

Type 1 Surgical key is to extract poly without damaging locking mechanism. Various way to remove the poly by using proper instrumentation provided by company. The trilogy (Zimmer) liner can be pulled out by opening the locking ring. Duraloc has thin poly extractor. The other method to remove the poly is to use 6.5 cancellous screw which can be pushed into the poly after drilling with 3:2 drill, this distracts the poly from the shell. If locking ring is damaged you can use same size locking new ring. Thin osteotomes may be used at the junction of metal and poly. Once poly is out then stability of the cup should be tested. Inserter should be used and long lever arm can be used to remove the cup. Unstable cup which have
movement with acetabular inserter, reverse hammering can be done to test the stability loose cup which requires revision. CT scan gives idea of location and size of lesion. Anterior column and pubic area are not amonable for grafting. Dome and ischial area are amenable for grafting.

A) Through screw hole

B) Trap door procedure in supraacetabular area.

Lesions are gently curretted and allograft are packed by using special designed instruments. Ischial and post column can be also delt with trap door entry by posterior approach.

Type 2  Well fixed socket but needs removal. This can be done without much bone loss by explant system by Zimmer. This is followed by assessment of osteolytic areas instability of pelvis. If there is no pelvic discontinuity gentle reaming, allografting and new uncemented cup with multihole is choice. The new trabecular metal cups (TM) which have better osteointegration have good promise. The poly liner should be highly cross poly which has shown low wear rate.

Newer pharmacological drugs are under trial with some hope. Early attempts have been made:

a) Anti inflammatory drugs (NSAIDS)

b) Indomethacin blocks PGE2

c) Bisphosphonates appears to hold some promise.

Till today we do not have conclusive results of their role, safety and duration of treatment of these drugs. Pharmacologic drugs can be considered in non progressive lesion with close monitoring.

Gene therapy provides exciting possibilities in future. Dramatic results have been shown in small animal studies. Delivery of gene using viral vector remains unsolved and controversial.

Arthroplasty surgeons are now looking into how to reduce particle load or look for new bearing surface which will not produce particles leading to wear or get the pharmacological drug which will stop cytokinin secretion. The gene therapy today look experimental but can be the future due to advance in genetic science engineering.

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**Dislocation following primary total hip arthroplasty**

**Authors:** Dr SKS Marya.

**Introduction:**

Primary total hip arthroplasty (PTHA) over the years has become the most successful surgery providing adequate relief and improving the quality of life for many patients suffering from an arthritic hip. However, dislocations following PTHA are a frequent and serious complication. Reported dislocation rates by multiple authors vary greatly and have ranged from less than 1-5% in PTHA.\(^1\)\(^3\)

Cause for dislocation are multifactorial, ranging from patient factors, previous surgery, cognitive and neurological disorders to surgical factors like surgical approach, soft tissue handling, implant selection and surgeon experience.

Unstable hips can be divided into the following types - early dislocators (within 3-6 months post-surgery) and late dislocators. (any time after 6 months).\(^4\)

More often than not, two thirds of early dislocations will occur within first 3 months following PTHA.\(^5\)

Prevention is by far the best strategy to reduce the incidence of dislocation following THA. Stress on proper
patient selection, approach, implants and correct surgical planning prior to surgery will optimize results followed by patient education about hip precautions and post op rehabilitation.

**Risk Factors:** Risk factors for hip dislocations can be attributed to patient specifics, surgical procedure and implant features.

**Patient Factors:** Age above 80 years and female gender have been associated with higher dislocation rates owing to weak muscles and muscular incoordination, while differences in body fat and muscle mass distribution patterns attribute dislocation in the sexes. Neuromuscular and cognitive disorders like dementia influence of alcohol and drugs alter proprioception leading to non compliance of hip precautions. Dislocation rates significantly higher in obese patients possibly owing to extra articular soft tissue impingement during adduction and flexion.

**Surgical Factors**

Surgical approach is an important variable that is directly under the control of the surgeon. Dislocation rates owing to surgical approach has been found to be 1.27% for transtrochanteric, highest with the posterior approach without capsular repair (3.23%), and least with the lateral approach (0.55%). A comparison between dislocation rates with anterior approach versus posterior approach was 2.3% and 5.83% respectively.

Abnormal Cup placement with excessive ante or retro version usually leads to anterior or posterior dislocation. Increasing angles of cup abduction are known to increase probability for dislocation. Horizontal cup placement can cause impingement in abduction.

Abductor muscle dysfunction owing to trochanteric avulsion / non union or muscle avulsion more so with lateral approach is known to cause instability and dislocation.

Certain implant features like femoral offset, head size and inlay design are important factors in hip stability. Low head neck ratio facilitates impingement thereby leading to dislocations. Larger femoral heads (36mm or more) increase hip stability by increasing the jump distance and increasing the range of movement before impingement.

Insufficient neck length and femoral offset are important determinants for hip stability and should be considered while trying to retain optimal soft tissue tension.

**Evaluation**

History and physcials: Follow a standardized and methodical approach to formulate an ideal treatment plan.

History becomes important to understand the sequence of events that preceded the dislocation. Elucidate how the present dislocation occurred, what was the activity being carried out at the time of the dislocation and the position of the limb. An insight into past dislocation is very important.

Always look for signs of sepsis or past / present infection, a review of previous documentation which includes operative notes that documents surgical approach, position of implant with any intra or post operative complications.

Physical examination should include assessment of both lower limbs, gait, range of motion, strength (mainly abductor musculature) neurovascular status, limb length and location of previous incision.

Additionally, if infection is suspected then white blood count, ESR, C-reactive protein along with aspiration and cultures become mandatory.

**Radiography**

Standard AP involving pelvis and upper half of femur along with the lateral views of the affected side.

Femoral component should be assessed for head to neck ratio, loosening, neck lengths and, offset with angulations and evidence of subsidence.
Treatment:

Initial management of dislocated THA is closed reduction. Early dislocations are most often positional, trauma related or violation of hip precautions. Dislocation during the first week most often is attributed to disturbed abductor motor function and incomplete capsular healing. Hence these carry better prognosis with less recurrence rates.

These cases are best treated, following closed reduction by bracing and patient education. Bracing is advised for 6 to 12 weeks. Important pre requisites for long time stability are-correct implant position, adequate soft tissue tension and acceptable range of motion before impingement.

If recurrent dislocation is persistent and is because of prosthesis malposition, abductor dysfunction or soft tissue laxity then surgical revision should be considered.

Severe cup misalignment will require cup repositioning, however minor cup malposition can be treated by modular exchange of liners with the use of elevated, deep, antverted or lateralized inlays which is superior to component revision in terms of surgical time, tissue damage and bone loss.

Reduced soft tissue tension is difficult to assess as the underlying cause. However loss of femoral offset as well as limb shortening correlates with hip instability.

In the past trochanteric advancement was put to good use, but nowadays with the introduction of modular components, the surgeon can change the neck offset and length without revising the stem.

With introduction of large femoral heads (LFH), issues arising out of femoral neck impingement on the acetabular rim leading to dislocation could be addressed. Significant reduction of dislocation rates were noted when large head were used in comparison to smaller heads (22mm and 28mm). The main draw back with large heads is the increased volumetric wear that is generated leading to higher revision rates.

If these options fail or likely to result in unsatisfactory stability then constrained acetabular liners and bipolar hemi-arthroplasty are good salvage procedures.

Constrained sockets are indicated if cause for dislocation is unidentifiable, abductor musculature inadequacy or cognitive and neuromuscular disorders are present.

The disadvantages with constrained liners are decreased ROM, increased impingement, wear, acetabular loosening or component separation.

Bipolar hemi- arthroplasty is another viable option as a salvage procedure. However the disadvantages with it as a procedure involves re dislocation with rates ranging from 1.923 to 19%, continuing hip pain owing to acetabular bone erosion.

A newer addition is the dual mobility acetabular component or unconstrained tripod implant which is made up of a fixed acetabular component articulating with a bipolar prosthesis. It aims at providing greater stability with increased ROM.

In conclusion, patient at risk for hip dislocation should be identified prior to surgery so that the surgeon can adopt strategies to enable a more stable hip. Prevention by far is the best treatment for a displaced THA. Good patient education with stress on hip precautions is essential in preventing dislocations following THA. Closed reduction must be attempted initially and is usually successful in many cases. Recurrent dislocation should be surgically corrected following well laid guidelines to deal with individual issues like prosthesis mal-alignment and abductor insufficiency. Constrained acetabular components and bipolar hemi- arthroplasty can be used as salvage procedures at the cost of increased complications like loosening or hip pain.
References:


Post operative infection in THR

Authors: Dr. Shubhranshus S. Mohanty.

Introduction

Sir John Charnley reported 9% rate of periprosthctic joint infection (PPII) in his first 109 hips and it has come down to 1-2% in recent literature due to availability and understanding of better prophylactic antibiotics, concept of clean laminar airflow operating theatre environment, body exhaust suits and antibiotic laden bone cement. Associated medical co-morbidities like Rheumatoid arthritis, Diabetes mellitus, previous transplant surgery or any other previous hip surgery poses a 2.5 times higher risk factor for development of infection. The diagnosis varies from simple clinical examination to various laboratory investigations. The treatment varies from Antibiotic suppression, Debridement and retention of prosthesis, one stage or two-stagereimplanation and excision arthroplasty.

Classification

Based on onset and cause of infection, Fitzerald (1995) has classified post THR infection into 3 types. However, now Tsukayama et al (2003) have brought out a new entity of positive intraoperative cultures. Now the accepted classification of PPJI is as follows:

Type-I: Positive intra-operative cultures supposedly for aseptic revision
Type-II: Early postoperative infection <1month post-op
II A- Superficial to jt. capsule, II B- Deep to joint capsule
Type-III: Acute haematogenous infection >1m post-op, acute onset
Type-IV: Late chronic infection >1m post-op, insidious onset

Diagnosis

Osmond et al in 2005 stated that in order to prove periprosthctic joint infection one need to reveal the Joint Prosthetic Dysfunction and able to demonstrate microorganism in prosthesis/periprosthctic tissue. But the concept has changed recently and Parvizi et al in 2011 from AAOS working group has recommended that one of the following criteria should meet in order to prove infection:

1) Sinus tract communicating with prosthesis
2) At least two positive culture from separate tissue or fluid samples obtained from prosthetic joint
3) Four of the following six criteria exist:
   a) Elevated serum ESR & CRP (b) Elevated synovial leukocyte count
   c) Elevated synovial PMN% (d) Presence of purulence in joint,
   e) Isolation of organism in one culture of periprosthetic tissue/fluid
   f) Greater than five neutrophils/hpf in five HPFs observed from histologic analysis of periprosthetic tissue at x400 magnification

An ESR more than 30mm/hr and CRP more than 10mg/L is considered to be significant. The leucocyte cell count of 3000cells/μL and 80% polymorphonuclears (PMN) has been taken as threshold for hip infections.

Most infections occur due to Coagulase negative staphylococcus or Staphylococcus aureus. However, there is evolution of more resistant organisms during last couple of years. The author had shown that more than 55% of periprosthetic infections around the hip are due to Methicillin resistant Coagulase negative staphylococcus. Hence the surgeon needs to give a first generation/second generation cephalosporin only for 1day postoperatively as prophylactic antibiotic to prevent resistance.
**Management**

Type-I infection is essentially diagnosed after surgery and hence requires antibiotics to be given IV for 6 weeks depending upon the sensitivity report.

Type-II infection is basically classical fulminant wound infection like any other implant surgery. It is a clinical diagnosis and does not require any laboratory investigation to prove it. Wound dehiscence, necrosis of wound margins, infected haematoma all comes under this group. One needs to be aggressive in decision making to go ahead with debridement early within 2 weeks of onset of symptoms to have an optimum outcome. The success rate has been 71% in published literature.\(^4\)

Type-III infection is due to haematogenous spread from some source other than hip. The period between the index surgery and onset of infection remains normal. The patient may be febrile, but usually presents with pain on weight bearing and/or movements of the hip. It needs debridement with component retention or removal depending upon its stability.

Type-IV infection requires removal of components and one stage/two stage reimplantation. One stage exchange is recommended for elderly patients, infection with sensitive organisms and in an adequately debrided joint. However it is not suitable for immune-compromised, resistant Gm-ve/MRSA organism or with major skin/soft tissue/osseous defect. A review of 12 studies in 1299 patients with an average follow up of 4.8 yrs shows an overall success rate of 83%. The authors have used antibiotic cemented THR in 99% cases.\(^5\)

The first stage of two-stage surgery involves surgical debridement to remove sinus tracks, non-absorbable sutures, hardware, cement, restrictors, cables and wires etc. At least 5-6 samples of joint fluid, tissue specimens are sent for culture and sensitivity. One may need intraoperative radiography to check retained material. Then high dose heat stable antibiotic containing Cement beads/ cement spacer is put for direct delivery of antibiotics and to maintain soft tissue tension. The interval treatment consists of antibiotics administration, ESR/CRP evaluation. Second stage reimplantation is done after observing a downward trend of ESR/CRP values with clinical improvement.\(^10\)

The author uses autoclavable and reusable Polysiloxane (medical grade silicone) templates to prepare cement spacer, which is very useful and cost-effective.\(^11\)

Excision Arthroplasty remains the last option in medically unfit, mentally impaired, patients on immunosuppressant therapy, IV drug abusers or in failed two-stage Arthroplasty. But it leads to poor function and residual pain more or less remains.

Current problem in literature is that antibiotic resistant organism requires antibiotics having higher potential toxicity to the patient and the success of direct exchange of cementless prosthesis.

**References**


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**Decision making in malignant bone tumours**

**Authors:** Dr. Rakesh Bhargav

The growing trend to try and salvage limbs afflicted by malignant bone tumors has imposed certain responsibility and liability upon the orthopaedic surgeon attempting to do so. It becomes imperative that he should have correct and unambiguous answers to certain questions. I wish to first deal with those concerning the patient with the malignant tumor reporting to him

1. He must have a fair idea of what he is dealing with after the initial clinical examination and X-Rays. He must have a good idea of the natural history of the lesion and its growth and growth pathways, and possible metastasis site

2. He must be aware of the surgical staging system including preoperative staging using angiography, CT scan and other investigations for specialized staging and mets

3. The lesion must then be assessed with the surgical considerations of margins with the surgical intentions in mind, and the possible surgical operations

4. The most important consideration at this point is about the biopsy, from where to take it, that is the site, how to take it, whether needle, core or open, and adequate representative tissue for definitive histological examination

5. Once the pathology is established the tumor's natural history must again be considered in totality, and only then should definitive surgery be planned. This planning may require involvement of the plastic surgeon, vascular surgeon and pathologist, in case a frozen section may be needed

6. The imperative question to be answered now is whether limb salvage is possible. The considerations, other than the surgical ones, of just as great an importance are the patient's occupation, and the possibility of his return to it, his economic situation and that of his family, the possible duration of rehabilitation and its financial, social and psychological consequences for him. How far will the salvaged limb be acceptable to the patient in physical appearance, functionality and, again, psychologically

7. The merits and demerits of the alternative, that is, amputation have to be discussed in all honest terms both by him and for him.

8. He has to be honestly and correctly apprised of the chances of recurrence and metastasis on the basis of the surgeon's own database.

The other important consideration is the facility available to the surgeon in terms of infrastructure, availability of critical care and allograft facility. He should be confident of his own competence to not only perform the complex resections and reconstruction surgery required according to the individual lesions, but should be able to handle the intra and post operative complications as well

Some illustrative example are being projected of what can be done, in which malignant lesion and at what stage and the complexities that may be encountered during and after surgery
The patient needs to be followed up for recurrence of distant metastasis and this involves maintaining a proper database.

The bottom line is 'Surgery in orthopaedic oncology is not to be trifled with, for any half hearted attempts at management by way of facility, availability and surgical training and competence are acceptable. As with everything else, either do it right or don’t do it'.

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**Decision making in GCT**

**Authors**: Dr Sudhir K Kapoor

**Introduction**

Giant-cell tumor of the bone accounts for 4-5% of primary bone tumors and 20% of benign bone tumors. It is a well-known fact that incidence of GCT, in Asian countries, is much higher. It has been reported that in countries like China, Philippines, Hong Kong, Pakistan is as high as 20% of all primary bone tumors. Further the presentation is generally late in these developing countries. Management of Giant cell tumor ranges from surgical curettage to wide resection. Postoperative recurrence rate ranges from 4% to 50%. There is no uniform accepted treatment protocol for these tumors. Curettage, although an accepted method of treatment, carries a high local recurrence rate. GCT of the bone has sometimes unpredictable behavior. The best treatment should ensure local control of disease and maintain limb function. Earlier studies had shown very high (25–50%) local recurrence rates after simple curettage and bone grafting.¹

There are several dilemmas in the management of GCT, in diagnosis and various aspects of treatment, they can be discussed one by one.

**Dilemma in diagnosis**

Sometimes a histopathologist gives a report of not GCT but of a giant cell rich lesion. There are several osteolytic lesion in metaphyseo-epiphyseal region of long bones which may be rich in Giant cells e.g Hyperparathyroidism, chondromyxoid fibroma, osteosarcoma, aneurysmal bone cyst, foreign body granuloma, tubercular lesions etc. an orthopedic surgeon should never proceed till the time a clear cut diagnosis of giant cell tumor has been obtained by histopathology. Key features in differentiating GCT of bone from other lesion is multinucleated osteoclastic type giant cells surrounded by rounded mononuclear stromal cells.

**Treatment options**

Campanacci et al¹ proposed a grading system for GCTs that is based on the radiographic appearance of the tumors.

- A grade 1 lesion (latent) has a well-defined margin and an intact cortex.
- A grade 2 lesion (active) has a relatively well-defined margin but no radiopaque rim, and the cortex is thinned and moderately expanded.
- A grade 3 lesion (aggressive) has indistinct borders and cortical destruction.

In Campanacci Grade I and II GCT extended Curettage is the treatment of choice but because of high recurrence rate in campanacci Grade III GCT, its treatment is still debatable.

**Extended Curettege**

This is the treatment of choice for grade 1 and II tumors. However many people have confusion regarding the full spectrum of means to achieve the extended curettage. Extended curettage is a technique of intralesional excision where the margins of the excision are extended by a surgical, chemical, or thermal...
adjuvant. Surgically, the surgeon must ensure that with the help of a burr, all the ridges within the cavity have been taken care of and the wall of the tumor cavity has been thoroughly curetted. What additional chemical/thermal adjuvant is to be used is still debatable. Various adjuvant options available are:

- Bone cement
- Liquid nitrogen / Cryotherapy/Argon laser
- Phenol, ethanol, sterile water
- Hydrogen peroxide
- Chemotherapy
- Embolization
- Bisphosphonates
- Immunomodulators

Curettage alone results in high rate of local recurrence. On the other hand, curettage and adjuvant cryosurgery followed by bone cement or bone grafts give low rate of local recurrence.²

Prosser GH, Baloch KG3 et al retrospectively reviewed 193 patients of GCT treated during period of 27 years. 137 pts. had curettage as primary treatment of which 26 pts. (19%) had local recurrence. The local recurrence rate of giant-cell tumors confined to bone (Campanacci Grades I and II) was only 7% compared with 29% in tumors with extraosseous extension (Campanacci Grade III). They recommended that the primary curettage for intraosseous giant-cell tumors without adjuvant treatment or filling agents, but tumors with soft tissue extension or with local recurrence require more aggressive treatment.

Cryosurgery

Cryosurgery is recommended as a physical adjuvant to curettage in the treatment of giant cell tumor of bone. It extends the margin of a simple curettage or resection curettage and makes it biologically equivalent to that of a wide resection. Compared with other techniques, cryosurgery with composite fixation not only preserves joint function but also significantly decreases the rate of local tumor recurrence. From retrospective studies, adjuvant liquid nitrogen, or cryosurgery, has been reported to provide the highest cure rate. Its use has not gained popularity, because of cost, elaborate setup required and difficulty in handling this product.

Phenol acts by causing chemical necrosis of residual tumour cells. Most studies examining its use fail to demonstrate a significant reduction in local recurrence. Phenol should be used along with other adjuvants like cementation or cryotherapy.

Hydrogen peroxide has been demonstrated to be toxic in vitro to GCT cells.³ Hydrogen peroxide is used clinically as a chemical adjuvant for removal of residual tumor cells, presumably by effervescent cleansing with minimal damage to surrounding soft tissue and bone cells.

Certain drugs in addition to chemical adjuvants, drugs which have specific activity at the molecular level have been shown to have anti-GCT activities. These molecular drugs include Denosumab and bisphosphonates. Intrallesional bisphosphonate therapy⁴- Zolendronate, and to a lesser extent pamidronate, have been demonstrated to cause apoptosis of giant cells in vitro.

RANKL (Receptor Activator of Nuclear factor Kappa B), an essential molecule for osteoclast differentiation in bone metabolism, was found to be highly expressed in the cells of GCT. The possible involvement of RANKL10 in the pathogenesis of GCT have been established in recent studies. This led to the idea of using RANKL-targeting drugs, such as Denosumab, to combat against this bone tumor.

Dilemmas in unresectable GCT's

Unresectable GCTs (e.g., certain sacral and pelvic tumors) can be managed with transcatheter embolization of their blood supply. Embolization is performed at monthly intervals until significant pain palliation is achieved. Subsequent embolizations are performed when there is symptomatic or radiographic relapse of the tumor.
External beam radiation has been utilized in situations where patients had inaccessible sites, multiple recurrences, where complete surgical resection would detrimentally affect the patient’s function, or where complete tumour removal is not possible, such as in the sacrum or spine. In these difficult cases, which are likely pre-selected to have a higher local recurrence rate, low dose external beam radiation results in local control comparable to most other series of extremity lesions.

The curettage and cementation technique is usual practice in GCT treatment. The cement mechanical and cytotoxic properties as well as its innocuity and ease of handling make curettage and cementation one of the top-ranking GCT treatment options. It is simple and reproducible with lower rate of recurrence and dual benefit of excellent mechanical and functional qualities. The diagnosis of recurrence can be made earlier.

Campanacci Grade III GCT - management of grade III GCT is still controversial. Options include-

- Extented curettage- but it has high recurrence rate
- Excision- excision is the treatment of choice in grade III GCT but another debatable issue following excision is Arthrodesis or reconstruction by Megaprosthesi

Cartilage repair: newer horizons

Authors: Prof Mandeep S Dhillon, Dr Siddhartha Sharma.

Introduction

The articular cartilage is unique; it can withstand endless cycles of loading without incurring damage, yet it does not have the potential to repair after even a minor degree of trauma. This fact was noted by Hunter in 1743 who stated that “Ulcerated cartilage is a troublesome thing, once destroyed is not repaired.” Damage to the articular cartilage ultimately leads to joint damage and degenerative arthritis.

References

**Structure and function of articular cartilage**

The articular cartilage serves to act as a cushion and helps in even dissipation of forces. Articular cartilage is hyaline cartilage. Its acellular elements are water, collagen, predominantly Type II and lesser amounts of proteoglycans, matrix proteins and lipids. The predominant cells are the chondrocytes. It is avascular, aneural and alymphatic and is believed to derive its nutrition from the synovial fluid, synovium or the underlying bone.

That cells involved in tissue repair cannot migrate to the injured site to initiate repair. Furthermore cartilage also lacks undifferentiated cells that can initiate and participate in repair.

If the cartilage defect is superficial to the tidemark (the region between the calcified and the uncalcified cartilage), a healing response is not elicited. Chondrocytes near the defect proliferate and may even secrete new matrix, but do not migrate towards and heal the defect. This is attributable to the lack of hemorrhage and the ensuing inflammatory response.

Deep defects penetrate past the tidemark into the subchondral bone and elicit a healing response. The undifferentiated mesenchymal stem cells in the subchondral bone differentiate and proliferate into fibrocartilage, whose mechanical properties are quite different and which is not as durable as hyaline cartilage.

**Natural history of cartilage damage**

Why does the articular cartilage have such a poor healing potential? The reasons are manifold and somewhat poorly understood. Perhaps the most important reason is the lack of vascularity which means...
Advances in understanding of cartilage repair mechanisms

Several studies have added to our understanding of cartilage formation and may pave the way for successful cartilage repair techniques in future. Chondrocytes, the cells of the articular cartilage, are derived from mesenchymal stem cells (MSCs). Several growth factors that may regulate and promote differentiation of MSCs into chondrocytes have been identified. Chondrogenic differentiation in vitro is promoted by upregulation and production of type II collagen and aggregans, both of which are articular cartilage specific matrix components [loken]. TGF β1 and 2 have shown to be potent in vitro stimulants of MSC differentiation into chondrocytes. Other factors that may promote cartilage differentiation include bone morphogenic proteins (BMP), fibroblastic growth factors (FGF) 2 and 18, insulin like growth factor (IGF) 1 and signalling molecules of the Wnt family.

Cartilage repair techniques

Kim et al have classified cartilage repair techniques into 3 broad categories viz., endogenous stem cell therapy, exogenous cell therapy and osteochondral grafts and we will look at them one by one.

1. Endogenous stem cell therapy techniques

These techniques rely on the body's own stem cells to differentiate, proliferate and repair the defect. This may be achieved by bone drilling, abrasion arthroplasty or microfracture. The basic principle behind all these techniques is the same; a blood clot filled rich in mesenchymal stem cells is induced at the defect site with the hope the MSCs would form fibrocartilage. Such techniques work best for low demand patients with defects > 2 – 2.5 cm.

Perhaps the most widely used of these techniques is the microfracture which involves making multiple small holes through the defect into the subchondral bone. This results in formation of a blood clot at the defect site within hours, which is invaded by MSCs within days. Chondryocytic differentiation and formation of hyaline cartilage like tissue is seen at around 3 weeks, however at 36-48 weeks, this hyaline tissue gets replaced by fibrocartilage, for reasons unknown as yet.

The histological changes also correlate well with the clinical outcomes; most patients experience short term improvement but the results deteriorate at 24 months.

Some recent advances to improve the microfracture technology are as follows:

a. Increasing the number of MSCs at the defect site: Research has shown that the number of MSCs increase with the use of wider bore needle (17gauge versus 22gauge), increasing the depth of the holes (6mm vs 2mm) and maximizing the number of drill holes. It is thought that the key to improving the number of MSCs is to create as many holes in the defect so as to expose the subchondral bone, without fracturing the subchondral bone itself.

b. Addition of growth factors: Growth factors that promote chondrogenesis and chondrocyte proliferation are also being used. Of note are perforated decalcified cortical bone matrix (DBCM), TGF β, IGF, BMP-7 and FGF.

c. Clot stabilization techniques: some researchers believe that addition of natural or synthetic biomaterials, that act as scaffolds, to the blood clot help to provide an improved milieu for cartilage regeneration, although the how such materials
exactly help is still unclear. Natural scaffolds include hyaluronic acid (HA) and chitosan glycerol based scaffolds. Polyglycolic acid (PGA) and Poly-l-lactic acid (PLLA) are two synthetic biomaterials that have been tried in sheep models. Most of this research is based on animal models and only a few Phase I clinical trials have looked into their use.

d. Biomembranes: it is postulated that biomembranes may delay clot degradation and improve overall results. Porcine collagen I and III matrices and extracellular matrices made from porcine chondrocytes have been used as biomembranes.

2. Exogenous cell therapies. Exogenous cell therapies rely on cells cultured in vitro and then implanted into the defect site. Implanted cells could be the patient's own (autologous) chondrocytes or mesenchymal stem cells.

a. Autologous chondrocyte implantation (ACI)

Chondrocytes harvested from the patient's own cartilage (autologous) chondrocytes have been extensively studied and the ACI technique has evolved over the years. Common to all ACI techniques is the harvest of chondrocytes from the non weight bearing portion of the femoral condyle, invitro culture and subsequent implantation into the cartilage defect [Campbell].

First generation ACI techniques used implantation of chondrocytes as a gel directly into the defect site and coverage by a periosteal flap. However, this was associated with graft hypertrophy in about 18% of the cases, which may be attributable to the use of chondrocytes in liquid form.

Second generation ACI techniques use absorbable collagen matrices in place of a periosteal flap. This is also known as 'matrix' assisted ACI or MACI technique.

Third generation ACI techniques use chondrocytes incorporated into a type I or III collagen matrix often along with fibrin glue.

ACI techniques can be used to repair defects 3.5 – 10 cm in size. The advantages of ACI are low donor site complications and the ability to repair large defects. However, the two stage nature of the procedure is both cumbersome and costly, graft hypertrophy may occur (mainly with first generation ACI techniques) and graft delamination and underfilling of the defect has also been reported [kim]. Also, prolonged immobilization and strict adherence to weight bearing protocols is necessary to ensure good outcomes.

b. Implantation mesenchymal stem cells

Implanted chondrocytes tend to degenerate and sometimes dedifferentiate into fibroblasts and this may partly explain some of the failures seen with ACI. In an effort to overcome these problems, recent research has focussed on implanting mesenchymal stem cells into the defect. Such MSCs may be derived from the bone marrow, adipocytes or umbilical cord blood. Although quite promising, MSC implantation is an evolving technique which needs to be studied extensively before routine use can be recommended. Some of the disadvantages include donor site morbidity (in case of bone marrow and adipocyte MSC harvesting) and inconsistent harvesting in case of umbilical cord MSCs.
3. Osteochondral grafts

Osteochondral grafts are small plugs of bone and cartilage that may be used as fillers. Such grafts may be obtained from the patient (autografts) or from cadavers (allografts).

a) Autologous osteochondral transplantation (OATS) or Mosaicplasty

The OATS procedure may be used to fill up defects up to 2 cm in size. Autografts are obtained from the peripheral, non weight bearing part of the femoral condyle. The defect is debrided to match the harvested grafts and the grafts are placed in the defect without any fixation. The cited advantages include one stage nature of the operative procedure, transplantation of viable hyaline cartilage and shorter rehabilitation times. The disadvantages, however, include donor site morbidity, limited area available for harvest and graft subsidence that may occur with progressive weight bearing.

b) Allogenic osteochondral transplantation

Fresh osteochondral allografts are taken from cadaveric donors. A size matched hemicondyle is used to harvest the allograft, which is placed at the defect site after debridement. Chondrocyte viability of upto 80% after 4 weeks has been reported with this procedure. The advantages of this procedure are the ability to cover larger defects (2-3.5cm), single stage nature of the procedure and no donor site morbidity. However, owing to the fact that only fresh allografts may be used, the patient has to be available 'on call' when a suitable donor becomes available. Also, there is at least a theoretical risk of infectious disease transmission.

Future directions

Most of the research on cartilage repair is relatively new and confined to the past four decades. However, researchers are focussing on almost all aspects of cartilage repair and how to make them better. From improving the MSC yield after microfracture to decreasing the cell loss and graft hypertrophy after ACI, use of MSCs instead of chondrocytes and tissue engineering techniques to generate cartilage rather than using osteochondral grafts, the future holds tremendous promise.

Recommended Further Reading


Rational antibiotic therapy

Authors: Dr Alok C Agrawal.

Orthopaedic surgery with its recent advancements relies largely on the availability of modern antibiotics. Joint replacements now are considered not only in absolute infection free indications but the indications in post infective cases which started initially from 10 infection free years, then 5 infection free years, then 2 infection free years then 6 months of infection free period and now they are being considered for only a negative CRP and normal ESR. Antimicrobials are considered as the greatest discovery of the twentieth century. In the pre-antibiotic era, infectious diseases accounted for significant morbidity and mortality and invasive medical procedures were fraught with the risk of infection. All this changed with the use of antimicrobial agents. But the miracle seems to be short lived. Irresponsible and erratic use of these life-saving instruments has resulted in the development of drug resistance in many organisms and deaths due to resistant infections is slowly increasing; in the U.S., mortality due to nosocomial infections is now 4 times that due to road traffic accidents. The question is as to why do doctors over-prescribe antibiotics?

1. Is it lack of confidence: While it is very easy to scribble a prescription, it takes a fair amount of courage to avoid unnecessary prescriptions. Inability to make a fairly accurate clinical diagnosis is one of the most common causes for over-drugging. Inability to convince the patient about the nature and simplicity of the illness and about the non-requirement of antibacterials is another reason. Some doctors may harbour a notion that it is better to give "something powerful" for every patient so as to achieve "dramatic" results (Shot Gun therapy). But the fact remains that most patients do not demand any particular prescription from their doctor and many are indeed happy if they are explained about their problem and prescribed as less drugs as possible. Fear of law-suits for 'negligence' ('act of omission') and hence 'defensive' practice may also be another reason.
2. Peer pressure: Some doctors may have a fear that if they do not prescribe, their 'next door' colleague may prescribe these 'powerful' drugs and get all the credit for 'curing' the patient. To avoid this 'loss of practice' they tend to prescribe these 'powerful' remedies. This is another face of 'defensive' practice.

3. Patient pressure: Rarely, however, one may come across patients, some of them with half-knowledge, who insist on a prescription for antibacterials so as to "get better at the earliest" (because they are "very busy and have no time to lie down in bed") or to "avoid any hassles", particularly in cases of children and the elderly. Although in such situations it is the duty of the doctor to resist any such pressures, some doctors may yield to these pressures, often to appease the patients and to 'save' their practice.

4. Company pressure: With hundreds of pharmaceutical companies and thousands of medical representatives, it is natural to come under some pressure for prescribing these drugs, which earn handsome profits for the drug industry. ("Volume building products, Sir", the representative would tell us). With competition hotting up, the companies seem to mislead the doctors about the indications, suppress the facts on adverse effects and hide the facts on cost of therapy. Recently there is a dangerous trend of 'combining' antibacterials and marketing them for imaginary diseases. Many of the so called 'newer' antibiotics (which are in fact nothing more than modifications of existing molecules) are priced exorbitantly (even hundred times more than their older congeners) without offering any benefits over the older, time tested drugs. But it has become rather fashionable to prescribe these drugs, with many doctors feeling that 'costlier must be better'.

Rational Use of Antibiotics

Antibiotics are the most important weapons in our hands. Each one of them have been invented after spending considerable amount of time, energy and money. Therefore, we cannot afford to lose them. We must exercise considerable restraint in prescribing antibacterials and restrict the use of antibacterials to only certain definite indications.

Indications for antibacterial therapy:

1. Definitive therapy: This is for proven bacterial infections. Antibiotics (read antibacterials) are drugs to tackle bacteria and hence should be restricted for the treatment of bacterial infections only.

2. Empirical therapy: Empirical antibacterial therapy should be restricted to critical cases, when time is inadequate for identification and isolation of the bacteria and reasonably strong doubt of bacterial infection exists: septicemic shock/ sepsis syndrome, immunocompromised patients with severe systemic infection, hectic temperature, neutrophilic leukocytosis, raised ESR etc. In such situations, drugs that cover the most probable infective agent/s should be used.

3. Prophylactic therapy: Antimicrobial prophylaxis is administered in orthopaedic patients with implant surgery or Joint replacements and the drug of choice remains first generation cephalosporin Cefazolin 1 gm ideally 30 minutes prior to the incision. The dose may be repeated 8 hourly but never beyond 24 hours.

Some of the factors to be considered prior to starting antibiotics are as follows:

Type of infection: Infections can be localised or extensive; mild or severe; superficial or deep seated; acute, sub acute or chronic and extracellular or intracellular. For extensive, severe, deep seated, chronic and intracellular infections, higher and more frequent dose, longer duration of therapy, combinations, lipophilic drugs may have to be used.

Culture and antibiotic Sensitivity: Ideal management of any significant bacterial infection requires culture and sensitivity study of the specimen. If the situation permits, antibacterials can be started only after the
sensitivity report is available. Narrow spectrum, least toxic, easy to administer and cheapest of the effective drugs should be chosen. If the patient is responding to the drug that has already been started, it should not be changed even if the in vitro report suggests otherwise.

**Source of infection:** Community acquired infections are less likely to be resistant whereas hospital acquired infections are likely to be resistant and more difficult to treat (e.g. Pseudomonas, MRSA etc.).

**Host factors:** Age of the patient, immune status, pregnancy and lactation, associated conditions like renal failure, hepatic failure, epilepsy etc. should be considered in choosing the antibacterial agent.

**Age:**

- **Infants:** Chloramphenicol (Can cause grey baby syndrome) and sulfa (Can cause kernicterus) are contraindicated.
- **Below the age of 8 years:** Tetracyclines are contraindicated because they are known to discolor the teeth.
- **Below the age of 18 years:** All fluoroquinolones are contraindicated because they are known to cause arthropathy by damaging the growing cartilage.
- **Elderly:** In the Elderly, achlorhydria may affect absorption of antibacterial agents. Drug elimination is slower, requiring dose adjustments. Ototoxicity of aminoglycosides may be increased in the aged.

**Compromised immune status:**

In patients with extremes of age, HIV infection, diabetes mellitus, neutropenia, splenectomy, using corticosteroids or immunosuppressants, patients with cancers / blood dyscrasias, Only bactericidal drugs should be used. And it is indeed debatable whether antibacterials should be used to treat infections like aspiration pneumonia, UTI, catheter infections, infections through life support systems, pressure sores etc. in patients who are terminally ill (brain dead, patients with massive stroke, terminal cancers, advanced age, terminal AIDS etc.).

**Pregnancy:** Drugs with known toxicity or un-established safety like tetracyclines, quinolones, streptomycin, erythromycin estolate and clarithromycin are contraindicated in all trimesters and sulfa, nitrofurantoin and chloramphenicol are contraindicated in the last trimester. Drugs with limited data on safety like aminoglycosides, azithromycin, clindamycin, vancomycin, metronidazole, trimethoprim, rifampicin and pyrazinamide should be used with caution when benefits outweigh the risks. Penicillins, cephalosporins, INH and ethambutol are safe in pregnancy. In lactating mothers sulfa, tetracyclines, metronidazole, nitrofurantoin and quinolones are contraindicated.

**Renal failure:** Tetracyclines are absolutely contraindicated; aminoglycosides, cephalosporins, fluoroquinolones and sulfa are relatively contraindicated; and penicillins, macrolides, vancomycin, metronidazole, INH, ethambutol and rifampicin are relatively safe. It is better to avoid combinations of cephalosporins and aminoglycosides in these patients because both these classes of drugs can cause nephrotoxicity.

**Hepatic failure:** No drugs are absolutely contraindicated; chloramphenicol, erythromycin estolate, fluoroquinolones, pyrazinamide, rifampicin, INH and metronidazole are relatively contraindicated and penicillins, cephalosporins, ethambutol and aminoglycosides are safe.

**Drug Factors**

1. **Hypersensitivity:** If the patient has prior history of hypersensitivity the concerned antibacterial agent should be avoided. It is therefore important to elicit this history in all patients.

2. **Adverse reactions:** Certain adverse reactions warrant discontinuation of therapy and the doctor should adequately educate the patients on these adverse effects.

3. **Interactions:** Interactions with food and other
concomitant drugs should be considered before instituting antibacterial therapy so as to maximize efficacy and minimize toxicity.

4. Cost: Lastly, but not the least, the cost of therapy should be considered in choosing the antibacterial agent and in a developing country like India with limited spending on healthcare, this does assume significance. It should always be remembered that just because a particular drug is expensive, it need not be superior to the cheaper ones. For example, cheaper drugs like doxycycline or co-trimoxazole would be as effective as the costlier clarithromycin or cephalosporin in the management of LRTI

**Combinations:** Judicious and intelligent combination of different antibiotics can be very useful in treating certain difficult infections and in preventing or overpowering resistance. On the other hand irrational and unnecessary combinations can add to the cost and adverse effects and help in the development of drug resistance.

Antibacterial combinations can be useful in the following situations:

1. To sharpen the effect: Synergistic combination of two static drugs - e.g. Combination of Trimethoprim and Sulfamethoxazole - Co-Trimoxazole
2. Treatment of infections with multiple organisms: Mixed infections in lung abscess, peritonitis, soiled wounds etc., naturally require multiple antibiotics for complete clearance of the infection - *Penicillins* (for gram positive and certain anaerobes) + *Aminoglycosides* (for gram negative); metronidazole for bacteroides etc.
3. To prevent resistance: Use of combinations is a well known method of preventing drug resistance. The classic example is the antitubercular therapy.
4. To overcome resistance: Combination of specific drugs can be useful in overcoming the resistant infections. Examples include *Penicillins + β-lactamase inhibitors*/β-lactamase resistant penicillins for *S. aureus*; *Penicillins/cephalosporins + aminoglycosides* for *Pseudomonas* etc.

The following combinations are irrational, not useful or even harmful:

1. Combinations of bactericidal with bacteriostatic drugs (e.g. *Penicillins* with tetracyclines);
2. Combinations of drugs with similar toxicity (e.g. chloramphenicol and sulfa)
3. Combining drugs for non-existing 'mixed infections' (e.g. tablets of ciprofloxacin + metronidazole/tinidazole).

Response to treatment: It depends on the nature and sensitivity of the agent, specificity of the drug, bioavailability and dosage. Longer the doubling time of the organism, longer the time it takes to respond. Thus a Streptococcal pneumonia can respond within 24 -48 hours, but tuberculosis may take 2-8 weeks to respond. One should have the patience to wait for the adequate period before changing the drug (e.g. *S. pneumoniae* infections - 24-48 hours; *E. coli* - 24-48 hours; *S. typhi* - 4-7 days; *M. tuberculosis* - 2-8 weeks etc.). Drugs should be changed midway only when there is absolutely no response or there is no expected response and the sensitivity report also suggests resistance.

**Resistance to Antimicrobial Agents**

Resistance to antimicrobial agents is one of the greatest problems faced by the medical community. These powerful weapons, developed by spending millions of dollars and years of dedicated research, have been rendered less effective or totally ineffective only because of our own negligence and complacency. This is indeed frustrating. The following table provides an overview of some of the recent examples of resistance to antimicrobials:
Resistance may be acquired by mutation and passed onto the next generations. It may also be acquired by horizontal transfer from a donor cell by transformation, transduction or conjugation.

Control of use of antimicrobial agents: The following methods can be used to control the use of antimicrobial agents in hospitals: Education programmes like staff conferences, lectures and audiovisual programmes; availability of clinical pharmacist consultants; control of contact between pharmaceutical representatives and staff physicians and of various sponsorships from companies; restriction of hospital formulary to minimum number of agents needed for most effective therapy; availability of diagnostic microbiology laboratory sensitivity tests and appropriate selection of sensitivity tests for organism and site; automatic stop orders for specific high-cost agents and written justification for high-cost agents etc.

In the current Orthopaedic Practice several routes of antibiotic treatment exist. Oral antibiotics are still the most commonly used. Intravenous application may be required for more serious infections that do not respond to oral antibiotics. Local delivery of antibiotics also can be beneficial. Polymethyl methacrylate (PMMA) beads impregnated with heat-stable antibiotics (tobramycin, vancomycin, and gentamicin) have been used since the early 1970s. A 2- to 3-cm area around each bead has a high concentration of antibiotic. With tobramycin and vancomycin, the peak concentration of antibiotic delivered to local tissue occurs on the first day and lasts for only approximately 1 week. This local delivery system avoids systemic toxicity; however, it requires removal (usually surgical) within 4 weeks. A more attractive biodegradable system is the collagen-gentamicin sponge, which obviates the need for surgical removal and delivers higher concentrations of antibiotics than PMMA beads. It has been suggested that antibiotic release by this method may be complete within 4 days. Lactic acid polymerase may be the next step in local biodegradable antibiotic delivery systems. This system

<table>
<thead>
<tr>
<th>Organism</th>
<th>Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram Positive coci</td>
<td>Methicillin resistant Staph. aureus and coagulase negative <em>Staphylococci</em>, penicillin resistant <em>Pneumococci</em>, macrolide resistant <em>Streptococci</em>, vancomycin resistant <em>Enterococci</em>.</td>
</tr>
<tr>
<td>Gram negative coci</td>
<td>Penicillin, quinolone resistant <em>gonococci</em>.</td>
</tr>
<tr>
<td>Gram negative bacilli</td>
<td>Enterobacteriaceae resistant to B lactams and B lactamase inhibitors, multi drug resistant pathogens include <em>Shigella, E. Coli, Salmonella</em>.</td>
</tr>
<tr>
<td>Acid fast bacilli</td>
<td>Multi drug resistant <em>M. tuberculosis</em>.</td>
</tr>
</tbody>
</table>

Factors contributing to antimicrobial resistance:

Antimicrobial resistance, initially a problem in hospitals and developing countries, today affects the world at large. The reasons for resistance are many. The WHO reports that the antimicrobial agents are used by too many people to treat the wrong kind of infection in the wrong dosage and for the wrong period of time in both industrialized and developing countries. Increase in poverty, overcrowded living areas, crowded day care centers have all contributed in spreading the resistant bacterial infection. The tremendous increase in the size of the high risk populations because of immune-compromise, the increased frequency of invasive medical interventions and prolonged survival of patients with chronic debilitating disease have amplified the problem.

Resistance to antimicrobial agents can be due to various mechanisms:

1. Inability of the drug to reach the organisms
2. Inactivation of the drug
3. Alteration in the target
delivers a high concentration of quinolines (bactericidals for probable pathogens of chronic osteomyelitis) for 60 days, with a peak release of antibiotics at day 15. An additional method of local antibiotic delivery is that of mixing autogenous iliac crest bone graft with piperacillin or vancomycin. Antibiotics must be chosen carefully. For example, heat-stable antibiotics are required for PMMA applications; quinolones have shown detrimental effects on chondrocytes and fracture healing; and tobramycin at intermediate levels of concentration (400 µg/mL) can decrease cell replication. In general, vancomycin is less toxic to osteoblasts at high local concentrations than other aminoglycosides and rifampin and the quinolones should not be administered when bone regeneration is an issue. An infectious disease consult can help guide the appropriate antibiotic in each patient and can be especially useful with the ever-changing microbial picture. Even though many surgical techniques have been described for the treatment of osteomyelitis, prevention is still the best course, and adherence to the basic principles of treatment of infections helps achieve success.

**Acute Septic Arthritis:**

**Empirical Antimicrobial Therapy**

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Empirical Antimicrobial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram-positive cocci in clusters with MRSA risk factor or β-lactam allergy</td>
<td>Vancomycin 15 mg/kg IV q12h</td>
</tr>
<tr>
<td>Gram-positive cocci in clusters, no MRSA risk factors</td>
<td>Nafcillin or oxacillin 2 g IV q4h</td>
</tr>
<tr>
<td>Gram-positive cocci, no MRSA risk factors</td>
<td>Cefazolin 2 g IV q8h</td>
</tr>
<tr>
<td>Gram-positive cocci in chains (streptococci presumed)</td>
<td>Penicillin G 12-18 MU/d or ampicillin 2 g IV q4h</td>
</tr>
<tr>
<td>Gram-negative cocci (presumptive Neisseria)</td>
<td>Ceftriaxone 1-2 g IV/IM q12-24h or cefotaxime 2 g IV q8h</td>
</tr>
<tr>
<td>Gram-negative rods</td>
<td>Ceftazidime 2 g IV q 8 hr or cefepime 2 g IV q 8 hr</td>
</tr>
<tr>
<td>Negative Gram stain, previously healthy, no MRSA risk factors</td>
<td>Cefazolin 2 g IV q8h</td>
</tr>
<tr>
<td>Negative Gram stain, health-care associated or other MRSA risk factors</td>
<td>Vancomycin 15 mg/kg IV q12h plus ceftazidime 2 g IV q8h, cefepime 2 g IV q8h or piperacillin/tazobactam 4.5 g IV q6h</td>
</tr>
<tr>
<td>Human, dog, or cat bite</td>
<td>Ampicillin sulbactam 1.5-3 g IV q4h</td>
</tr>
</tbody>
</table>

Data from Nuermberger E: Septic arthritis community acquired. Available at http://hopkins-abxguide.org

Risk factors for methicillin-resistant Staphylococcus aureus: recent hospitalization or nursing home admission, hemodialysis, diabetes, intravenous drug use, recent antibiotic exposure, recent incarceration, recent skin or soft tissue infection in patient or close contact. Community-acquired MRSA often occurs without preexisting risk factors.
<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Antimicrobial Antimicrobial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus (methicillin sensitive)</td>
<td>Nafcillin or oxacillin 2 g IV q4h × 3 wk</td>
</tr>
<tr>
<td></td>
<td>Cefazolin 2 g IV q8h × 3 wk</td>
</tr>
<tr>
<td>Staphylococcus aureus (methicillin resistant or type I penicillin allergy)</td>
<td>Vancomycin 15 mg/kg IV q12h × 3 wk</td>
</tr>
<tr>
<td>Streptococcus including penicillin-sensitive</td>
<td></td>
</tr>
<tr>
<td>S. pneumoniae [MIC &lt; 4 mg/L]</td>
<td>Penicillin G 12-18 MU IV qd divided dose or ampicillin 2 g IV q4h × 2 wk</td>
</tr>
<tr>
<td>S. pneumoniae (penicillin-resistant)</td>
<td>Ceftriaxone 1-2 g IV q12h or cefotaxime 2 g IV q8h if susceptible, or vancomycin 15 mg/kg IV q12h × 2 wk</td>
</tr>
<tr>
<td>Enteric gram-negative bacilli</td>
<td>Ceftriaxone 1-2 g IV q12h or cefotaxime 2 g IV q8h × 3 wk</td>
</tr>
<tr>
<td>Gram-negative bacilli (Pseudomonas aeruginosa)</td>
<td>Ceftazidime 2 g IV q8h or cefepime 2 g IV q8h, plus gentamicin or tobramycin 5 mg/kg IV q24h × 3 wk</td>
</tr>
<tr>
<td>Gram-negative bacilli</td>
<td>Ciprofloxacin 400 mg IV q8-12h or 750 mg PO q12h or levofoxacin 750 mg IV or 750 mg PO qd × 3 wk</td>
</tr>
<tr>
<td>Polymicrobial</td>
<td>Ampicillin/sulbactam 1.5-3 g IV q4h × 3 wk</td>
</tr>
<tr>
<td></td>
<td>Clindamycin 600 mg IV q6-8h × 3 wk plus ciprofloxacin 400 mg IV or 750 mg PO q12h or levofoxacin 750 mg IV or 750 mg PO qd × 3 wk</td>
</tr>
<tr>
<td>Gram-positive etiology and type I penicillin allergy</td>
<td>Vancomycin 15 mg/kg IV q12h × 3 wk</td>
</tr>
</tbody>
</table>

Data from Nuernberger E: Septic arthritis community acquired. Available at http://hopkins-abxguide.org.

MIC, minimal inhibitory concentration.

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WHAT IS RESEARCH? HOW TO START?

In the broadest sense, research is defined as gathering of data, information and facts for the advancement of knowledge. Every field of study has its own research problems and methods. As a researcher you seek answers to questions of great interest to you. Medical research is research conducted to aid the body of knowledge in the field of medicine. This can be divided into two general categories: new treatments that are tested in clinical trials, and all other research contributing to the development of new treatments.

What is a research question?

The first step in conducting a research study is to pose a research question and it is undoubtedly the most important step towards a successful study. The research question should be framed in a manner that is easily understood as a poorly designed question can affect your research efforts and make it difficult for readers to interpret the results and ultimately jeopardize publication. A clear and relevant question will “determine the research architecture, strategy and methodology.” In all areas of research, asking the right question is perhaps the most important part of research. How the research problem is stated determines the trial design used, the data collected, the analyses conducted and the conclusions (i.e., interpretation) that can be drawn. The research question can relate to diagnosis, prognosis, treatment, iatrogenic harm, quality of care or health economic. Evaluate your research question based on significance and feasibility.

Once the research question is determined, it is essential that you find its relevance in your practice i.e. it should be relevant with your flow of patients and how it would benefit your patients. For example for an arthroplasty surgeon it will be very important to know what is the functional outcome and satisfaction rate in his cohort of patients and he will require designing a study to answer this essential question.

What is importance of literature review?

After formulating a research question and assessing its relevance in your current practice, the next step is to perform a complete and thorough literature search to know what is already done on the topic. This information is important

- to learn about other ongoing and completed research in your area,
- to ascertain that your hypothesis/ research topic has not been tested already by other researchers
- to build your case for funding requests

Further, you can learn from other study mistakes and limitations and try to prevent such problems in your own study. The next step is to discuss your research questions with knowledgeable peers, mentor and biostatistician.

Significance of study design

Consider the steps necessary to conduct your study for example, type and phase of the clinical trial, budget, informed consent, sites, and resource constraints of both personnel and facilities, study duration. Before you start a particular study, it is essential to know the extent of your resources so that accordingly you can work towards your goal. Now that you have posed the appropriate research question and performed a literature review and are sure of the resources at hand, you can start by writing a research protocol and decide the best suitable study design. Once the Investigator has decided upon the question, the next step involves embarking on a study design that will ensure the proper analysis of data and a higher level of evidence.

Scientific study design is the most aspect of study planning. The significance of study design for subsequent quality, the reliability of the conclusions, and the ability to publish a study are often underestimated (study design sets the end points for fulfilling the study objectives long before the volunteers
are recruited). In comparison to errors in the statistical evaluation, errors in design cannot be corrected after the study has been completed. This is why the study design must be laid down carefully before starting and specified in the study protocol.

**Different types of study design**

In general, there are two broad classifications of study designs: Analytic studies and descriptive studies. Analytic studies focus on the causes of a disease through testing the outcome of a particular exposure. Specifically, there are two types of analytic studies: Observational studies include case-control and cohort studies, whereas experimental studies include randomized controlled trials.

Descriptive studies focus on the distribution of a disease in relation to factors such as age, location, and sex. Studies that fall into this category include cross-sectional studies and case reports. It is important to distinguish between retrospective and prospective studies as well. Retrospective studies involve patient follow up after the desired outcome, whereas prospective studies involve following up on patients prior to the desired outcome. Once the study design is finalized and other requirements to conduct a study are in place, the investigator can start the study and move successfully towards completion and generation of data.

**Data collection and documentation**

The importance of collecting data is to determine the type of data and scales you are using for your observations and this will ultimately dictate the types of statistical analysis you can do to interpret your results. The statistical data can be divided into two broad categories i.e. Qualitative and Quantitative data. Qualitative data are discrete in nature such as number of deaths in different years, population of different towns, and so on. This is further categorized as nominal and ordinal data. Quantitative data describes a characteristic in terms of numerical value and comprises of two categories of data i.e. continuous and discrete data.

To ensure the accuracy of the measurements, it is necessary to plan a proper method of data collection and documentation. Forms are designed to capture the data and complete information on each subject known as Case Record Form (CRF). This is important because the analysis and reporting of trial outcome is based on the completeness and accuracy of data recorded from each patient recruited in the trial. The CRF can be paper-based or in the electronic format allowing direct data entry into the database. The CRF is designed in such a way that allows accurate input, presentation, verification, audit and inspection of the recorded data.

**Statistical analysis**

After the patients have been followed for specified period of time and data collected, the next step is analysis of data. We have Parametric and Nonparametric tests for statistical analysis of data. Parametric means that it meets certain requirements with respect to parameters of the population (for example, the data will be normal-the distribution parallels the normal or bell curve). Parametric statistics are considered more powerful than nonparametric statistics. Nonparametric data are lacking those same parameters and cannot be added, subtracted, multiplied, and divided. A nonparametric test is distribution free which means that the data are not assumed to come from any specific distributions. Now that the data collection and analysis is complete, the traditional approach to reporting a result requires you to say whether it is statistically significant by generating a $p$ value from a test statistic. A significant result indicates “$p<0.05$”

It is important to keep in mind that no statistical test can rescue the poorly conducted experiment. Utmost care needs to be taken to monitor entire conduct of the study appropriately involving right kind of professional at right time throughout the study.

**Summary**

Research is important for the advancement of knowledge. Asking the right question is the most important part as it determines the trial design used, the data collected, the analyses conducted and the conclusions (i.e., interpretation) that can be drawn. Start by writing a research protocol and decide the best
suitable study design. Scientific study design is the most important aspect of study planning and the choice of study design depends on the type of study being conducted i.e. observational or experimental study. Once the study design is in place, start by collecting the data. Forms are designed specifically for proper collection and storage of data known as Case Report Form (CRF). Data collection by these forms can be either paper based or in an electronic format. Finally, after all the data has been collected and entered into the database, the database is locked and after proper quality checks the data is analyzed statistically. Different tests are available for statistical analysis of data such as parametric and non-parametric tests. Parametric statistics are considered more powerful than nonparametric statistics. Proper analysis of data determines the statistical significance by generating a p value and a significant result is indicated by “p<0.05”.

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Author: Dr J Naresh Babu.

doi: 10.4103/0019-5413.30520
PMCID: PMC2981888
Planning a clinical research study
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In planning any research protocol, we should consider two questions: 1. Is there a real need for the trial? 2. Is the study design and methodology robust? We focus on the second issue-study validity.

A randomized controlled trial (RCT) is the most valid of
the clinical research designs. It is a prospective study where allocation to the treatment groups is random. Recently, RCTs have become widespread in the medical literature. In 1998, more than 12000 RCTs were being published each year, more than double the annual publication rate of just a decade previously. This growth can be traced to the growing acceptance of RCTs as the most reliable experimental design for investigating therapeutic interventions. Although preferred, RCTs are just one of many research designs.

While outside factors such as cost or time may influence the choice of design, the most suitable research design is dictated by the research question being asked. For example, it would be unethical to randomize patients to an exposure suspected as being harmful. A cohort study would be an appropriate and ethical design to answer such a question. Nonetheless, for questions of therapy, RCTs have moved to the top of what is known as the therapeutic hierarchy. The validity of the evidence is highest for a single, large randomized trial. Randomization limits bias and controls for unknown prognostic variables. Careful deliberation of some simple questions can help to ensure a valid, robust RCT.

WILL THE RESULTS BE VALID?

This first section of this paper deals with internal validity.

HOW WILL POTENTIAL SOURCES OF BIAS BE AVOIDED?

Bias is “a systematic tendency to produce an outcome that differs from the underlying truth”. Bias in clinical trials falls into four categories: selection bias, performance bias, detection bias and attrition bias.

Selection bias

The goal when enrolling patients is to create comparison groups that are similar with respect to all known or unknown confounding factors. This is accomplished by randomizing patients. Reviews comparing randomized with observational studies have found that a lack of randomization can lead to both underestimation and overestimation of the treatment effect. The process of randomization depends on two procedures: generation of an allocation sequence and allocation concealment.

Randomization

Fundamental to RCTs is the random allocation of patients to comparison groups. Nonrandom methods of allocation subvert the whole purpose of an RCT. Some methods are described as “pseudorandomization”. Examples include allocating patients by chart number, date of presentation or by alternating assignment. There is the risk of introducing bias into your study. As an example, in some populations the day of week on which a child is born is not a completely random event. There is also the risk of compromising allocation concealment if your allocation sequence is predictable.

While there are complex methods of generating an adequate allocation sequence, the most elegant and simple designs are underused. These include a table of random numbers or a computer-generated sequence.

Groups are more likely to be balanced as the sample size increases when using a random number generator. For example, in a sample size of 20 patients, investigators should expect that roughly 10% of the sequences generated via simple randomization would yield a ratio imbalance of three to seven or worse. Manual methods of randomization such as coin-tossing or dice are technically correct, but are less preferable since they allow the implementer to sabotage the randomization. For example, when flipping a coin, a series of heads or a series of tails may occur. An investigator may be tempted to alter the result of a coin toss in order to rectify what they perceive to be a nonrandom sequence, when in fact their actions serve to do just the opposite. Another disadvantage of these manual methods of randomization is that they leave no paper trail and so cannot be checked at a later date.
Concealment of allocation

A proper allocation concealment scheme keeps investigators and patients unaware of upcoming assignments. In an ideal world, allocation concealment would be unnecessary and patients would enter into the trials groups to which they were originally assigned. It is important to realize however, that the process of randomization often frustrates clinical inclinations. In cases of poor allocation concealment (for example, posting of the allocation sequence), knowledge of upcoming assignments could lead to the exclusion of patients the care provider felt were unsuited for a particular treatment group.

Recognize also that the forces being placed upon healthcare providers may be stronger than the forces pushing for adherence to an RCT protocol. In these cases, even good attempts at allocation concealment may be subverted, as was the case in one study where residents held envelopes up to bright light to decipher upcoming assignments to avoid hassling their attendings with the more involved treatment late at night. The importance of allocation concealment in protecting against bias has been shown in a study that showed greater heterogeneity in trials with improperly concealed allocation.

Development of a robust method of allocation concealment requires thought and effort. In addition to the demands of day-to-day medicine which frequently trump the desire to maintain good research methodology, one must also contend with human nature and the natural inclination of some to decipher the concealed allocation for curiosity’s sake alone.

When designing a trial, use of additional elements to ensure that your concealment is tamper-proof is advised [Table 6].

Performance bias and detection bias

Performance bias arises when the treatment assignment is known to patients or caregivers, and detection bias arises when outcome assessors or data analysts are similarly aware. They will be considered together since the solution for both is the same. Blinding is the process of ensuring that such parties are kept unaware of whether patients have been assigned to a treatment or a control group. Without blinding securely in place, an RCT is vulnerable to bias from a number of sources [Table 7].

The importance of blinding to preventing personal bias from clouding judgment is especially important when assessing subjective outcomes. One study has shown that nonblinded assessors were more likely to see the benefit of an intervention than blinded assessors. Blinding of certain parties may be impossible in some trials. As an example, it may not be possible to blind caregivers or outcome assessors in surgical trials. The absence of blinding does not preclude the ability to create a methodologically strong RCT. As an example, use of objective outcome measures or assessment by a third party not involved with the RCT are viable methods to avoid bias when blinding of outcome assessors is not possible. Sometimes the administration of a noneffective treatment can have a positive effect on outcomes because the patient believes it will work. This phenomenon is known as the placebo effect. Aside from helping to compensate for the placebo effect, use of a placebo in the control group is an important aspect of blinding. Patients and physicians would quickly discern allocation assignments if the treatment between comparison groups was readily observed to be different. Whenever possible, an inert, but otherwise identical placebo should be used.

Attrition bias

Throughout the course of a trial, there will be participants who deviate from the study protocol or those who drop out and refuse any further participation. This population of patients may differ in a relevant and systematic way from the patients who have adhered to the trial protocol. As an example, patients may have dropped out and become unavailable for further follow-up due to acute exacerbations of their illnesses.
Likewise, it would not be surprising if those patients who suffered the most serious side-effects were those who chose to deviate from the study protocol. For these reasons, the analysis should include all randomized patients, not just those who adhered to the treatment protocol. In addition, all patients should be analyzed according to the groups to which they were originally allocated, regardless of what treatment they actually received. This type of analysis is known as intention-to-treat and guards against the introduction of attrition bias. However, exclusion from the analysis is sometimes unpreventable. This occurs if some participants become lost to follow-up before outcomes can be recorded. In such circumstances, it is important to report explicitly the number of subjects excluded and to discuss the possibility of attrition bias in the written report. Strategies to maximize patient follow-up are presented in Table 8. Tips for avoiding bias in a clinical trial are presented in Table 9.

SAMPLE SIZE, HYPOTHESIS-TESTING AND STUDY POWER

The goal of any RCT design is to use the smallest sample size necessary to attain a prespecified level of power to detect an effect of interest. Power is just one factor to consider when determining sample size. It is not the intent of this article to show how sample size calculations are derived. The focus will instead be on the four key factors that must be considered in all sample size formulae [Table 10].

When testing a hypothesis, we risk making two types of fundamental errors [Table 11]. Type I errors occur when we conclude that the treatment had an effect, when in fact it did not. The probability of making a Type I error is known as the significance level of the test and is denoted as α. Type II errors occur when we conclude that the treatment had no effect, when in fact it did. The probability of a Type II error is denoted by β. Power is 1-β and it represents the probability of avoiding a false-negative conclusion. Typically, α is set at 0.5 and β is set at 0.20, giving rise to a power of 0.80. Stated in words, this means that we're willing to accept a 5% chance of making a false-positive conclusion and that we have an 80% chance of detecting a difference between comparison groups, if a true difference exists.

Variance and effect size have opposite effects on sample size. As the effect size increases, the necessary sample size decreases. The larger the effect size, the more easily it would be detected, so it makes sense intuitively that fewer subjects (less information) would be needed. As the variance increases, the necessary sample size increases as well. This can be illustrated by imagining a population where the variance was zero, which is to say that each member of the population was identical. In this case, the sample size could be very small and still be a good representation of the population. As the level of significance (β) and power (1-β) of the test are often set at β =0.05 and 1-β =0.80 respectively, our influence on the sample size comes from our estimations of variance and effect size. Variance will depend upon the population under investigation and the reliability of the tool being used to measure outcomes. Estimations of both variance and effect size can come from historical data and from examination of similar populations. While much subjective judgment is involved, it is important to temper optimism when making these estimations. Overestimation of effect size will result in too few subjects and an RCT that is under-powered. It may be worthwhile to undertake a pilot study to ensure that your estimations of variance and effect size are realistic. This may also be helpful in helping predict the anticipated rates of noncompliance and loss to follow-up. Again, failure to account for these factors will lead to a decrease in sample size. The resulting study would then lack the power to impact clinical practice and research in a meaningful way.

WILL THE RESULTS BE APPLICABLE?

The second half of this article deals with the issues of
applicability and clinical utility. A study is said to have good external validity if its results will generalize to the larger population.

Has sufficient account been taken within the study design of the issues of generalizability and representativeness?

The trial setting is often a source of concern regarding generalizability. Physicians in primary care often wrestle with the applicability of RCT results obtained in tertiary and secondary centers.26 Often, primary care patients suffer numerous comorbidities that would have been exclusion criteria in the very studies that examine the efficacy of the therapies relevant to them.27

The differences between countries with regards to their demographics and healthcare systems can also affect external validity. Racial differences can affect the natural history or susceptibility to a disease.28 Regional differences in the diagnosis and treatment of the same disease may be strikingly different. This can lead to differences in the use of adjuvant, nontrial treatments. For example, in an international RCT of aspirin and heparin for acute ischemic stroke, glycerol was used in 50% of the 1473 patients in Italy versus 3% elsewhere.29 In addition to adjuvant therapies, consideration should also be given to the generalizability of the entire treatment protocol. In order to have broad applicability, the RCT protocol should diagnose and manage patients pretrial and posttrial in a manner that mirrors actual clinical practice.30

Is the trial population reflective of the target population so that the results will have meaning?

To maintain external validity, it is important that the sample population be representative of the whole. For many reasons, this may not be the case. To begin with, recruiting for trials is often undertaken by specialists in tertiary care centers. From the outset, this group of patients will differ from those patients being managed in the community by primary care physicians. Often, this threat to validity can never fully be eliminated since a certain proportion of the population never presents at a location or time that is conducive to entry into a trial. However, attempts to rectify it can be made by sampling before other selection pressures impose themselves. A trial’s eligibility criteria are then applied to arrive at an even more selective group. Attempts to remove confounding factors and diagnoses can lead to stringent eligibility criteria and very high exclusion rates. An average exclusion rate of 73% was found in a review of 41 US National Institutes of Health RCTs.31 Strict eligibility criteria create a sample that is again less representative of the population, which limits external validity. This is compounded by the fact that participating clinicians may apply additional selection criteria beyond that of the eligibility criteria. While usually done with altruistic intentions (clinicians seek to enroll those they feel will do well in the trial.), this practice further deteriorates the representativeness of the sample population.

Have the outcome measures been well chosen and adequately defined?

As noted previously in this paper, we typically accept a 5% probability of obtaining a false-positive when testing a hypothesis. For this reason, it is important to limit the number of investigated outcomes. The more the outcomes evaluated, the greater the chance of obtaining a false-positive result.

The applicability of an RCT depends on the clinical relevance of the measured outcomes. There has been a shift towards the use of simple, clinically relevant outcomes and away from surrogate outcomes.32 Surrogate outcomes are often misleading. Observational studies may show correlation between a surrogate outcome and a relevant clinical outcome and a treatment may show a positive effect on that same surrogate outcome, yet the treatment may still be ineffective harmful. Antiarrhythmic drugs used to be prescribed for postmyocardial infarction to reduce ECG abnormalities (the surrogate outcome). This ceased becoming the standard of care when RCTs showed increased mortality (clinically relevant outcome) due to this treatment.33
The use of inappropriate scales or composite scores is also harmful to external validity. Unvalidated scales have been found to be more likely to show significant treatment effects than validated scales. In addition, the clinical relevance of an apparent treatment effect (i.e. a 5-point mean reduction on a 50-point outcome scale made up of various signs and symptoms) is impossible to determine.

Trials can gain statistical power by combining multiple outcomes to form a composite outcome. Unfortunately, composite outcomes can hurt the applicability of an RCT result. The treatment may affect each individual outcome in different ways. The results of an RCT reporting a composite outcome may not be applicable to a patient who is particularly predisposed to developing one of the specific outcomes. Another danger is when outcomes of varying severities are combined. Less serious outcomes often occur more frequently. In this case, the least clinically significant outcome would have an inordinate impact on treatment effects.

Careful consideration should also be given to the patient and disease process. Patients typically prioritize quality of life issues more than clinicians, who tend to focus on the physical aspects of a disease. Since the final goal is to uncover therapies that improve things for patients, it makes sense to adopt patient-centered outcomes.

The RCTs investigating chronic diseases have often suffered from inadequate duration of follow-up. Clinicians treat these patients over months and years and the results of a RCT with follow-up measured in weeks are of limited applicability.

**SUMMARY**

RCTs provide the most reliable data when investigating questions of therapy. For this reason, they play a central role in helping clinicians make evidence-based decisions. However, it requires much planning and thought to design a robust RCT that possesses good internal and external validity. Care should be taken to use proper methodology to avoid bias. An adequate sample size should be obtained so as to avoid an underpowered study. Efforts should be made to make the sample as representative of the population as possible. Simple, clinically relevant outcomes should be used.

Even the perfectly designed and executed RCT would be useless if those reading the report are not aware of its quality. Issues of quality of reporting are intertwined with issues of methodological quality. The use of quality of reporting as an indicator of methodological rigor is problematic because the two do not always correlate. A well-conducted but poorly reported study may not receive proper credit, while a biased but well reported study may wield undue influence. Guidelines on the reporting of clinical trials have been developed to combat this problem. As a final point, this author would also like to encourage investigators to think longitudinally. Try and stay one step ahead of your participants and anticipate any problems or concerns that may arise [Table 12]. The process of conceiving, developing and organizing an RCT can be long and arduous, but if done properly, can serve to advance clinical medicine.

**Footnotes**

Disclaimer: Dr. Bhandari is supported, in part, by a Canada Research Chair, McMaster University.

No funds were received in preparation of this manuscript.

Simon Chan was supported, in part, by a scholarship from the Canadian Institutes of Health Research.

Source of Support: Nil