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# Overview about Current Acetabulum Fracture Management

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**Abstract:** Current acetabulum fracture management represents a complex interplay of surgical and non-surgical approaches tailored to the unique characteristics of each injury. The initial assessment hinges on a thorough clinical examination, complemented by advanced imaging techniques such as CT scans, enabling precise fracture classification according to established systems like the Judet and Letournel classification. This detailed assessment guides treatment strategy, considering factors such as fracture displacement, patient age, comorbidities, and functional demands. Non-operative management, primarily indicated for minimally displaced fractures in select patients, often involves strict weight-bearing restrictions and rigorous physical therapy. However, the majority of acetabulum fractures require surgical intervention to achieve anatomical reduction and stable fixation. Surgical techniques have evolved significantly, with a shift towards minimally invasive approaches whenever feasible. These include open reduction and internal fixation (ORIF) using a variety of implants, including screws, plates, and cannulated screws, chosen based on fracture morphology and location. The aim is to restore articular congruity and joint stability while minimizing iatrogenic damage. Recent advancements include the increasing use of computer-assisted navigation and 3D-printed implants, enhancing precision and potentially reducing surgical time and complications. Post-operative management focuses on early mobilization and targeted rehabilitation programs, crucial for optimizing functional outcomes. Challenges remain in managing complex, highly comminuted fractures, and achieving optimal long-term results necessitates meticulous surgical planning, precise execution, and diligent post-operative care. Ongoing research focuses on refining surgical techniques, improving implant designs, and developing novel rehabilitation strategies to further enhance patient outcomes and reduce the incidence of complications such as post-traumatic arthritis and avascular necrosis. The field continues to evolve, striving for improved functional recovery and a higher quality of life for patients with acetabulum fractures.

**Keywords:** *Acetabulum Fracture Management*

## Introduction.

The annual incidence of acetabulum fractures is around 8.1 cases per 100,000.1 Acetabular fractures are most common in two age groups: young patients and the elderly. In young people, high energy trauma (e.g., automobile accidents and sports injuries) and direct or transmitted force resulting in acetabular fractures are the main mechanisms, whereas in the elderly, low energy trauma (e.g., drops or falls) is the predominant mechanism, but treatments are more difficult. 2,3,4

Comorbidities are not the sole factor that influences how well an acetabulum fracture recovers. Patient variables, injury factors, and therapy factors are three types of prognostic factors. Age, osteoporosis severity, comorbidities, existence of degenerative joint disease, premorbid activity level, and mental function are all issues to consider. The presence of associated injuries, the degree of intra-articular comminution, articular damage, and the fracture pattern are all injury factors. The management chosen, the management of perioperative problems, and the quality and timeliness of the chosen management are all important treatment variables.

Comorbidities, poor bone quality, and delayed presentation are all linked to poor outcomes, making acetabulum fractures difficult to treat. To avoid unfavorable results, a thorough understanding of acetabulum fractures is required, including definition, anatomy, cause of damage, and proper therapy. From diagnosis to treatment, the goal of this study is to describe the required procedures in reaching a good result.4

Anatomy of Acetabulum and Clinical Consideration

In the field of orthopedics, the acetabulum fracture remains a challenge. The sacrum, coccyx, and two innominate bones combine to form the pelvis. The ilium, ischium, and pubis create the innominate bones, which are linked by triradiate cartilage before fusing. The iliac bones articulate with the sacrum via the sacroiliac joint posteriorly, while the two pubic bones articulate anteriorly to form the pubic symphysis, forming a ring of pelvic bones. The acetabulum is located on the lateral side of each innominate bone and articulates with the femoral head. The cotyloid fossa, which is the central non-articular part of the acetabulum beneath the acetabular roof, is a critical reference point in the acetabulum. The anterior column and the posterior column are the two columns that make up the pelvis. The illio-pubic column, also called the anterior column, is a bony strut that runs from the sacroiliac joint to the ipsilateral pubic ramus. The superior ramus pubis, the anterior portion of the acetabulum, the anterior superior and anterior inferior iliac spines, and the anterior iliac crest make up the anterior column. On radiographs, the iliopectineal line approximates the anatomic anterior column. The bony strut stretching from the posterior superior iliac spine to the sciatic tuberosity is known as the posterior columns, or illio-ischial columns.

The ischiopubic junction from the obturator foramen to the larger sciatic notch, as well as the posterior portion of the acetabulum, make up the posterior column (Figure 1). On radiography, the ilio-ischial line approximates the anatomic posterior column.5

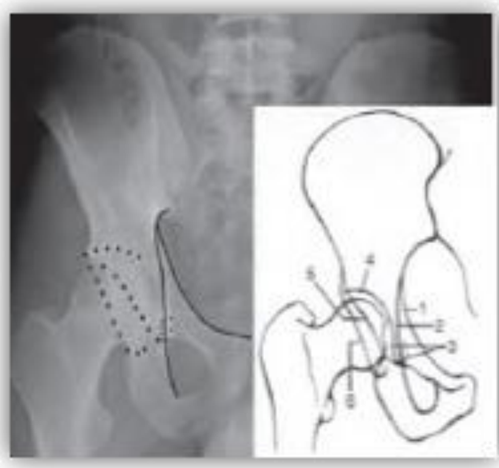

Figure 1. Radiographics lines of the acetabulum on Anteroposterior views. 1, iliopectineal line 2. Illioischial line 3teardrop, 4. Acetabular roof, 5. Anterior rim of the acetabulum, 6. Posterior rim of the acetabulum.17

Acetabular Fracture Classification Acetabular fractures are classified in a variety of ways, the most common of which is the Judet-Letournel classification. Acetabular fractures are divided into two types in this classification: elementary and associated type fractures If the fracture involves a single wall, column, or transverse fracture, it is classified as elementary. This type of fracture is easily remembered by visualizing the acetabulum's basic functioning structure..6,7 A two-part fracture is the most basic type of fracture. It is critical to remember that the word "transverse fracture" should only be used to designate anspecific diagnostic kind of transverse fracture,nnot the direction of the transverse fracture line

in acetabular fractures. In this class, anterior and posterior column fractures separate the complete column from the intact innominate, whereas anterior and posterior wall fractures merely separate the articular surface portion/s.

There are five fundamental types:

1. Fractures of the posterior wall of the acetabulum;
2. Fractures of the posterior column;
3. Fractures of the anterior wall of the acetabulum;
4. Fractures of the anterior column; and
5. Transverse fractures (single fracture lines that transverse anterior and posterior columns).

At least two of the primary patterns above, or an elementary pattern with an additional fracture component, make up Associated Fractures. It is a more complex pattern that

6. Anterior with posterior hemitransverse;
7. Posterior-column with posterior wall;
8. Transverse with posterior-wall;
9. T-shaped; and
10. Associated Both Column fractures.

includes the following elements:

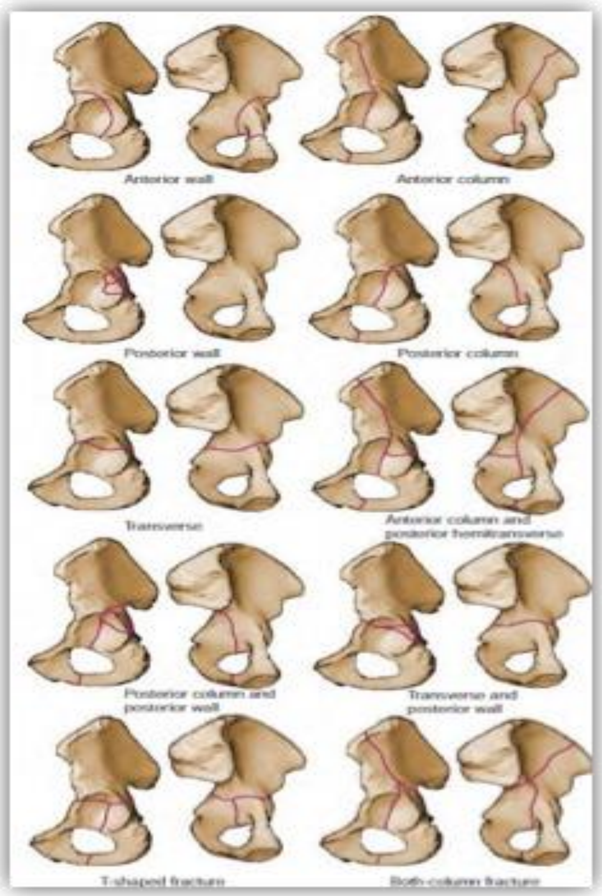

Figure 2. Letournel Acetabulum Fracture Classification17

Algorithm for Diagnosing Acetabular Fractures

The radiographic evaluation of the antero-posterior pelvis X-ray and two 45o Judet Oblique views are used to classify acetabular fractures in Judet and Letournal classifications.

Understanding complex fracture patterns and being able to classify them into one of five primary types or five associated types is a challenging subject to grasp, especially for people who do not evaluate pelvic radiography on a daily basis. The ability to correctly diagnose acetabular fractures is extremely critical, especially in the next phase of determining the fracture's ultimate treatment. The most challenging fracture patterns to classify, according to previous study, include posterior column/posterior wall fractures, anterior column/posterior hemitransverse fractures, and anterior column fractures. This could be related to the difficulties in detecting whether an ilium or ischial ramus fracture is non-displaced or minimally displaced. For less experienced doctors, computerized tomography (CT)-scan has proven to be useful in diagnosing minimally displaced iliac wing and obturator foramen fractures. Figure 3 illustrates the algorithm.8

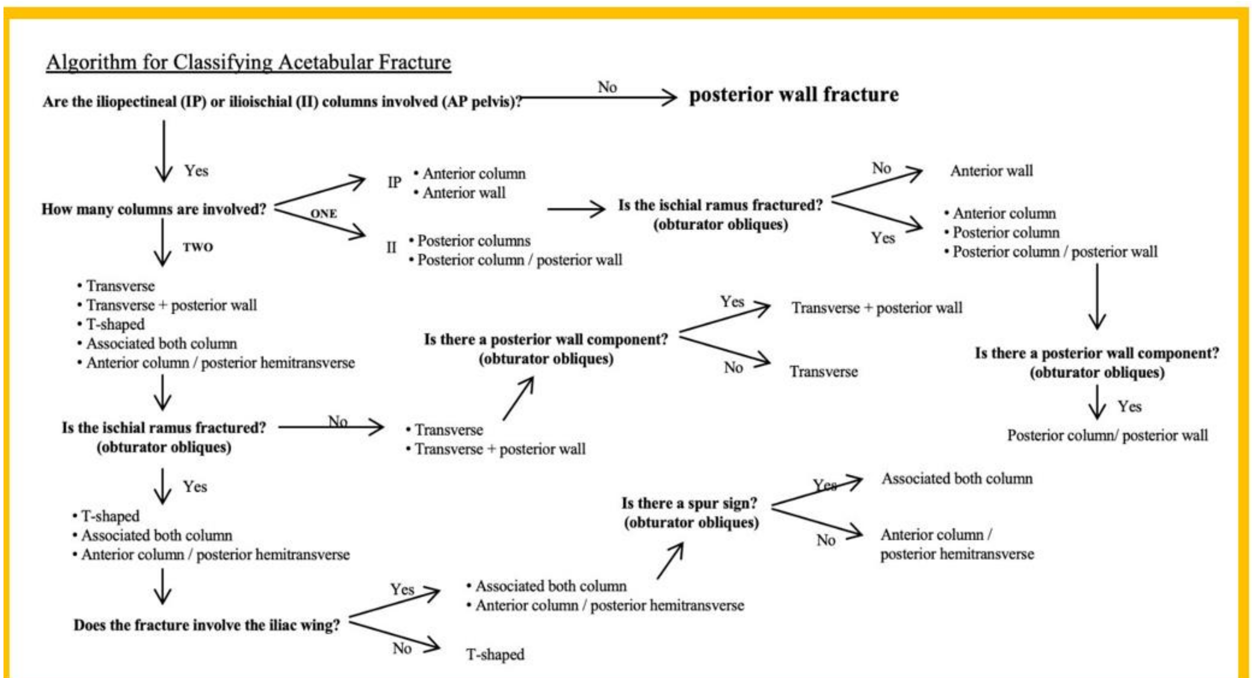


**Figure 3.** Algorithm for classifying acetabular fracture.[8]

Elementary type Fracture

***Anterior wall Fracture***

Despite their simple pattern, anterior wall fractures have the worst outcomes. Only 34% of the implants and reductions survived after twenty years, according to Matta et al. The majority of patients who suffer from these fractures are elderly people with severe osteopenia, which explains why. Not only is reduction difficult to achieve, but this type of fracture is also more likely to lose reduction, especially because it involves the roof of the acetabulum. As a result, joint failure is more common. The diagnosis was made by adopting the iliopectineal algorithm.line involvement without involvement of the ischial ramus fracture (Figure 4).9

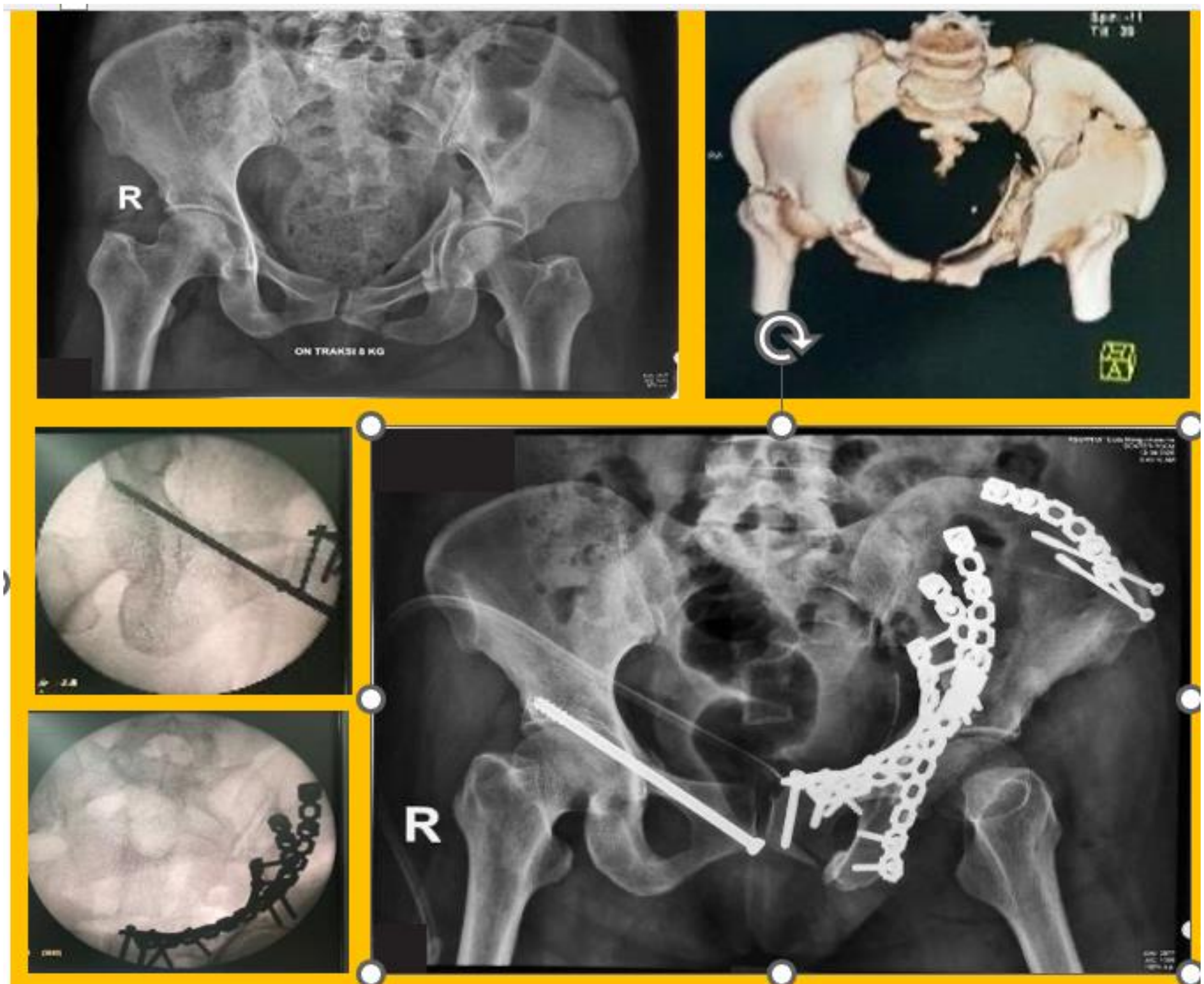


**Figure 4.** Female, 54 years old hit by a motorbike on left side. She experienced Closed fracture of Pelvic Marvin Tile 2, Young and Burgess LC 2 that consists of Right Acetabular fracture Judet-Letorunel elementary anterior wall type, left acetabular fracture Judet Letournel associated both columns. After couple days of traction using 8 kg weight,

***Anterior Column Fracture***

The iliopectineal line indicating the anterior column is disrupted in anterior acetabular column fractures, which can be seen more clearly in the obturator oblique projection The occurrence of anterior fractures is generally associated with anterior wall fractures. In such circumstances, it is critical to reduce the anterior column and accompanying anterior wall. Even a minor shift in the fracture line in the anterior column might cause joint incongruity by interfering with the reduction of the anterior wall.10


**Figure 5.** Male, 29 years old fell from 5 m height and landed in siting position. We can note that ilioischial line was intact while the iliopectineal line was disrupted with involvement of left ischial ramus fracture. Therefore, this was an anterior column acetabular fracture and was treated with cannulated screws

***Posterior Wall fractures***

As the most prevalent type of acetabular fracture (20-35%), fractures with this pattern are not as simple to treat as they appear. Unlike other acetabulum fractures, this one exclusively affects the posterior section of the posterior column and frequently occurs in conjunction with hip dislocation. Although conservative care is strongly suggested for stable joints with small fragment sizes, unstable stage joints or big posterior wall fragments necessitate Open Reduction and Internal Fixation.

The iliopectineal and ilioschial lines were not disrupted, hence these fractures were detected using an algorithm The accuracy of the reduction and avoiding an increase in contact pressure due to steps and gaps are the most critical aspects of the management of posterior wall fractures. The posterior wall fragments' vascularity is frequently disrupted, which leads to femoral head necrosis and resorption.11

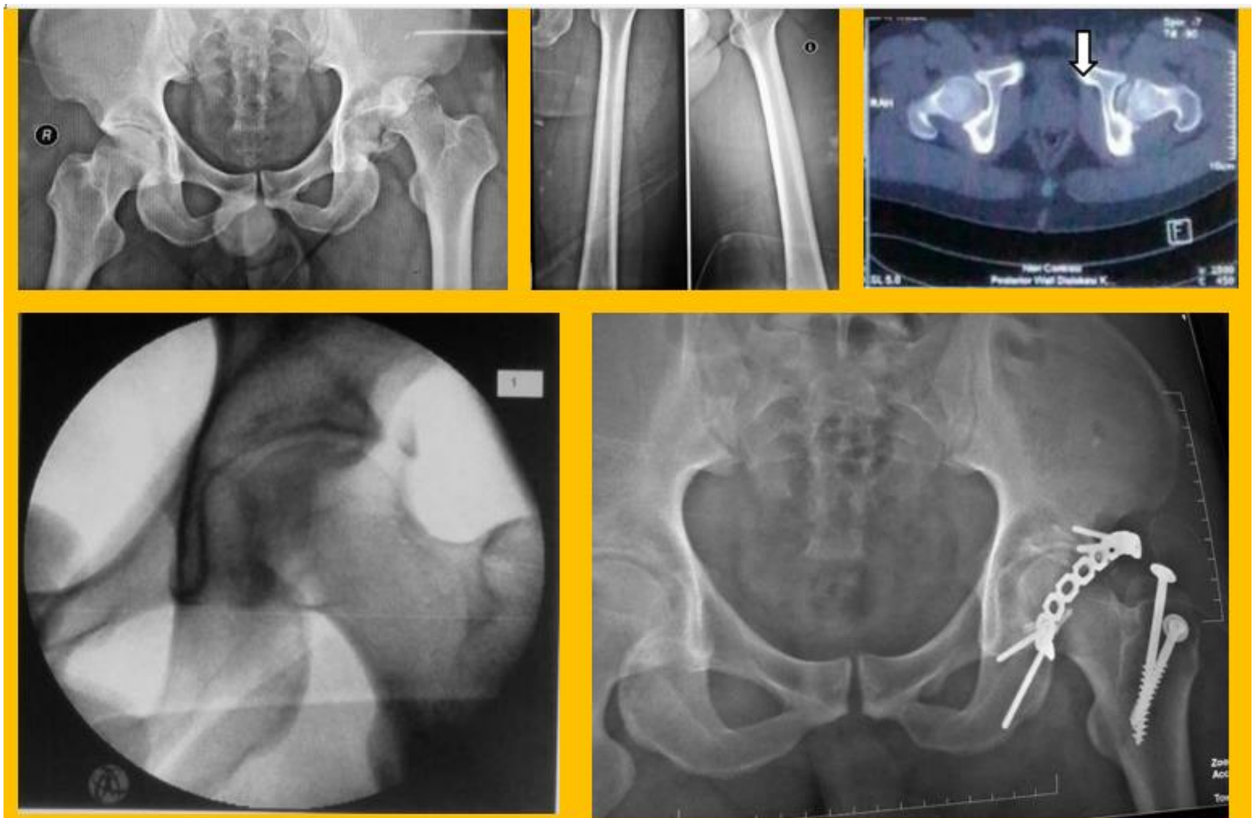

**Figure 6.** Male, 26 years old with posterior dislocation of left hip and left posterior wall acetabular fracture. As we can note that the ilioischial and iliopectineal line are intact. Closed reduction under anesthesia was performed and it was unstable. Due to dynamic instability & femoral head and posterior wall fracture pipkin type 4, ORIF was performed using 2 herbert screw for femoral head fracture, 2 herbert screw and buttress plate at the posterior wall, and interfragmentary screw for trochanteric osteotomy.

***Posterior column***

Following a diagnostic algorithm, fractures of the posterior acetabular column can be diagnosed by noticing the disruption of the ilioischial line and fracture of the ischial ramus without any involved posterior wall components. Isolated posterior column fractures are uncommon and usually occur in conjunction with a posterior hip dislocation.

Letournel's study found that out of 492 patients with isolated posterior column fractures, 81.82% had a favorable outcome. The success rate was reduced to 29.4% when the posterior wall was involved. Treatment of the posterior column without surgery is uncommon. It is usually misplaced and necessitates reduction and fixation.10,12

***Transverse Fracture***

Transverse fractures split the innominate bone into upper iliac and lower ischio-pubic fragments via the acetabulum. Letournel separates transverse fractures into three categories based on fracture locations - on radiographs: trans-tectal, juxtatectal, and infratectal. The iliopectineal and ilioischial lines are disrupted, but there is no fracture of the ischial ramus and no posterior wall component, therefore transverse fractures can be detected using the algorithm (Figure 7).13

**Figure 7.** Male, 28 years old, with Transverse type acetabular fracture. As we can note that both the iliopectineal and ilioischial columns were involved without fracture of ischial ramus and no posterior wall component. Patient was treated using iliopectineal plate and screw

***T-type Fracture***

A T-type fracture is a three-part fracture that appears on the roof of the acetabulum and has a sagittal fracture line. Type T fractures can also extend inferiorly, disrupting the obturator foramen. It is crucial to know the difference between T-tpe and elementary transverse

because the reduction's complexity will be drastically different. The ichiopubic ramus will be free-floating in a T-type acetabular fracture, making it difficult to reduce this section in addition to the roof acetabulum

As a result, anatomic reduction is critical to attaining the best results.14

***Anterior with Posterior hemitransverse***

In the obturator oblique view, an anterior with posterior hemitransverse fracture pattern can be recognized by detecting both a disrupted iliopectineal line and an ilioischial line with fracture of the ischial ramus and iliac wing fracture with no spur sign. This fracture pattern is more common in the older population and has a similar outcome to both column fractures. Matta et al, found that this form of fracture has an 88% 10-year survival rate.15

***Posterior wall/posterior column***

A fracture of the posterior column with posterior wall component is indicated by disruption of the ilioischial line without involvement of the iliopectineal line and fracture of the ischial ramus with involvement of the posterior wall component. This fracture pattern has a substantially worse prognosis than isolated posterior column fractures because of the involvement of the posterior wall.

***Transverse Fracture with Posterior Wall Involvement***

In up to 20% of all acetabular fractures, associated transverse fractures with posterior wall involvement occur. It is widely agreed that fractures with this pattern should be surgically treated. Prior to reducing the posterior column and posterior wall, the anterior column must be reduced until anatomical reduction is achieved and fixed. The optimum treatment for this sort of anterior column is a cannulated screw, whereas the best treatment for the posterior column is a plate and screw. The anterior column will be more stable if the posterior column is well-fixed 16

***Associated both column***

The presence of a spur sign and disruption of both the iliopectineal and ilioischial lines, as well as involvement of the ischial ramus fracture and iliac wing, were used to identify both column fractures. This fracture pattern is distinguished from the anterior column-posterior hemitransverse pattern by the spur sign In this fracture pattern, anatomical reduction is a metric that determines a good clinical result. If two of the - three criteria (femoral head dislocation, femoral head injury, or damage to the acetabular joint surface) are present, the patient is more likely to have joint degeneration. Secondary surgical congruence occurs when the acetabulum joint fragments follow the femoral head in a supero-medial orientation and retain congruence with the femoral head in this type of fracture. As a result, the roof- arc measurement is erroneous in this fracture pattern. CT scans were found to be more effective in assessing these fractures.

Surgical Treatment

All acetabulum fractures that result in hip joint instability and/or incongruity, regardless of classification type, require surgical treatment. Injuries involving fragments of bone or tissue within the hip joint that cause incongruity necessitate operational repair, as do posterior and anterior wall fractures with hip joint instability. One of the most common indications for open reduction and internal fixation is fracture displacement in the weight- bearing dome, which causes joint incongruity (ORIF). Loss of parallelism between the femoral head and the acetabulum articular surface detected on any of the three radiographic views is also an indication for operational care.

Anatomic acetabulum reduction achieved and sustained through healing, retained femoral head, and lack of perioperative problems are all predictors of good functional results in young and old patients. Furthermore, the timing of surgery has been found to be critical in achieving positive results. This is attributable to anatomical reductions in callus, organizing hematoma, and granulation tissues.20,22

There have been no particular rules for determining which patients would be most suited for surgery other than ORIF, hence the decision has been highly subjective. There are some indicators that can predict the necessity for a total hip arthroplast early on. (1) anterior dislocation, (2) femoral head cartilage lesion,
(3) posterior wall involvement, (4) marginal impaction, (5) marginal impaction, (6) initial displacement greater than 20mm, (7) non- anatomical reduction, (8) postoperative incongruence of the acetabulum roof, and (9) use of the extended iliofemoral approach.2,3

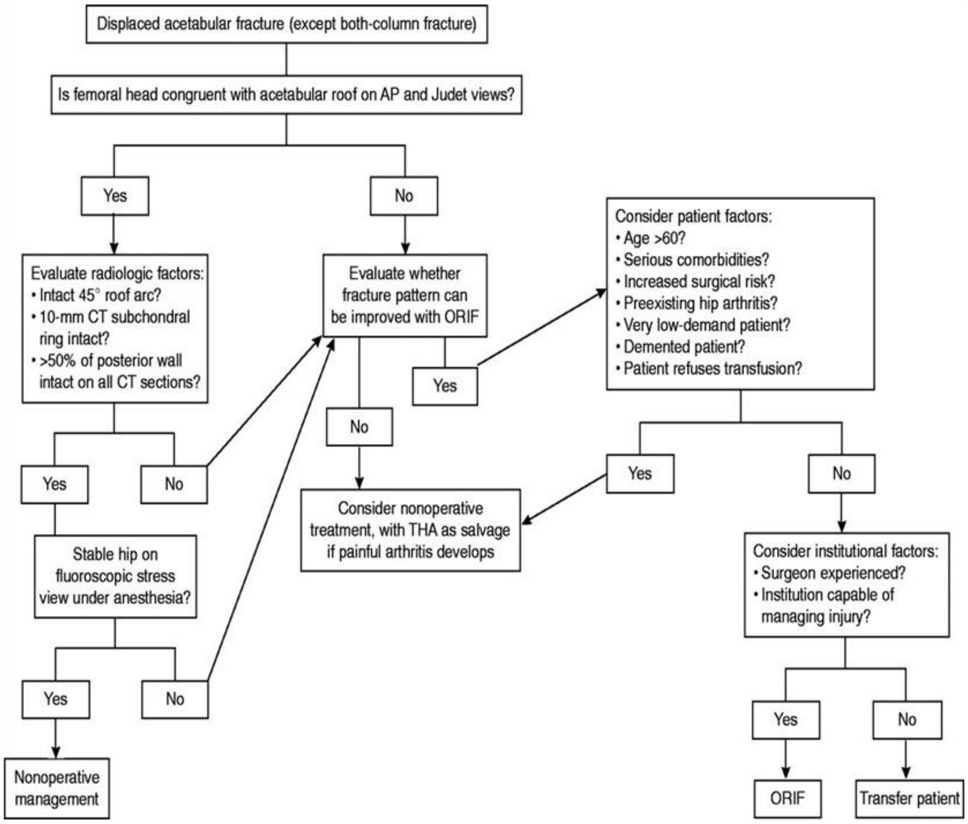


Figure 8. Algorithms in choosing optimal management for patients17

Patients with acetabulum fractures who are older have worse results than those who are younger. The elderly may require a variety of treatments, including non-operative, percutaneous methods, and ORIF with or without total hip replacement (THR). Although the percutaneous approach has a shorter operating time and less blood loss, it also has the potential of necessitating a second surgery. Internal Open Reduction Fixation is a technically difficult procedure, and even young patients may have poor outcomes. ORIF + THR necessitates a longer procedure with more blood loss, but the results may be better if the fractures are assessed individually.2,4,19

Because of the high number of revisions seen after ORIF of acetabulum fractures after months or years, arthroplasty is increasingly being evaluated as an alternative to secondary total hip replacement (THR), particularly in the elderly. Initial surgery may have resulted in scar tissue, heterotopic ossifications, soft tissue or bone abnormalities, avascularity, and the likelihood of concealed infection, making arthroplasty difficult. Aseptic loosening following cup insertion remains the most difficult perioperative hurdle in executing acute THR. The effects of THR on acetabulum fractures are still being debated. Individual solutions can give excellent outcomes, therefore a full understanding of the fracture pattern, a clear assessment of the patient's risk and prognosis, and the proper choice of the implant are all prerequisites for providing satisfactory outcomes in the elderly.3,4

Involvement of quadrilateral plate fractures in acetabular fracture

The quadrilateral plate is the acetabulum's thin medial wall, which fractures with less force than the acetabulum's superior weight-bearing zone. Central fracture dislocation of the hip with medial migration of the quadrilateral plate is common in patients with both column, transverse, T-shaped, and anterior column-posterior hemitransverse fractures. An incongruent hip and a bad outcome will occur if the medial wall's buttressing role is not adequately restored and central displacement is reduced. Conservative treatment of quadrilateral plate acetabular fractures resulted in poor results, a higher risk of pin-track infection, and a rapid progression of post-traumatic degenerative disease. 23

***Intrapelvic plate***

Fractures of the quadrilateral surface, particularlythose involving theanteriorcolumn, anterior column posterior hemi transverse, or linked both column fracture patterns, are common in the elderly. In traditional extra pelvic fixation, a reconstruction plate is implanted at the pelvic brim with screws angled caudally to capture the posterior column of the fracture fragment. Quadrilateral fractures, on the other hand, are more difficult to treat because they are close to the articular surface of the hip joint, are located in the true pelvis, and have a paucity of bone stock, especially in older patients with osteoporosis or osteopenia.

The intrapelvic plate is a pre-contoured plate that mimics the anatomy of the medial wall of the pelvis below the pelvic brim to help buttress the fracture. Despite being more invasive, requiring additional dissection, and lasting longer, the addition of an intrapelvic plate in addition to extrapelvic plating increases the force required for clinical failure and increases the biomechanical strength of the joints, especially in geriatric patients, according to a cadaveric study by Gillispie et al.24 In their analysis using infra-pectineal plating, Qureshi et al. demonstrated that infra-pectineal plating provides rigid attachment and applies the plate in the same plane as the displacement. The results of a displaced quadrilateral plate fracture in 21 osteoporosis patients over the age of 60 were published in 2011 by Laflamme et al. Using a modified stoppa strategy, they used an infra-pectineal plating procedure. Anatomical reduction (less than 1mm) was achieved in 52.4 percent of cases, imperfect (1- 3mm) in 38.1 percent, and poor (greater than 3mm) in 9.5 percent, with a functional outcome ranging from good to very good in 70.6 percent of cases. Even in poor reductions, plating in osteoporotic fractures yields a favorable functional and radiological outcome, as long as the femoral head stays concentric with the superior dome, according to this study.25,26 Kistler et al. compared 35 pelvic models with transverse transtectal fractures treated with five different fixation instruments (anterior column plate + posterior column lag screw, posterior column plate + anterior column lag screw, anterior and posterior column lag screws only, infrapectineal plate + anterior column plate, and suprapectineal plate only) in a study published in 2014. The maximum load to failure was proven by the quadrilateral surface buttress plates on the anterior and posterior columns, which used the infrapectineal plate.

In between plating procedures for quadrilateral plate fractures, spring plates bent across the pelvic brim can be used to maintain the medial wall. T-shaped, H-shaped, one-third tubular, and rebuilding can all be employed in this case.30 Contouring plates to provide enough medial buttress to all individuals, on the other hand, may be difficult. Failure frequently results in non-union and the requirement for future arthroplasty. The usage of a pelvic brim plate with periarticular screws and an H-plate spring plate was found to offer no biomechanical advantages over the pelvic brim plate alone.

According to the findings of many studies, the intrapelvic plate gives stronger biomechanical stability to the QS fragment31, while the results are still unclear and further research is needed to directly compare the two.

Surgical Approach

One of the most significant components of acetabulum surgery preoperative planning is the selection of the optimal surgical technique. The fracture type, the period between injury and operative intervention, and the amount and location of maximal fracture displacement are the most important factors in the decision-making process. In most cases, a single surgical method is used in the hopes of completing the fracture reduction and fixation in one go. The surgical approaches to the acetabulum are those described by Letournel and Judet: The Kocher-Langebeck, The illioinguinal, the illiofemoral and the extended illiofemoral, Alternative procedures, on the other hand, have been presented that could provide significant benefits over current methods. The modified Gibson approach, the trochanteric flip osteotomy, the modified Stoppa approach, and the simultaneous use of the standard and posterior approaches are among them. 19,21,32

Table 1: Choice of surgical approach for each fracture pattern17

| Fracture type | approach |
|---|---|
| - **Elementary** | |
| - Posterior wall | - Kocher langenbeck |
| - Posterior column | - Kocher langenbeck |
| - Anterior wall | - Illioinguinal or illiofemoral |
| - Anterior column | - Illioinguinal or illiofemoral |
| - Transverse | - Kocher-langenbeck or illioinguinal |
| infratectal/juxtatectal | - Extended illio fermoral or kocher langenbeck |
| - Transverse transtectal | |
| | - Kocher langenbeck |
| Associated | - Illioinguinal |
| - Posterior column + wall | - Kocher langenbeck |
| - Anterior + posterior hemitransverse | - Extended iliofemoral or kocher langenbeck |
| - Transverse infratectal/juxtatectal + posterior wall | - Kocher langenbeck or combined |
| | - Extended iliofemoral or combined |
| - Transverse transtectal + posterior wall | - Illioingunal or extended iliofemoral or combined |
| - T-shaped infratectal/juxtatectal | |
| - T-shaped transtectal | |
| - Both column | |

The illioingunal technique for anterior column or T-shaped or bicolumn fractures with minimal comminution in the posterior column, as well as the Kochen-langebeck route for posterior column injuries, are the most widely used standard approaches.

Alternative ways to treating anterior wall, anterior column, transverse, T-shaped, anterior column/wall, and posterior hemitransverses, as well as both column fractures, are gaining popularity. The trochanteric flip osteotomy is a variant of the Kocher-Langebeck method that is utilized to gain more anterosuperior exposure and facilitate femoral head dislocation during surgery. Femoral head posterior wall acetabulum fractures, posterior wall and column fractures, as well as t-shaped and transverse fracture patterns, are all indications for this method. The Modified Gibson technique differs from the Kocher-Langenbeck approach in that it has a straight skin incision, making it visually pleasing and allowing it to be used with a trochanteric flip osteotomy. The anterior ilioinguinal or iliofemoral approach can be paired with the posterior iliofemoral approach and executed sequentially.18,19

Post-Operative Care

The goals of postoperative care are to maximize the patient's function, allow an early return to function, and detect and address issues rapidly. One of the most critical components of postoperative treatment is pain control, which is best achieved with a continuous opiates epidural infusion. DVT prevention is critical, particularly in high-risk patients. Starting at 6–12 weeks, the patient should be actively mobilized.2.

To avoid heterotopic ossification, indomethacin is commonly prescribed at a dose of 25 mg three times per day for six weeks17. Heterotopic ossification is a common consequence following acetabulum fracture surgery, occurring in 7% of cases. The surgical method chosen has been demonstrated to influence the chance of ectopic bone formation.8,9 According to a recent study, race is linked to varying rates of severe heterotopic ossification, with African Americans experiencing greater rates than Caucasians.33 The use of extended mechanical breathing may result in severe heterotopic ossification, necessitating the administration of indomethacin.34 Postoperative radiographs should include anteroposterior and oblique views. Patients are examined at two weeks after discharge for wound inspection and suture removal, then at six weeks, three months, one year, and once a year. At these visits, radiographs in the AP and oblique views should be obtained to examine the maintenance of reduction and fracture healing, as well as the possibility of posttraumatic arthritis. Patients are expected to resume ordinary activities six months after surgery and rigorous activity one year later, but this varies by person.17

Expected Outcome and Complication

In the literature, the outcomes of ORIF for acetabulum fractures vary. Certain types of injuries seem to respond better to surgery than others. Both types of column fractures are difficult to treat due to their complexity. However, they do have a better outcome than any other type of fracture. Every treatment option for acetabulum fractures may result in complications. Post-traumatic arthritis is the most common consequence after an acetabulum fracture. The effectiveness of fracture reduction appears to be the most important factor in determining the likelihood of late traumatic arthritis. Wear of the femoral head against a malreduced fracture is the most prevalent cause, and osteonecrosis is a common complication17. The most common consequence of operatively treated fractures is acetabulum fracture infection. An open fracture and local soft tissue injuries such as Morrel-Lavale lesions, as well as abdominal and urological injuries, increase the risk of infection. Infection management is similar to that of other anatomic locations, with culture and antibiotics administered as soon as possible.20

Iatrogenic nerve injury is a rare complication of acetabulum fracture therapy, although it is a serious problem. The posterior and extended surgical methods, which include direct exposure and retraction of the sciatic nerve, are the most typically associated with these injuries. Management of sciatic nerve damage is expectant and the prognosis for functional recovery is variable.19 Other acetabulum fracture consequences include venous thromboembolism, which should be treated with a thromboprophylaxis regimen, as previously mentioned. Heterotopic ossification is another acetabulum fracture complication that occurs in up to 90% of cases after surgical treatment.17,21

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