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## **Original Research Article**

# Outcome and complications of open reduction and internal fixation in ankle fractures at a tertiary care center

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### ABSTRACT

**Background:** Closed reduction used for management of ankle fractures usually result into delayed healing. It inhibits the healing of the ankle fractures. On the contrary, open reduction and internal fixation helps to preserve the supply of blood not only to soft tissues but also bones. This way it helps in proper and timely healing.

**Objective:** To study outcome and complications of open reduction and internal fixation in ankle fractures **Materials and Methods:** A hospital based prospective study was carried out among 40 cases of ankle fractures. Detailed history, general examination were carried out as per the pre-tested, pre-designed study questionnaire. Once patient was found to be eligible for present study, surgical profile and pre-anesthetic check-up was done as per standard guidelines. All patients were treated with open reduction and internal fixation method.

**Results:** Most commonly affected age group was 31-40 years (40%). Males were affected more than females (4:1). Vehicular accident was most common cause (65%) of ankle fracture. 95% had closed fracture. Most common injury pattern (57.5%) was Pronation external rotation. K-wire was most commonly used (40%) operative technique. Among the variables, open type of fracture and other mode of injury were significantly associated with painful gait. There were no other complications recorded. 70% had excellent outcome and 25% had good outcome. Among all factors studied, only open type of fracture was found associated with functional outcome that is not excellent.

**Conclusion:** Thus open reduction and internal fixation is the treatment of choice in case of fracture ankle joint, with very less change of complications

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#### 1. Introduction

In the United States, most commonly treated fracture is the ankle fracture by the orthopedic surgeons.<sup>1</sup> Population - based studies suggest that the incidence of ankle fractures has increased dramatically since the early 1960s<sup>2</sup> as well as there is increase in the severity of fractures, especially in elderly individuals.

Ankle is the most congruous joint in the lower extremity, bearing up to five times the body weight. It was demonstrated by Ramsey and Hamilton that there can be 42% reduction in the articulation of tibiotalar if there is even one millimeter lateral displacement. This will be enhanced with further lateral displacement. In all fractures through the articular surface of a major weight bearing joint, restoration of the normal anatomy is required to prevent development of secondary arthritis and ankle joint is no exception.<sup>3</sup>

\* Corresponding author. E-mail address: gvvvsiva@gmail.com (Venkata Sivaram G V). Despite the general perception that operative treatment of ankle fracture yields better clinical results than closed treatment, this advantage has not been demonstrated scientifically in most studies.<sup>4</sup> The primary difficulty in evaluation of the literature in this regard is that, in most clinical studies, the fractures have not been stratified by type but, rather, have been evaluated as a heterogeneous group.

After 1970, ankle fractures are usually managed by operative methods.<sup>5</sup>The goal of treatment is to restore biomechanical stability to the ankle, therefore it is imperative to have a clear definition of the altered biomechanical status caused by a specific injury.<sup>2</sup>

Many clinical studies of ankle fractures have proven that good results depend upon an anatomic reduction of the fracture, and there is a direct correlation between displaced fractures and the occurrence of degenerative arthritis.<sup>5</sup>

In ancient times injuries of the ankle were diagnosed chiefly as "Luxation." Not until the middle of the eighteenth century were there attempts in the literature to clarify the position of malleolar fractures in relation to "luxation" of the ankle. Among the earliest observations on the pathomechanics of ankle injuries were those by Sir Percival Pott, who in an article entitled "Some Few General Remarks on Fractures and Dislocation" published in 1768, attempted to relate the clinical findings in a given case to the injuries that caused them. After that most experimental studies on the production of ankle fractures were done by the French.<sup>6</sup>

The next significant advance in our understanding of ankle fractures had to wait nearly 50 years before Baron Guillaume Dupuytren's described- Dupuytren's fracture dislocation of ankle in 1819 and commended Pott on his powers of acute observation. Both Pott and Dupuytren were the first to point out the type of ankle injury in which the fracture of fibula occurs proximal to level of syndesmosis. They indicated that mechanism of injury was abduction of the foot in relation to the tibia, but they failed to recognize that rupture of the ligaments of syndesmosis accompanied the fracture.<sup>6</sup>

Considering the fact that the original description was in English, it is surprising how little has been written in English language on the subject. The French on the other hand have written extensively, beginning with Baron Dupuytren's description in 1819 of the fracture that eponymous bears his name. According to Boning, the period 1815- 1872 was dominated first by Dupuytren and then by one of his pupil Maisonneuve, who described a fracture dislocation after his name, experimentally produced in 1840, but clinically described for the first time by hundred an eight years later.<sup>6</sup>

The most significant contribution was made by Lauge Hansen in 1950 when based upon his cadaver experiments and a careful study of both clinical and radiological points of view a new classification was proposed – 'Genetic classification of ankle injuries.<sup>7</sup>

By this time – the 1960s – the concept of internal fixation in ankle fractures was fast gaining grounds. R.A. Denham &

C.L. Colton advocated internal fixation for unstable ankle fractures and fracture dislocations. This was based on the concept that perfect anatomical reduction was the crux of the issue and absolutely essential for optimum functional results. Yet, the concept of early mobilization had not gained great popularity due to lack of sufficiently rigid fixation.<sup>8</sup>

Management of ankle fractures by internal fixation became popular after the work of "Muller, Allgower and Willenegger (1970)".<sup>2</sup> The motto was "Life is Movement, Movement is Life". However they utilized the classifications introduced by Weber in 1964 –66, for analysis of ankle fracture and making decision as to choice of implants.<sup>3</sup>

Hughes (1980) reported a comparative study of ankle fractures from three major centers. They reported that "open reduction and internal fixation" of ankle fractures was superior to closed method. <sup>8,9</sup>

Closed reduction used for management of ankle fractures usually result into delayed healing. It inhibits the healing of the ankle fractures. On the contrary, open reduction and internal fixation helps to preserve the supply of blood not only to soft tissues but also bones. This way it helps in proper and timely healing. Hence, present study was carried out to analyze the outcomes & complications among patients treated for ankle fractures with open reduction and internal fixation method

#### 2. Materials and Methods

A hospital based prospective study was carried out from Aug 2016 to Aug 2018 among 40 cases of ankle fractures at a tertiary care hospital. Institutional Ethics Committee permission was taken and informed consent was taken from all study participants.

During the study period, it was possible to include 40 cases of ankle fracture. Patients with ankle fracture belonging to age group of 20 years and above of either gender or consenting were included in the present study. Those with complicated fracture and with severe comorbidities were excluded from the present study.

Detailed history, general examination were carried out as per the pre tested, pre designed study questionnaire. Once the patient was found to be eligible for the present study, surgical profile and pre-anesthetic check-up was done as per the standard guidelines. In the present study we have taken three radiographs Anteroposterior, Lateral & Mortise view of all clinically diagnosed ankle fractures. All patients were treated with open reduction and internal fixation method.

First to start with, giving the priority to fibula, we first fixed lateral malleolus followed by fixing the medial malleolus. After every anatomical reduction, it is necessary to carry out temporary stabilization. For provisional stabilization of the lateral malleolus K wires are used and similarly the medial malleolus is also provisionally fixed. The internal fixation is then carried out, using a 4 mm cannulated cancellous screw, or a four – hole plate

with/without interfragmentary screw. All Kirschner wires are removed at the end, except when they provide additional fixation.

The ideal time for the procedure is within the first 6 to 8 hours before any true swelling or fracture blisters develop. The leg is then kept elevated to reduce the swelling before the open reduction is undertaken.

Standard post-operative care was taken. All patients were followed up for six months to study the functional outcome. Regarding post-operative protocol in present study, all patient were given Below Knee cast for at least 2 weeks and then mobilized with Physiotherapy along with partial weight bearing followed by full weight bearing after 6 weeks. Period of immobilization recommended in below knee cast is for 2 weeks in monomalleolar, bimalleolar and Trimalleolar fractures with additive and its 2 more weeks in partial or complete diastasis fractures. Non-weight bearing was however started two weeks after operation. Functional results were assessed and graded at the end of plaster immobilization and patient sent for partial weight bearing and physiotherapy. At this time patient was also assessed for painful gait, infection, instability and persistent subluxation.

#### 2.1. Statistical analysis

The data was expressed as proportions. Chi square test was applied to study the factors related to the outcome. P value <0.05 was taken as statistically significant.

#### 3. Results

Most commonly affected age group was 31-40 years (40%) followed by 20-30 years (25%). Males were affected more than females in the ratio of 4:1. Vehicular accident was the most common cause of ankle fracture in 65% of the cases. 95% of the cases had closed fracture. Most common injury pattern was Pronation external rotation in 57.5% of the cases. K wire was most commonly used operative technique in 40% cases (Table 1)

Among the variables, open type of fracture and other mode of injury were significantly associated with the painful gait. (Table 2)

Only one case (2.5%) had painful gait at the end of six months follow-up period. There were no other complications recorded (Table 3)

70% of the cases had excellent outcome and 25% had good outcome. Fair outcome was recorded in only two cases (Table 4)

Among all the factors studied, only open type of fracture was found to be associated with functional outcome that is not excellent (Table 5)

#### 4. Discussion

Following the operation, a good or excellent result was obtained in 95% of patients in the present study. Majority

of cases fall in age group of 31-40 years. Males were more in number compared to females. As far as ankle fractures are concerned sexual variation has no clinical significance. The higher proportion of male cases could be because cases were more of vehicular accidents and males are usually at the wheel in most instances. Most common mode of injury is vehicular accidents with Closed type of fractures which are diagnosed as mono, bi, or Trimalleolar Fractures with having pronation external rotation type of injury pattern in among more than 50% of cases.

In the present study we have taken three radiographs Anteroposterior, Lateral & Mortise view of all clinically diagnosed ankle fractures. Anteroposterior, Lateral view & Anteroposterior with slight medial rotation Views are essential for appropriate classification of fracture and their management. Several investigators have studied the necessity for the use of three radiographs- Anteroposterior, Lateral & Mortise view for classification of fracture and their management.<sup>10,11</sup>

Lauge - Hansen pointed out that little reliance can be placed on patient's interpretation of how ankle was injured because he usually has little idea of the forces involved. It is more satisfactory to take account only of information obtained from radiology and clinical examination.<sup>12</sup>

In our study the accurate anatomical reduction with stable internal fixation preferably rigid is responsible for superior result and early functional recovery with minimum possibility of mal-union or non-union as compared to results after conservative treatment.

We found that "open reduction and internal fixation using the AO–ASIF method" gave very good results. Previous studies also found the same.,<sup>11,12</sup> that sometimes anatomical reduction can give rise to fair/poor functional result but fair / poor reduction always give poor functional result. It requires serial manipulation and further immobilization in cast which leads to further increase in duration in hospital stay and delayed physiotherapy for the joint and delay in rehabilitation. In any case, results from closed treatment frequently reveal that the fractures were inadequately reduced or inadequately maintained after an original adequate reduction and, as would be expected, had comparatively poor results.<sup>13</sup>

In the study reported by Brounstein and Wade (1959) of 57 patients whose ankle injuries had been treated by close reduction, 28 required a second manipulation and 8 a third or fourth manipulation.<sup>14</sup> These authors comment on difficulty in maintaining the position by plaster splintage during the first few weeks as the edema subsides.

Extent of immobilization is necessary after closed reduction but that lead to osteoporosis, with more risk in elderly females.<sup>3</sup> There is always risk of mal-union and residual subluxation and non-union if there is soft tissue interposition between fragments of medial malleolus.<sup>15</sup>

Table 1: Socio-demographic and clinical characteristics

Variable		Number	%
	20-30	10	25
	31-40	16	40
Age (years)	41-50	7	17.5
	51-60	4	10
	> 60	3	7.5
Corr	Male	32	80
Sex	Female	8	20
	Fall from height	3	7.5
Mode of injury	Vehicular accident	26	65
	Other	11	27.5
T (( )	Open	2	5
Type of fracture	Closed	38	95
	Supination adduction	8	20
	Supination external rotation	2	5
Injury pottern	Pronation abduction	4	10
Diagnosis	Pronation external rotation	23	57.5
	Pronation dorsiflexion	1	2.5
	Other	2	5
	Monomalleolar	12	30
	Bimalleolar	12	30
	Trimalleolar	16	40
	K wire as well	16	40
Operative technique	Only TP and cortical screw	12	30
	Malleolar screw as well	10	25
	CC screw as well	2	5

Table 2: Association betweensocio-demographic, clinical variables with painful gait

Variables		Painful gait		Chi annon	_
		Yes	No	Chi square	р
Sex	Female	0	8 (100%)	0.256	0.613
	Male	1 (3.1%)	31 (96.9%)	0.230	
Mode of injury	Fall from height	0	3 (100%)	0.552	0.759
	Vehicular accident	1 (3.8%)	25 (96.2%)		
	Other	0	11 (100%)		
Type of fracture	Open	1 (50%)	1 (50%)	10 497	< 0.0001
	Closed	0	38 (100%)	19.40/	
Injury pattern	Supination adduction	0	8 (100%)		< 0.0001
	Supination external rotation	0	2 (100%)		
	Pronation abduction	0	4 (100%)	16.022	
	Pronation external rotation	0	23 (100%)	10.932	
	Pronation dorsiflexion	0	1 (100%)		
	Other	1 (50%)	1 (50%)		
Diagnosis	Monomalleolar	0	12 (100%)		
	Bimalleolar	0	12 (100%)	1.538	0.463
	Trimalleolar	1 (6.3%)	15 (93.8%)		

## Table 3: Complications among the cases at the end of six months

Complications	Number	%
Painful gait	1	2.5
no wound infection	40	100
No implant failure	40	100

Functional outcome	Number	%
Excellent	28	70
Good	10	25
Fair	2	5
Total	40	100

Table 4: Functional outcome at the end of six months

Table 5: Association between socio-demographic, clinical variables with functional outcome at the end of six months.

Variable		Functional outcome at six months			<b>v</b> 2	
		Excellent	Good	Fair	Λ-	þ
Sex	Female	5 (62.5%)	3 (37.5%)	0	1.205	0.547
	Male	23 (71.9%)	7 (21.9%)	2 (6.3%)		
Mode of injury	Fall from height	3 (100%)	0	0	2.740	0.602
	Vehicular accident	19 (73.1%)	6 (23.1%)	1 (3.8%)		
	Other	6 (54.5%)	4 (36.4%)	1 (9.1%)		
Type of fracture	Open	0	1 (50%)	1 (50%)	10.526	0.005
	Closed	28 (73.7%)	9 (23.7%)	1 (2.6%)		
	Supination adduction	6 (75%)	2 (25%)	0		
Injury pattern	Supination external rotation	2 (100%)	0	0	17.848	0.058
	Pronation abduction	1 (25%)	3 (75%)	0		
	Pronation external rotation	18 (78.3%)	4 (17.4%)	1 (4.3%)		
	Pronation dorsiflexion	1 (100%)	0	0		
	Other	0	1 (50%)	1 (50%)		
Diagnosis	Monomalleolar	10 (83.3%)	2 (16.7%)	0	4.119	0.390
	Bimalleolar	8 (66.7%)	4 (33.3%)	0		
	Trimalleolar	10 (62.5%)	4 (25%)	2 (5%)		

By doing open reduction and internal fixation one can achieve anatomical reduction by removing soft tissue interposition if that is causing problems in reduction and end result are likely to be excellent. In the present study, no any soft tissue interposition interfering the reduction was found or probably ORIF of medial and lateral malleolus caused a fall of the soft tissues to their original anatomical positions.

In our study 2 cases came within 6-12 hour of injury and got operated immediately. One case was 45 year old male having compound grade II fracture of ankle joint. Irrigation, debridement and ORIF with a malleolar screw was performed for medial malleolus and one third tubular plate with 3.5 mm cortical screws was used for fracture of lateral malleolus. Tag sutures were taken in view of compound wound. Later on STSG was performed. Patient was initially maintained in BK slab. BK cast was given after STSG took over for 8 weeks and mobilize thereafter. Final outcome was fair functional end result in view of painful gait, restricted movement and edema of foot. Timothy J. Bray, in his study of 31 compound ankle fractures treated with ORIF, concluded that it is better than conservative management in view of speedy recovery and rehabilitation.<sup>16</sup>

In present study standard medial approach used for fixation of medial malleolus. In some cases, 4mm cannulated cancellous screws of proper length were used. Large fragment required two screws. All patients had complete union of medial malleolus.

The lateral malleolus is fixed by standard lateral approach. The lateral malleolus has a key role to play in achieving reduction and stability of ankle fractures. Yablon IG et al from Boston University Medical Center produced an important and interesting paper in 1976. Till then it had been wrongly believed for a long time that if the medial malleolus was reduced and fixed, the fibular fracture fell into place. They provided evidence that in patients with bimalleolar fracture cases, first it is necessary to reduce the lateral malleolus so that we can reposition the talus.<sup>17</sup>

In present study, the same principal described by Yablon IG et al<sup>17</sup> was followed and lateral malleolus fixed first in each bi-malleolar and tri-malleolar fracture and anatomical reduction with excellent functional end results was achieved.

Fixation of posterior malleolus is not always required. Posterior malleolus fracture is first describe by Destol 1911 occurs primarily as a consequence of avulsion by the posterior–inferior tibio–fibular ligament of because of pressure from the externally rotating talus when associated with medial and lateral malleolar fracture called as trimalleolar fracture. Intra-articular fragment that are big allowed to heal in the displaced position lead to intra articular incongruity lead to post traumatic arthritis. In our present study, 16 cases of posterior malleolus fractures were found and ORIF was not done. All of these cases had excellent functional result. Mcdaniel WJ et al in their paper concluded that when posterior fragment involved 25% of the articular surface or more operative treatment of the posterior malleolus was associated with better functional result than of close treatment.<sup>18</sup>Harper MC et al concluded that fracture of posterior malleolus is not at all required to fix by ORIF if both malleoli reduced anatomically and fixed with rigid internal fixation, the posterior malleolus got reduced by its own and remain stable.<sup>11</sup>

Finsen V et al in their study of 56 patients of fracture ankle conclude that there is no added advantage of postop. Mobilization with or without BK cast, if the fixation is stable.<sup>19</sup>

In this study, patients were asked to use crape bandage for 6 weeks after removal of the cast to prevent rebound edema. Patients were assessed every two weeks in general. The following criteria were adopted for rehabilitation. If the patient is light and sedentary worker early rehabilitation at about two weeks after the expected period of union. Heavy manual worker requires walking and standing, had to wait for two weeks to eight weeks after the period of union.

In present study there were no complications like infection and implant failure except painful gait in one patient till after end of one year. In our study there is a significant association of painful gait complication with open type of fractures.

A compound fractures of ankle joint which resulted in fair function end result was found comparable with the study published by Burwell HN et al.<sup>14</sup> Wilson FC in his paper on fracture of the ankle joint- pathogenesis and treatment, concludes that, bimalleolar fracture and posterior malleolar fracture with fracture fragment more than 25% of the tibial plafond should be fixed with ORIF for better result.<sup>20</sup>

#### 5. Conclusion

Maximum period required by majority of the patient after operation to return back to work was 12-14 weeks; however some were able to go back to work as early as 8 weeks. Successful results were seen in 95% of cases and complications were observed only in 5% patients. The main complication found was painful gait. Surgical intervention with anatomical reduction and stable internal fixation yields superior results with minimal complications and earlier rehabilitation. It is essential to treat all ankle fractures by accurate anatomical reduction and stable internal fixation. Thus open reduction and internal fixation is the treatment of choice in case of fracture ankle joint, with very less change of complications.

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### 7. Conflict of Interest

The authors declare they have no conflict of interest.

#### References

- Ahl T, Dalen N, Selvik G. Mobilization after operation of ankle fractures. Good results of early motion and weight hearing. *Acta Orthop Scan.* 1988;59(3):302–6. doi:10.3109/17453678809149368.
- Ahl T, Dalen N, Selvik G. Ankle fractures. A clinical and roentgenographic stereophotogrammetric study. *Clin Orthop.* 1989;(245):246–55.
- Ahl T, Dalen N, Lundberg A, Bylund C. Early mobilization of operated on ankle fractures. Prospective, controlled study of 40 bimalleolar cases. *Acta Orthop Scand.* 1993;64(1):95–9. doi:10.3109/17453679308994541.
- Ali MS, Mclaren CA, Rouholamin E, O'Connor BT. Ankle fractures in the elderly: non-operative or operative treatment. *J Orthop Trauma*. 1987;1(4):275–80. doi:10.1097/00005131-198701040-00002.
- Bauer M, Jonsson K, Nilsson B. Thirty-year follow-up of ankle fractures. Acta Orthop Scand. 1985;56(2):103–6. doi:10.3109/17453678508994329.
- Amendola A. Controversies in diagnosis and management of syndesmosis injuries of the ankle. *Foot and Ankle*. 1992;13(1):44–50. doi:10.1177/107110079201300108.
- Baird RA, Jackson S. Fractures of the distal part of the fibula with associated disruption of the deltoid ligament. Treatment without repair of the deltoid ligament. *J Bone Joint Surg.* 1987;69(9):1346–52.
- Bauer M, Bengnér U, Johnell O, Redlund-Johnell I. Supination-eversion fractures of the ankle joint: changes in incidence over 30 years. *Foot Ankle*. 1987;8(1):26–8. doi:10.1177/107110078700800107.
- Bauer M, Bergstrom B, Hemborg A, Sandegard J. Malleolar fractures: non-operative versus operative treatment. A controlled study. *Clin Orthop.* 1985;(199):17–27.
- Goergen TG, Danzig LA, Resnick D, Owen CA. Roentgenographic evaluation of the tibiotalar joint. *J Bone Joint Surg.* 1977;59(7):874– 7.
- Harper MC. The deltoid ligament. An evaluation of need for surgical repair. *Clin Orthop Relat Res.* 1988;(226):156–68.
- Lauge-Hansen N. Combined experimental-surgical and experimentalroentgenologic investigations. *Arch Surg (1920)*. 1950;605:957–85.
- Joy G, Patzakis MJ, Harvey JP. Precise evaluation of the reduction of severe ankle fractures. J Bone and Joint Surg. 1974;56(5):979–93.
- Burwell HN, Charnley AD. The treatment of displaced fractures at the ankle by rigid internal fixation and early joint movement. *J Bone and Joint Surg.* 1965;47(4):634–60.
- Boden SD, Labropoulos PA, Mccowin P, Lestini WF, Hurwitz SR. Mechanical considerations for the syndesniosis screw. A cadaver study. J Bone Joint Surg Am. 1989;71(10):1548–55.
- Bray TJ, Endicott M, Capra SE. Treatment of open ankle fractures. Immediate internal fixation versus closed immobilization and delayed fixation. *Clin Orthop Relat Res.* 1989;(240):47–52.
- Yablon IG. The key role of the lateral malleolus in displaced fractures of the ankle. J Bone Joint Surg. 1977;59(2):169–73.
- Mcdaniel WJ, Wilson FC. Trimalleolar fractures of the ankle. An end result study. *Clin Orthop*. 1977;(122):37–45.
- Finsen V, Saetermo R, Kibsgaard L, Farran K, Engebretsen L, Bolz KD, et al. Early postoperative weight-bearing and muscle activity in patients who have a fracture of the ankle. *J Bone Joint Surg.* 1989;71(1):23–7.
- Wilson FC. The pathogenesis and treatment of ankle fractures : historical studies. *Instr Course Lect*. 1990;39:73–7.

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