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Medial Clamp Tine Positioning Affects Ankle Syndesmosis Malreduction

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Abstract

Objectives—The purpose of this study was to determine if the position of the medial clamp tine during syndesmotic reduction affected reduction accuracy.

Design—Prospective Cohort.

Setting—Urban level 1 trauma center.

Patients—Seventy-two patients with operatively treated syndesmotic injuries.

Intervention—Patients underwent operative fixation of their ankle syndesmotic injuries using reduction forceps. The position of the medial clamp tine was then recorded with intraoperative fluoroscopy. Malreduction rates were then assessed with bilateral ankle computerized tomography.

Main Outcome Measurement—Fibular position within the incisura was measured with respect to the uninjured side to determine if a malreduction had occurred. Malreductions were then analyzed for associations with injury pattern, patient demographics and the location of the medial clamp tine.

Results—A statistically significant association was found between medial clamp position and sagittal plane syndesmosis malreduction. In reference to anterior fibular translation, there was a 0% malreduction rate in the 18 patients where the clamp tine was placed in the anterior third, a

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Conflicts of Interest

McAndrew	<i>Speaking Fees:</i> DePuy Synthes, AO North America, AO Trauma <i>Manuscript preparation:</i> JBJS American
Ricci	<i>Consultancy:</i> Smith & Nephew, Biomet, Stryker, Wright Medical <i>Royalties:</i> Smith & Nephew, Wright Medical, Lippincott <i>Research Support:</i> Smith & Nephew <i>Manuscript preparation:</i> JBJS American
Gardner	<i>Consultancy:</i> DePuy Synthes, Stryker, DGIMed, BoneSupport AB, Pacira Pharma, KCI <i>Royalties:</i> Lippincott <i>Research Support:</i> DePuy Synthes <i>Manuscript preparation:</i> JBJS American

The remaining authors (Cosgrove, Putnam, Cherney, Spraggs-Hughes) have no conflicts to report.

Level of Evidence : Prognostic Level IV

19.4% malreduction rate in the middle third and 60% malreduction rate in the posterior third ($p = 0.006$). In reference to posterior fibular translation, there was a 11.1% malreduction when clamp placement was in the anterior third, a 16.1% malreduction rate in the middle third and 60% malreduction rate in the posterior third ($p = 0.062$). There were no significant associations between medial clamp position and coronal plane malreductions (over- or under-compression) ($p = 1$).

Conclusions—When using reduction forceps for syndesmotic reduction, the position of the medial clamp tine can be highly variable. The angle created with off-axis syndesmotic clamping is likely a major culprit in iatrogenic malreduction. Sagittal plane malreduction appears to be highly sensitive to clamp obliquity, which is directly related to the medial clamp tine placement. Based on these data, we recommend placing the medial clamp tine in the anterior third of the tibial line on the lateral view to minimize malreduction risk.

Keywords

syndesmosis; malreduction; ankle fractures

INTRODUCTION

Injuries to the distal tibiofibular syndesmosis are common and are estimated to occur in up to 23% of all ankle fractures¹ and between 5 and 11% of all ankle sprains.^{2,3} A wide body of literature suggests that functional outcomes in these patients are largely dependent on the ability to obtain and maintain an anatomic reduction of the syndesmosis and ankle mortise.^{4–10} Despite the established importance of an anatomic reduction, syndesmotic malreduction occurs at a surprisingly high rate. Studies have reported malreduction rates ranging from 16% to 52% of patients.^{10–13} Off-axis clamping and screw trajectory,^{14–16} along with difficult intra-operative radiographic reduction assessment, are commonly cited factors for such high malreduction rates.^{3,17,18} The use of computed tomography (CT) scanning has been validated as a more reproducible and sensitive means of assessing the accuracy of syndesmotic reductions.^{19,20}

The historic standard for syndesmotic fixation has been the use of trans-syndesmotic screws after reduction with a clamp. Alternative techniques, like the suture-button, have been developed to allow for physiologic motion during healing as well as for some degree of spontaneous “natural correction” of a potentially malreduced syndesmosis.²¹ Regardless of the type of fixation used, much interest and recent focus has been placed on attempting to find reproducible radiographic parameters for assessing intra-operative syndesmotic reduction. Although some studies have attempted to use intra-operative CT scanning as a guide to reduction,^{22,23} this technique currently has limited utility as an intra-operative measurement tool at many institutions due to availability, cost, and other prohibitive factors.

The goal of this study was to evaluate fluoroscopic parameters that may be utilized to reduce the risk of off-axis clamping and syndesmotic malreduction. Using the mortise and talar dome lateral images from the contralateral ankle as a template, we sought to analyze the effects of medial tine positioning on reduction accuracy. Our hypothesis was that medial clamp tine positioning during syndesmotic reduction would directly affect malreduction rates.

MATERIALS AND METHODS

Patients who underwent operative intervention for ankle fractures with associated syndesmotic injuries from 2013 through 2015 were prospectively enrolled in an institutional study database after Institutional Review Board approval. To be considered for inclusion into this cohort, patients must have been diagnosed with a syndesmotic injury and undergone trans-syndesmotic screw fixation. Consent for enrollment was obtained in the perioperative period. All patients were treated by one of three orthopedic traumatologists at a Level I trauma center. Operative fixation of additional fractures about the ankle was performed by standard technique. Patients were excluded from the study if they did not have a sufficient talar dome lateral fluoroscopic image clearly demonstrating clamp tine positioning, or if they lacked necessary CT imaging for contralateral ankle measurements.

At the time of analysis, the cohort of patients enrolled in the prospective syndesmotic study consisted of 72 total patients, 31 of whom were male and 41 of whom were female, with an average age of 37.6 years. After exclusion criteria were applied, the final study group consisted of 54 patients, 22 male and 32 female, with an average age of 37.3 years (range, 18–79 years). There were a variety of ankle fracture patterns in this patient population, with the most common being pronation-external rotation (AO/OTA 44-C1) and supination-external rotation types (AO/OTA 44-B2/3), as described by Lauge-Hansen.²⁴ There were no significant differences in the demographic breakdown or fracture patterns between the exclusion group and those ultimately included in the data analysis (Table 1). The 19 excluded patients either did not have a talar dome lateral fluoroscopic image that was of adequate quality for accurate measurement or was not correctly saved into their electronic medical record. Radiology technician error, and other logistical challenges associated with saving fluoroscopic images to our hospital PACS system, left us with 75% of the study population who had appropriate imaging to evaluate. Of the three participating surgeons in this cohort, surgeon 1, 2 and 3 treated 15, 24 and 15 patients, respectively. Patients were assigned to each surgeon based on operating room availability and call schedule, without exception for patient demographics or fracture complexity.

Operative Protocol

Prior to sterile preparation of the surgical field, fluoroscopic imaging was performed to obtain a mortise and true talar dome lateral view of the contralateral uninjured ankle. These images were then saved and the patient was prepped and draped. Operative fixation of the ankle fracture was performed for the malleoli where applicable. The determination of a syndesmotic injury was based on standard criteria using ankle stress radiographs showing widening of the tibiofibular clear space using an intraoperative dynamic Cotton or external rotation stress test.^{25,26} If the syndesmosis was unstable, reduction and fixation was performed. Clamp reduction of the syndesmosis was achieved by placing the lateral clamp tine on the fibular tubercle, or on a screw head if the fibular tubercle was inaccessible. The medial clamp tine was placed on the distal tibia in accordance to each surgeon's standard technique. An ankle mortise view was then obtained to judge the restoration of anatomic landmarks relative to the uninjured side, including fibular length and rotation. The anterior-posterior relationship of the fibula and tibia on the talar dome lateral was also compared to

the contralateral side to judge reduction in the sagittal plane.²⁷ If necessary, the surgeon's positioning of the medial clamp tine was adjusted in the sagittal plane until a satisfactory reduction was felt to be achieved on both the mortise and lateral fluoroscopic views. Syndesmotic fixation was then performed using a minimum of three cortices and up to two screws per the individual surgeon's preference.

Post-operatively, bilateral ankle CT scans were then performed to evaluate the syndesmotic reduction. At our institution, these scans have been established as standard of care to assess syndesmotic reduction, requiring no external source of funding. Various standardized measurements were taken according to parameters previously described by Nault et al.¹⁹ (Figure 1). These measurements were chosen to provide an accurate description of the fibula's position in relation to the incisura. Measurement A was recorded as the distance between the most anterior part of the incisura and the nearest most anterior point on the fibula. Measurement B was recorded as the distance between the most posterior point of the incisura and the nearest most posterior point of the fibula. Lastly, measurement C was recorded as the distance between the tibia and the fibula in the middle of the incisura and was helpful in determining the degree of compression present. Sagittal malreduction of the fibula was correlated most closely with measurements A and B. Malreduction was defined as a difference of 2mm between the injured and uninjured sides on any of the CT scan measurements. Although the exact tolerance for clinically significant malreduction is unknown, these criteria were based on previous studies and were thought to provide a high sensitivity for malreduction in any plane.^{8,28,29}

Next, the intra-operative fluoroscopic radiograph of the talar dome lateral was used to measure the position of the medial clamp tine relative to the anterior-posterior dimension of the distal tibia (the "tibial line", Figure 2). The ratio of these distances was then used to group tine position into anterior, middle and posterior thirds of the total width of the tibia. This breakdown was chosen to provide meaningful statistical analysis and also to provide a basis for clamp positioning recommendations that could easily be reproduced by the surgeon after results were interpreted. Two investigators who did not directly participate in the care of the patients performed all radiographic and CT measurements. In an attempt to reduce study bias, data from both the injured and uninjured ankle CT scans, as well as intraoperative fluoroscopy measurements, were collected in a blinded fashion independently of each other. CT measurements were not repeated between investigators as excellent interobserver reliability scores have been described in the literature.¹⁹ Fluoroscopic measurements were performed by a single investigator in this study design.

Statistical Methods

A Fisher's exact test was performed to assess statistical association between medial clamp tine placement on intraoperative fluoroscopy and malreduction, as well as other categorical variables in our data. A 2mm threshold for each CT measurement was utilized to define a malreduction in any plane. A student's t-test was utilized to determine significance in number of cases performed by each participating surgeon.

Source of Funding

No external funding was received for this study.

RESULTS

In all patients, the average position of the medial tine along the tibial line was $40 \pm 18.4\%$ of the anterior-posterior distance starting from the anterior tibial cortex. The tibial line was divided into thirds. In 18 patients (33.3%), the clamp was placed in the anterior third of the tibial line; in 31 (57.4%) the clamp was placed in the central third, and in 5 (9.3%) the clamp was in the posterior third. There was no significant difference between the three treating surgeons regarding their individual average placement of the medial clamp tine along the tibial line. Although our data demonstrates an increased number of cases performed by surgeon 2 ($p = 0.027$), this is likely an artifact of enrollment and participation in our prospectively collected patient database, and not representative of surgeon predilection for ankle fractures. Surgeons 1, 2 and 3 averaged 47%, 34% and 42%, respectively, which was not statistically significant ($p = 0.552$). Of the ankles determined to have no malreductions in the sagittal plane, the average location of the medial clamp tine was $36\% \pm 15\%$ along the tibial line.

For measurement A, there were significantly fewer sagittal plane malreductions when the medial tine was placed in the anterior third of the tibial line (0%), compared to tine placement in the central third (19.4%) and posterior third (60%) ($p = 0.006$) (Figure 3). For measurement B, there was an 11.1% sagittal plane malreduction rate when the medial tine was placed in the anterior third of the tibial line, and sagittal plane malreduction rates of 16.4% and 60% when placed in the middle and posterior thirds, respectively. Although this trend was similar to that seen with measurement A, this did not reach statistical significance ($p = 0.062$) (Figure 3). Finally, for measurement C, there was an 11.1% malreduction rate when the medial tine was placed in the anterior third of the tibial line, a 12.9% malreduction rate when placed in the middle third, and a 0% malreduction rate when placed in the posterior third. There was no statistical association between these malreduction rates ($p = 1$) (Figure 3).

Additionally, there was no statistical difference between the malreduction rates in Weber B and Weber C fracture types in Measurements A ($p = 0.54$), Measurement B ($p = 0.55$) or Measurement C ($p = 0.34$). Furthermore, we found no correlation between the rates of malreduction and degree of syndesmotic instability (frank versus stress-positive) for Measurements A ($p = 0.724$), B ($p = 0.169$) or C ($p = 0.413$). Our study was not sufficiently powered for a meaningful statistical analysis of the relationship between the Lauge-Hansen pattern and malreduction rates.

The overall malreduction rate was 16% based on Measurement A, 18.5% based on Measurement B, and 11.1% based on Measurement C (Table 2). Malreduction rates were then stratified by participating surgeons, who had similar overall malreduction rates (33%, 37%, and 33% for surgeons 1, 2 and 3, respectively.) This data was underpowered to derive a meaningful statistical analysis but there is no evidence to support that surgeon or patient-specific factors influenced reduction accuracy.

DISCUSSION

Precise reduction of the ankle syndesmosis is crucial to restoring function and optimizing outcomes for patients with these injuries.^{4–10} Malreduction may lead to increased contact pressures and early degenerative changes of the ankle joint.^{8,30} Although some recent literature disputes the clinical importance of a 2mm malreduction threshold,³¹ surgeons should still strive to achieve as optimal of a reduction as possible without the routine use of advanced imaging to assess reduction in the axial plane. In this study, we utilized the talar dome lateral fluoroscopic view as a reproducible and readily available template to study the effects of medial clamp tine placement on syndesmotic malreduction. While the placement of the lateral tine was relatively fixed on the fibular ridge, we observed a wide variability with regard to the placement of the medial tine. Medial tine placement in the anterior third of the tibial line on the lateral view resulted in a statistically significant decrease in the malreduction rate in measurement A and the lowest malreduction rate in measurement B, as determined by validated measurements on CT imaging. Utilization of this approach allows for purposeful and reproducible placement of the medial clamp tine, which may decrease malreduction rates when indirect reduction with forceps is performed.

Achieving anatomic reduction of the syndesmosis has proven to be difficult, as evidenced by the consistently high malreduction rates in recent literature.^{10–14,32} The primary goal for improving syndesmotic injury treatment should be focused on finding methods that promote intraoperative anatomic reduction and secure fixation until healing occurs.³³ However, because of the high rates of malreduction following syndesmotic screw fixation, other fixation techniques, like the suture-button, have evolved to provide fixation without requiring initial anatomic reduction due to its self-centering effect.^{34–36} Despite early studies that report favorable outcomes data,^{34–36} it is still unknown whether or not the same laxity may also predispose to loss of reduction.³² Biomechanical studies have shown more anterior-posterior, rather than lateral, instability in syndesmotic injuries, reaffirming the importance of correct positioning in the sagittal plane.³⁷ Malreduction in this plane has been attributed to an incorrect clamping vector, eccentric trans-syndesmotic screw placement, or an incompetent posterior malleolus.¹⁴

Other reduction techniques, including the use of direct visualization of syndesmotic reduction, have improved, but not solved, the issue of malreduction rates.^{10,11} Whether or not open reduction internal fixation of the syndesmosis under direct visualization leads to improved reduction rates is a subject of current debate. Further studies will be needed to delineate the superiority of anatomic reduction techniques with direct visualization, isolated trans-syndesmotic stabilization, or a combination thereof. However, at this time both techniques are supported by the literature and commonly used in practice. The overall malreduction rate and injury patterns in our cohort is consistent with those previously reported in the literature.

Intraoperative CT is not widely available, and has not been shown to improve rates of malreduction.²⁹ Additionally, the lack of reliable radiographic parameters when using fluoroscopy hinders reduction accuracy. None of the 39% of patients who had malreduction in the study by Sagi et al. had intraoperative or postoperative radiographs suspicious for

malreduction.¹⁰ In a recent study, four orthopaedic trauma surgeons were able to identify a correct reduction only 68% of the time when analyzing the contralateral ankle lateral fluoroscopic view.⁴¹

There has yet to be a standardized approach to consistently achieve anatomic reduction exclusively using intra-operative fluoroscopy. Summers et al. described their technique of using contralateral mortise and lateral talar dome fluoroscopic views to create a template on which to evaluate the accuracy of their reduction.²⁷ Despite their promising results in a small cohort of patients, this study stops short of describing quantitative data that could aid in its reproducibility.

Similar to the methodology described by Summers et al., we used the uninjured ankle mortise and talar dome lateral fluoroscopic views as a template for the reduction of the injured syndesmosis. Postoperatively, we utilized three standardized measurements described previously in the literature to evaluate sagittal plane malreduction (A and B) and over-compression (C).¹⁹ Our results demonstrated a significantly lower sagittal plane malreduction rate with medial clamp tine placement in the anterior third of the tibia, as visualized intraoperatively with a true talar dome lateral fluoroscopic image. Conversely, malreduction rates in the sagittal plane were highest when the clamp tine was placed in the posterior third of the tibial line. Whether used to obtain or simply maintain a syndesmotic reduction, an incorrect clamping vector that deviates from the trans-syndesmotic axis may ultimately induce a malreduction.

The results of this study are consistent with the work of Lepojarvi et al. who reviewed 107 uninjured CT scans of the ankle and determined that the fibula was situated anteriorly or centrally within the incisura 97% of the time. In that same study, 67% were found to be anteriorly translated within the incisura and not centrally located.³⁸ Therefore, placing the medial clamp tine in an anterior position relative to the tibia should provide a more anatomically accurate clamping axis in the majority of ankles. This trajectory may also explain why statistical significance was reached in Measurement A when the medial clamp tine was placed in the anterior third, which would more adequately restore the distance between the fibula and anterior edge of the incisura. The lack of statistical significance in Measurement B when the clamp tine was placed in the anterior third may be attributable to an internal rotational change from a “too anterior” vector, which would potentially increase the distance between the fibula and posterior incisura. Whether this rotational change is primarily influenced by the instability imparted by the rotational injury or an inaccurate clamping vector cannot be concluded from our data.

Our study was underpowered to detect a range of clamp positions “too anterior,” thus causing increased susceptibility to a malreduction in Measurement B. Although our lowest malreduction rates occurred when the medial clamp tine was placed in the anterior third position, one must take caution in extreme anterior clamping along the tibial line. Clamping more anterior than a standard deviation from the average location where no malreductions occurred (ie. more anterior than 11% along the tibial line) may pose an increased risk for this type of malreduction. A larger number of patients would need to be enrolled to make this statistical assessment.

Malreduction by translation or rotation can occur with clamping in a non-centroidal axis, which some authors suggest passes between the lateral apex of the fibula and the region of the medial malleolus just anterior to its midline.¹⁶ In our methods, we primarily utilized the lateral fibular ridge when available, or a closely adjacent screw head in a posterolateral plate as a consistent fibular landmark that could be placed under direct visualization. It has historically been suggested that screw fixation should be at thirty degrees relative to the coronal plane of the ankle.³⁹ However, given the high degree of anatomic variability of the syndesmosis, without prior knowledge of an individual's precise anatomic location of the uninjured fibula within the incisura, it is possible that we may only be able to optimize the malreduction rate, rather than completely eliminate it.^{16,38,40}

It was also notable that there was a remarkably high variation in the medial clamp tine positioning in this sample set, despite being performed by orthopaedic traumatologists with significant experience in treating these injuries. This indicates the importance of developing useful and accurate intraoperative techniques for purposeful positioning of the medial clamp tine that can be verified with fluoroscopy. The necessity of clamping in a correct vector has been well-established,^{14,16} but without prior knowledge of where this axis may lie relative to a true talar dome lateral, positioning of the medial clamp tine can be highly variable.

Limitations of this study include a small sample size that prohibits more sophisticated statistical evaluation of the data, particularly those in which the medial clamp tine placed in the posterior third of the tibial line. Another weakness of this study is the moderate proportion (25%) of patients in the original cohort who did not have talar dome lateral fluoroscopic image available and were thus excluded from data analysis. However, we failed to identify any demographic or fracture characteristics that were significantly different between this group and those who were included in the study. Therefore, there is a low likelihood that the excluded group introduced any specific bias that could skew our final statistical analysis.

Another weakness of this study is the possibility for measurement variability when pelvic reduction forceps with a ball and spike configuration were used. Clamp obliquity inherently radiographically obstructs the exact position of the spike within the projection of the ball on the lateral view. However, these subtle measurement irregularities would not expect to produce meaningful changes in the overall clamp vector.

The surgical protocol for achieving and maintaining syndesmotic reduction, as detailed above, was followed for all patients. However, this study provided for some inherent biases with regard to surgeon preference for syndesmotic reduction within the generalized protocol. While there was no meaningful difference between the malreduction rates among the three participating surgeons, minor surgeon-specific variabilities regarding the diagnosis of syndesmotic disruption and surgical techniques may have some unappreciated influence on our study results. Therefore, there is a low likelihood that the excluded group introduced any specific bias that could skew our final statistical analysis.

In this cohort we analyzed only linear reduction parameters, which may serve as a proxy for, but does not provide a complete assessment of, rotational changes of the fibula within the

incisura. Additionally, while there is potential for bias regarding surgeon assignment, we believe this is very minimal as patients were assigned to surgeons on a rotating basis based on the call schedule. Other potential bias includes measurement error and the inherent difficulties in accurately performing radiographic measurements, especially with magnitudes within 1mm. We attempted to compensate for this by blinding assessments by two investigators who were not involved in treating these patients.

CONCLUSIONS

When using reduction forceps for syndesmotic reduction, the position of the fibular clamp tine is relatively constrained by the small size of the fibula, but the position of the medial clamp tine can be highly variable. The eccentric angle created with off-axis syndesmotic clamping is likely a major culprit in the previously reported high iatrogenic malreduction rates. A true talar dome lateral image during intraoperative fluoroscopy creates a reproducible template on which deliberate medial clamp tine positioning can be performed. Sagittal plane malreduction appears to be highly sensitive to clamp obliquity, which is directly related to the medial clamp tine placement. Moreover, clamp tine placement in the anterior third of the tibia, as seen on a talar dome lateral, may contribute to lowering the rate of off-axis clamping and ultimately syndesmotic malreduction. Regardless of the type of syndesmotic fixation chosen, it is critically important to develop intraoperative guidance for clamp positioning to reduce the unacceptably high rate of syndesmotic malreduction.

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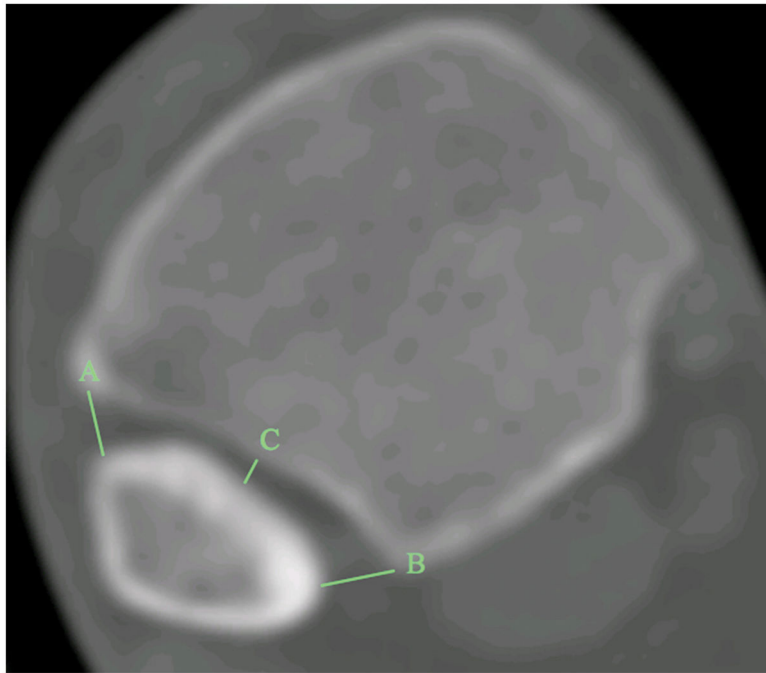


Figure 1.

Sample axial CT image 1cm above the tibial plafond with measurements of the ankle syndesmosis as described by Nault et al. Distance A: between the most anterior point of the incisura and the nearest most anterior point of the fibula. Distance B: between the most posterior point of the incisura and the nearest posterior point of the fibula. Distance C: between the tibia and fibula in the mid-point of the incisura.



Figure 2.

Talar dome lateral view using intraoperative fluoroscopy. The distance from the medial clamp tine (white dot) to the anterior tibial cortex (distance A) was divided by the anteroposterior width of the tibia (green line). This ratio was then used to group the tine position into anterior, middle and posterior thirds.

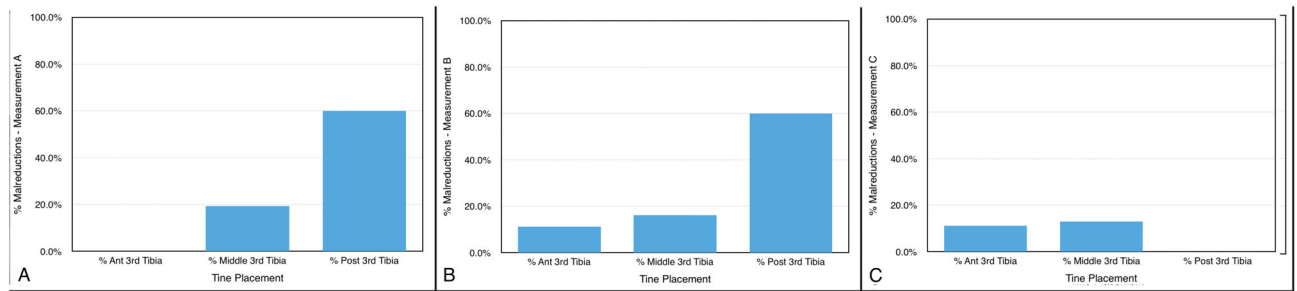


Figure 3.

A. Percentages of anterior (measurement A) syndesmotic malreductions recorded when the medial clamp tine was positioned in the anterior, middle and posterior third of the tibia. **B.** Percentages of posterior (measurement B) syndesmotic malreductions recorded when the medial clamp tine was positioned in the anterior, middle and posterior third of the tibia. **C.** Percentages of central (measurement C) syndesmotic malreductions recorded when the medial clamp tine was positioned in the anterior, middle and posterior third of the tibia.

Table 1

Patient Demographic and Injury Data

	Included Cohort	Excluded Cohort	P value
Total Number	54	18	
Average Age	37.3 (18–79)	38.3 (18–60)	p = 0.796
Sex			p = 0.492
Male	22	9	
Female	32	9	
BMI	31.6	31.9	
% Tobacco Use	48.1%	33.3%	p = 0.273
% Comorbid Conditions	61.1%	61.1%	p = 1.0
Side			p = 0.496
Right	25	10	
Left	29	8	
Lauge-Hansen Injury Pattern			p = 0.562
PER III	2	0	
PER IV	15	7	
SER IV	20	7	
PA III	4	3	
SAD III	1	0	
Other	11	1	
Maisonneuve			

	Included Cohort	Excluded Cohort	P value
AO 43-C1	1	0	
Weber Classification			p = 0.377
A	0	0	
B	17	9	
C	37	9	
AO/OTA			p=0.506
44-B2	13	3	
44-B3	8	4	
44-C1	17	7	
44-C2	4	3	
44-C3	11	1	
43-C1	1	0	
% Posterior Malleolus Fracture	38.8%	38.8%	p = 1.0
% Posterior Malleolus Fixed	16.7%	28.5%	p = 0.393
Avg Number of Trans-syndesmotic Screws	1.43	1.50	p = 0.858

Table 2

Dichotomous Groups of >2 mm Absolute Change Between Injured and Uninjured Sides

Measurement	Anterior Third (N = 18)	Middle Third (N = 31)	Posterior Third (N = 5)	P Value
A	0 (0%)	6 (19.4%)	3 (60%)	0.006
B	2 (11.1%)	5 (16.1%)	3 (60%)	0.062
C	2 (11.1%)	4 (12.9%)	0 (0%)	1