

Reamed Versus Unreamed Intramedullary Nailing of the Femur: Comparison of the Rate of ARDS in Multiple Injured Patients

By The Canadian Orthopaedic Trauma Society

Objective: To compare the rate of Acute Respiratory Distress Syndrome (ARDS) in multiply injured patients with femoral shaft fractures, treated with intramedullary femoral nails inserted with or without reaming.

Design: Prospective, randomized, multicenter, clinical trial.

Setting: Seven Level 1 trauma centers.

Patients: Three hundred fifteen patients with 322 femoral shaft fractures were stratified into 2 groups according to their estimated injury severity scores ($ISS \geq 18$ vs. $ISS < 18$) and then randomized to receive an IM nail with either reamed or unreamed insertion for primary stabilization of their femoral shaft fracture. One hundred forty seven patients with 151 fractures received an unreamed nail whereas 168 patients with 171 fractures, received a reamed nail. All fractures were nailed within 24 hours after their trauma.

Intervention: Closed intramedullary nailing for femoral shaft fractures.

Main Outcome Measurements: Determination of the rate of ARDS in patients undergoing intramedullary nailing of femoral shaft fractures.

Results: Three of the 63 multiply injured patients who received a reamed nail developed ARDS as compared with 2 out of 46 patients in the unreamed group. This difference was not statistically significant ($P = 0.42$). (The power for this difference is only 5%. 39,817 patients are needed in each group to detect a difference that small.) This difference was not statistically significant. There were a total of 4 deaths, 2 each in both the reamed and unreamed group. No death resulted from ARDS.

Conclusions: The overall incidence of ARDS was found to be low with primary stabilization of femoral shaft fractures with intramedullary nailing. There was no difference in the incidence of ARDS between the reamed and unreamed groups, given the sample size.

Key Words: femoral fractures, ARDS, intramedullary nailing, reaming

(*J Orthop Trauma* 2006;20:384–387)

Accepted for publication March 31, 2006.

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Supported by Synthes Canada, Calgary General Hospital, Foothills Hospital, AO North America, Alberta Heritage Foundation, Canadian Orthopedic Foundation.

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Closed locked intramedullary nailing is now the procedure of choice for the treatment of femoral shaft fractures. This procedure has been shown to result in high union rates and very good functional outcomes.¹

Several prospective and retrospective studies have shown that early stabilization of femoral shaft fractures within 24 hours of injury in patients with multisystem trauma results in better outcomes with both lower mortality rates and reduced incidence of pulmonary dysfunction and acute respiratory distress syndrome (ARDS).^{2–6}

In 1993, Pape et al⁷ challenged the wisdom of early femoral shaft stabilization in patients with significant pulmonary injury. In their retrospective study, a higher mortality and pulmonary morbidity was found in patients with significant chest trauma who received intramedullary fracture stabilization within 24 hours. A second publication by the same group⁸ reported an investigation of

reamed and unreamed insertion of intramedullary nails in multiple trauma patients. On the basis of their examination of lung function and pulmonary hemodynamics, the authors concluded that nails inserted without canal reaming offered a potentially better solution to reduce the risk of ARDS.

A number of subsequent publications have examined the timing and technique of fracture stabilization in polytrauma patients.⁷⁻¹⁸ Bosse et al¹⁰ reported a retrospective review of patients from 2 trauma centers who had femoral shaft fractures and AIS grades of chest injury similar to those in Pape's series. All fractures were stabilized within – 24 hours. Their rate of ARDS and the mortality rate were lower than the rate reported by Pape.

Pape's report was a retrospective, nonrandomized study. His conclusions seemed to be different from that of North American surgeons. Therefore, the Canadian Orthopedic Trauma Society undertook a prospective randomized, multicenter trial to evaluate the risk of ARDS and mortality in multiply injured patients with a fractured femoral shaft treated with intramedullary nailing.

METHODS

The study was a prospective randomized multicenter trial involving 7 level 1 trauma centers. Approval at each of the centers was received from the Research, Development and Ethics Committees.

Inclusion criteria for the study required a femoral shaft fracture, defined proximally from 1 cm distal to the lesser trochanter and distally no further than 6 cm from the distal physal scar. The time from injury to the initiation of the nailing was by design, less than 24 hours. The minimum canal diameter measurement required was 9.0 mm or greater using a preoperative template. All fractures were in patients that were skeletally mature. Exclusion criteria included a medical contraindication to surgery; history of myocardial ischemia; previous injury in the form of either a dislocation or severe fracture of the ipsilateral extremity with residual impairment of function; grade IIIB open fractures greater than 8 hours from the time of the injury; grade IIIC open fractures; and inability to obtain outpatient follow-up.

After obtaining informed consent, the eligible patients were stratified according to the estimated injury severity score (ISS). A determination was made as to whether the patient had a single system injury with an ISS less than 18 or an ISS greater than or equal to 18. The patients were then assigned to either a reamed or unreamed canal preparation group by drawing from sequentially marked, sealed envelopes. Patients with bilateral fractures were randomized once and the same technique was used for both femurs.

Reamed nailing was defined as insertion of the largest possible intramedullary nail after canal preparation by progressive reaming of the medullary canal until cortical chatter. Unreamed nailing was defined as insertion of a best-fit intramedullary nail, without any preparation of the medullary canal.

No distal femoral vent was used for either arm of the study. In the unreamed group, a Synthes (Davos, Switzerland) solid titanium nail was inserted without a guide rod. In the reamed group, a number of implants were used including Russell-Taylor femoral nail (Smith and Nephew Richards, Memphis, TN), Synthes universal femoral nail (Synthes USA, Paoli, PA), Grosse-Kempf nail (Howmedica, NJ) and ZMS (Zimmer, Warsaw, IN). All implants were FDA approved.

For data collection, standard demographic data was collected and details both about the injury to the limb, additional musculoskeletal or injuries, and other system injuries. Arterial blood gases were taken from both ventilated and nonventilated patients to determine the PaO₂. If the patient was not on a ventilator or a Venturi type mask, the patient remained off oxygen for 20 minutes before drawing blood for oxygenation assessment to ensure sufficient time for the PaO₂ to equilibrate. A baseline blood gas was obtained preoperatively and repeated 1 hour postoperatively and on postoperative days 1, 2, and 3. Particular attention was paid to the pulmonary complications.

Definitions

1. ARDS was defined as per the criteria outlined by the 1994 American-European consensus conference on ARDS¹⁷ and consisted of (a) acute onset, (b) bilateral chest infiltrate, (c) pulmonary artery occlusion pressure of 18 mm of Hg or less and no evidence of left atrial hypertension, (d) impaired oxygenation regardless of the level of positive end-expiratory pressure, and (e) a PaO₂/FIO₂ ratio of less than 200.
2. Pneumonia was defined by the formula as either A + B, B + C + D + E or B + F and 2 of C, D or E, where, (A) is positive blood or pleural cultures for the same microorganisms recovered in the tracheal aspirate, (B) new or progressive pulmonary infiltrate, (C) fever with temperature > 38°C (D) leucocytosis > 10,000/mm³, (E) sputum gram stain with > than 10 polymorphonuclear cells per high power field, (F) no other source of infection but the lungs.

Statistical Methods

As the clinical data available at the time had shown a very low rate of pulmonary complications after intramedullary nailing of femoral shaft fractures³, an impractically large sample size of 5000 patients in each group was deemed necessary to detect significant difference in the rate of pulmonary complications between the 2 groups.

Bone et al³ has demonstrated that 21.6% of patients who underwent a reamed nailing showed a decreased PaO₂ within 2 hours of the procedure as determined by blood gases. He considered this desaturation as an indicator of compromised pulmonary function.

With the assumption that 22% of patients who would receive a reamed nail would demonstrate desaturation, with $\alpha = 0.05$ and a power of 80%, 199 patients were required in each treatment arm. A drop out or loss to

follow-up rate of 10% was anticipated and hence a sample size of 220 patients would be needed in each group to detect significant difference.

χ^2 and Man-Whitney *U* tests were used to compare categorical outcomes by treatment and Student *t* test was used for continuous outcomes. As a secondary analysis bivariate testing was used to evaluate smoking, chest AIS, ISS and preoperative O₂ ratio, and age as factors that might be associated with development of ARDS. Logistic regression was used to model ARDS as a function of these variables including all 2-way and 3-way interactions.

Materials

Three hundred fifteen patients with 322 femoral shaft fractures were enrolled in the study between April 1, 1995 to February 28, 1999 across the 7 participating centers. There were 7 patients with bilateral fractures. One hundred forty seven patients with 151 fractures received unreamed nails. Forty-six had ISS \geq 18 and 101 had an ISS < 18. One hundred sixty eight patients with 171 fractures received a reamed nail. Sixty-three had an ISS \geq 18 and 105 had an ISS < 18. The 2 groups were found well-matched in their average age, sex, and injury severity scores (Table 1).

RESULTS

The rate of ARDS (5/315) and deaths (4/315) were low in this series of 315 patients. Three patients in the reamed group developed ARDS as compared with 2 in the unreamed group (*P* = 0.42). There were 2 deaths each in the reamed and unreamed group. No patient with ARDS died. Four out of the 5 patients who developed ARDS and all 4 patients who died had an ISS > 18. Of the 4 patients who developed ARDS in the group with ISS > 18, 3 received a reamed nailing and 1 received an unreamed nailing. There was only 1 case of ARDS and no deaths in the group with ISS < 18. The patient who developed ARDS in the ISS < 18 group received an unreamed nail. None of the patients who received a reamed nail in this group developed ARDS.

None of the 7 patients with bilateral fractures developed ARDS or died.

Bivariate testing was carried out for chest AIS (*P* = 0.13), PaO₂/FI₀₂ ratio (*P* = 0.82), and ISS (*P* = 0.27). None of these were found to be predictive of the development of ARDS.

DISCUSSION

The timing of femoral fracture stabilization in multiply injured patients is still controversial. Investigators

have examined the relationship of ARDS in femoral fractures stabilization and concluded that the injury to the chest cavity is the primary predictor of the development of ARDS and not the timing of femoral fracture stabilization.^{9,20} Pape’s article indeed showed that the chest injury was the most significant predictor of the development of ARDS.

Bosse and coauthors¹⁰ performed a retrospective review of the experience in 2 trauma centers with established trauma registries. Both centers treated a large number of patients with chest injury and associated femur fractures over the study period. Both centers had similar and notably lower rates of ARDS when compared with Pape’s series. There was one major difference between the 2 centers. The trauma center in Baltimore performed reamed intramedullary nailing, whereas the center in Pittsburgh performed primary stabilization by plating. Interestingly, there was no difference in the rate of ARDS between the 2 groups. A comparison of Pape’s group results with Bosse’s group and our own series (Table 2) shows the number of cases, who developed ARDS. Note the groups were comparable in that all had patients with chest injuries had an AIS \geq 2 and all had femoral shaft fractures, which were stabilized within 24 hours.

The rate of ARDS is clearly much lower in the reported North American series. Pape’s series, however, reports the results of a series of patients treated in the mid 1980s, which may explain the higher rate of ARDS and the higher mortality. A treatment bias may exist in Pape’s series as no rationale for assigning treatment to the early and late groups was given. Patients who were too ill to undergo early intramedullary nailing or plating were not reported in Bosse’s paper. His results, therefore represent only the “best cases,” that is, those patients who were physiologically able to withstand early surgery and may represent a selection bias. Pape’s series of consecutive patients reports the results of all patients and, therefore, does not have a selection bias.

The rate of ARDS, our primary outcome measure, was low in both the unreamed and reamed categories. The overall incidence of ARDS was only 3.7% in the multiply injured patients. There were no mortalities in our series in patients with multiple injuries from ARDS. The small number of patients that developed ARDS limits our ability to draw any conclusions from this. Within these limitations, we were unable to find significant difference in the rate of ARDS between reamed and the unreamed group. Certainly treatment of ARDS over the years has changed, and a reduction in the mortality rate has been noted.²¹

TABLE 1. Demographics Our Study

Groups	Reamed	Unreamed
Age	31.9	31.0
ISS	17	16
Male to female ratio	2.3:1	3.82:1

TABLE 2. Comparison of Pape’s, Bosse’s, and Our Study

Series	Number	ISS	ARDS	Deaths
Pape’93	24	33	8	5
Bosse’97 nail	117	30	3	3
Bosse’97 plate	104	28	1	2
COTS’00 reamed	28	27	3	1
COTS’00 unreamed	23	30	1	1

Our series was prospective and randomized but not a consecutive series. The rate of enrollment at each center was different. No record was made of the number of patients who were potential candidates for the study and were excluded and, therefore, we cannot determine whether those who declined enrollment had a patient profile and injury pattern similar to those who enrolled. Enrollment for the study was limited to those cases where consent was obtained from patient or by proxy. We note that a comparison of our unreamed nail series against the historical control in Pape's series would in fact have led to statistically significant difference in the rate of ARDS. This points out the difficulty with historical as opposed to concurrent controls.

Although our report does not indicate a reduced rate of ARDS using unreamed nailing, there may be enough difference in the biology at the molecular level between reamed and unreamed nailing to justify unreamed nailing if one elects to perform primary intramedullary nailing. Work by Giannoudis et al²² investigated the activity at the molecular level in patients with femoral shaft fractures treated by intramedullary nailing. The authors were able to demonstrate a measurable second hit manifested by an increase in serum IL6 and elastase levels which are known pro-inflammatory markers. These changes are of concern and may indicate that the risk of ARDS could be increased by nailing. Further work will need to be performed to explore this pathway.

In conclusion, the rate of ARDS and mortality in patients requiring intramedullary nailing is low even in the presence of multiple injury and chest injury. We noted no obvious detectable difference in the rate of ARDS whether intramedullary nails were inserted with or without reaming. As a result, the Canadian Orthopedic Trauma Society believes there is no clinical data to support a change in the current practice of primary stabilization of femoral fractures with reamed intramedullary nails, although subsequent investigations at a molecular level may lead to a different understanding of this process.

REFERENCES

- Scalea TM, Boswell SA, Scott JD, et al. External fixation as a bridge to intramedullary nailing for patients multiple injuries and femur fractures: damage control orthopedics. *J Trauma*. 2000;48:613–621.
- Berhman SW, Fabian TC, Kudsk KA et al. Improved outcome with femoral fractures: early versus delayed fixation. *J Trauma*. 1990;30:792–797.
- Bone LB, Johnson KD, Weigelt J, et al. Early versus late stabilization of femoral fractures: a prospective randomized study. *J Bone Joint Surg*. 1989;71A:336–340.
- Goris R, Gimbrere J, Van Niekerk J, et al. Early osteosynthesis and prophylactic mechanical ventilation multi-trauma patients. *J Trauma*. 1982;22:895.
- Johnson KD, Cadambi A, Seilbert B. Incidence of adult respiratory distress syndrome in patients with multiple musculoskeletal injuries; effect of early operative stabilization of fractures. *J Trauma*. 1985;25:375–381.
- Meek RN, Vivoda EE, Pirani S. Comparison of mortality of patients with multiple injuries according to type of fracture treatment—a retrospective age and injury matched series. *Injury*. 1986;17:2–4.
- Norris BL, Patton WC, Rudd JN Jr, et al. Pulmonary dysfunction in patients with femoral shaft fracture treated with intramedullary nailing. *J Bone Joint Surg Am*. 2001;83-A:1162–1168.
- O'Brien PJ. Fracture fixation in patients having multiple injuries. *Can J Surg*. 2003;46:124–128.
- Bone LB, Anders MJ, Rohrbacher BJ. Treatment of femoral fractures in the multiply injured patient with thoracic injury. *Clin Orthop*. 1998;347:57–61.
- Bosse MJ, MacKenzie E, Riemer BL, et al. Adult respiratory distress syndrome, pneumonia, and mortality following thoracic injury and a femoral fracture treated either with intramedullary nailing with reaming or with a plate. *J Bone Joint Surg*. 1997;79-A:799–808.
- Boulanger B, Stephen D, Brenneman FD. Thoracic trauma and early intramedullary nailing of femur fractures: are we doing harm? *J Trauma*. 1997;43:24–27.
- Pallister I. Current concepts of respiratory insufficiency syndromes after fracture. *J Bone Joint Surg Br*. 2002;84-B:464.
- Pape HC, Auf'm Kolk M, Paffrath T, et al. Primary intramedullary femur fixation in multiple trauma patients with associated lung contusion: a cause of posttraumatic ARDS? *J Trauma*. 1993;34:540–548.
- Pape HC, Regel C, Dwenger A, et al. Influence of different methods of intramedullary femoral nailing on lung function in patients with multiple traumas. *J Trauma*. 1993;34:540–547.
- Pape HC, Hilderbrand F, Pertschy S, et al. Changes in the management of femoral shaft fractures in polytrauma patients: from early total care to damage control orthopaedic surgery. *J Trauma*. 2002;53:452–462.
- Seibel R, LaDuca J, Hasset JM, et al. Blunt multiple trauma (ISS 36), femur traction and the pulmonary failure-septic state. *Ann Surg*. 1985;202:283.
- Van der Made WJ, Smit EJM, Van Luyt PA, et al. Intramedullary femoral osteosynthesis: an additional cause of ARDS in multiply injured patients? *Injury*. 1996;27:391–393.
- Winqvist R, Hansen S, Clawson D. Closed intramedullary nailing of femoral fractures. *J Bone Joint Surg*. 1985;66A:529–539.
- Bernard GR, Artigas A, Brigham KL, et al. The American-European consensus Conference on ARDS: definitions, mechanisms, relevant outcomes and clinical trial coordinations. (review). *Am J Respir Crit Care Med*. 1994;149:818–824.
- Carlson DW, Rodman GH Jr, Kahehr D, et al. Femur fractures in chest-injured patients: is reaming contraindicated? *J Orthop Trauma*. 1998;12:164–168.
- Houston P. An approach to ventilation in acute respiratory distress syndrome. *Can J Surg*. 2000;43:263–267.
- Giannoudis PV, Smith RM, Bellamy MC, et al. Stimulation of the inflammatory system by reamed and unreamed nailing of femoral fractures. An analysis of the second hit. *J Bone Joint Surg Br*. 1999;81:356–361.