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Reaming the intramedullary canal during tibial nailing does not affect in vivo intramuscular pH of the anterior tibialis

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Objectives: Many investigations have evaluated local and systemic consequences of intramedullary (IM) reaming and suggest that reaming may cause, or exacerbate, injury to the soft tissues adjacent to fractures. To date, no study has examined the effect on local muscular physiology as measured by intramuscular pH (IpH). Here, we observe in vivo IpH during IM reaming for tibia fractures.

Methods: Adults with acute tibia shaft fractures (level 1, academic, 2019–2021) were offered enrollment in an observational cohort. During IM nailing, a sterile, validated IpH probe was placed into the anterior tibialis (<5 cm from fracture, continuous sampling, independent research team). IpH before, during, and after reaming was averaged and compared through repeated measures ANOVA. As the appropriate period to analyze IpH during reaming is unknown, the analysis was repeated over periods of 0.5, 1, 2, 5, 10, and 15 minutes prereaming and postreaming time intervals.

Results: Sixteen subjects with tibia shaft fractures were observed during nailing. Average time from injury to surgery was 35.0 hours (SD, 31.8). Starting and ending perioperative IpH was acidic, averaging 6.64 (SD, 0.21) and 6.74 (SD, 0.17), respectively. Average reaming time lasted 15 minutes. Average IpH during reaming was 6.73 (SD, 0.15). There was no difference in IpH between pre-reaming, intrareaming, and postreaming periods. IpH did not differ regardless of analysis over short or long time domains compared with the duration of reaming.

Conclusions: Reaming does not affect IpH. Both granular and broad time domains were tested, revealing no observable local impact.

Keywords: pH, tibial nailing, anterior tibialis

1. Objectives

Locked intramedullary nail stabilization has become the standard of care in the treatment of diaphyseal tibia fractures (OTA/AO type 42 A-C).[1–3] Such implants may be placed either with or without reaming of the intramedullary canal. The comparative merits of these approaches have been studied extensively in recent decades, with mixed data yielding a consensus that reamed nails are, in general, preferred for closed fractures.[2–10] Although the effects of reaming on osseus tissue are better understood, the consequences of reaming on adjacent muscular tissue remain largely unknown at this time and are the primary focus of this research.

The physiologic effects of reaming the intramedullary canal of fractured long bones are complex and varied, and the contributions of these effects remain a topic of scientific inquiry.[11,12] It is understood that the effects are both local and systemic in nature and that these effects have aspects that are both favorable and unfavorable. Reaming has been shown to improve construct stability through increases in contact area between bone and nail[13] as well as to liberate and mobilize bone autograft,[14,15] osteogenic growth factors,[16,17] and multipotent stem cells.[17–19] In addition, data from meta-analyses have demonstrated that reamed intramedullary nails are associated with lower rates of implant failure and of reoperation when used in closed fractures.[3] Other phenomena are not clearly understood to be either favorable or unfavorable, such as the increased muscular blood flow in extremities stabilized with reamed intramedullary nails, which is hypothesized to be compensatory for the reduced circulation from the damaged endosteal vascular network.[20]

Deleterious systemic effects arise from venous intravasation of reamed intramedullary contents, particularly lipids, resulting in a dysregulated inflammatory milieu[21–23] leading to hemodynamic and pulmonary dysfunction.[12,21,24–27] Local unfavorable effects include damage to the endosteal vascularity,[20,28,29] thermal injury,[30–33] and both quantitative and qualitative deficiency in bony callous formation.[34] Furthermore, and of particular relevance to the present study, reaming has been shown to generate transient (and sometimes substantial) increases in intramedullary[11,27] and muscular compartment pressures.[35–39] These data suggest that reaming may cause, or exacerbate, injury to the soft tissues adjacent

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to fracture and hypothetically add a second insult in patients already at risk for acute compartment syndrome.

To date, however, no study has examined the effect on local muscle physiology as measured by intramuscular pH (IpH). IpH is an emerging measure of soft tissue health but is not yet widely studied. Systemic acid–base status, and venous pH specifically, is a widely used marker of systemic tissue damage and of the adequacy of resuscitation after traumatic injury.[40–43] Data on local acid–base status in the tissues adjacent to injury, however, remain scarce. It has been shown that IpH decreases during in vivo simulations of acute compartment syndrome with non-invasive measurement techniques.[44] Other studies have directly measured markers of tissue physiology in ex vivo models of acute compartment syndrome, although technical factors have prevented the measurement of IpH.[45] To the best of our knowledge, there are no published data that describe the invasive measurement of IpH in vivo in the setting of fracture.

The purpose of our work was to invasively study IpH in vivo during reaming of the intramedullary canal during intramedullary nailing of tibia fractures. We hypothesized that IpH (as a direct measure of tissue physiology and a marker of soft tissue damage) would decrease during reaming and that this acidic shift may last after the completion of surgical stabilization.

These data are potentially impactful to the concept of damage control, a now widespread concept that selects the minimum necessary amount of surgery during acute care and delaying definitive, larger operations until resuscitation and physiologic stability is reached.[41,42,46] The findings of this research may alter clinical decision making in the delivery of care in patients with open fractures, severe polytrauma with systemic consequences, and acute compartment syndrome.

2. Materials and Methods

The study protocol was reviewed and approved by the local institutional review board (OHSU IRB: #00017959). Adults ages 18–89 years with acute fractures of the tibial shaft (OTA/AO type 42 A-C) treated at a single, Level 1 academic medical center between September 2019 and February 2021 were offered enrollment in an observational cohort. Patients with pathologic fractures or active infection were excluded, as were pregnant women, prisoners, and non-English speaking patients. Decisionally impaired patients (specifically including polytraumatized, obtunded, and/or intubated patients) were offered enrollment if a legally authorized representative, identified preoperatively, offered informed consent on behalf of the patient. Patients sustaining acute compartment syndrome were not included in this study. Patients sustaining open fractures of types 1 or 2 but not 3 were included if the treating surgeon felt the wound was manageable for definitive debridement and treatment with intramedullary nailing in the same operation.

2.1. Surgical Technique

Fractures were treated by fellowship-trained orthopaedic traumatologists in a manner consistent with standard of care through locked, reamed, intramedullary nail implants. If a diagnosis of acute compartment syndrome was made, treatment was through four-compartment fasciotomy. Postoperatively, subjects remained nonweightbearing on the operative extremity in a posterior foot splint until the completion of data collection, regardless of the stability of the fracture and construct.

2.2. Intramuscular pH Measurement Device

A commercially available esophageal pH probe was procured (Digitrapper, Medtronic, Minneapolis, MN, Fig. 1). In preparatory work, a process to sterilize the probe was developed using low temperature gas-based techniques and the probe validated for intramuscular use. Validation was performed by comparing the Digitrapper probe with a commercially available USDA grade meat pH meter (Hanna Instruments, Woonsocket, RI) in the muscle of 2 living and 5 deceased rats. This showed an accuracy of 99.7%, with no greater than 0.72% error in any measurement. The pH of tested specimens ranged from 6.95 to 7.47.

Before the start of surgical stabilization, the probe was assembled in sterile fashion and standardized in pH solutions of 4 and 7. The probe was then placed percutaneously into the musculature of the anterior compartment (Fig. 2-A). The location of the probe was verified fluoroscopically, ensuring that the end of the catheter was within 5 cm of the fracture, a threshold selected to remain consistent with existing literature on the spatial decay of intramuscular pressure adjacent to fracture[47] (Fig. 2-B). The probe was then secured to the operative leg, connected to the data logger, and recording initiated. IpH data were collected at a sampling rate of 1 Hz, continuously, for a period of 48 hours. After completion of data collection, the probe was removed without anesthesia in the inpatient setting.

All study procedures were performed by a separate research team. No study data were available to the treating surgeon.

2.3. Statistical Methods

An independent research team recorded the time of reaming for data matching. IpH before, during, and after reaming was averaged and compared through repeated measures ANOVA. The appropriate interval over which to analyze IpH during reaming is unknown; thus, the analysis was repeated over various time domains (0.5, 1, 2, 5, 10, and 15 minutes prereaming and postreaming time intervals), with a

Figure 1. Commercially available pH probe used for intramuscular pH measurement.

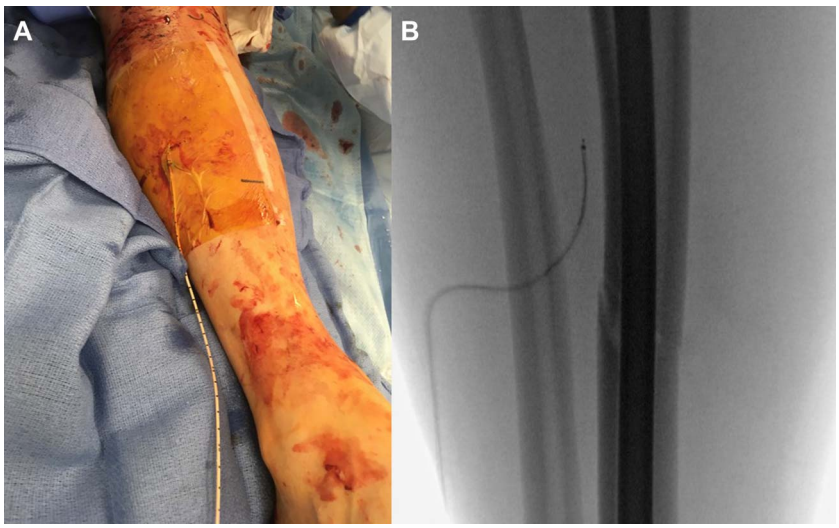

Figure 2. Clinical example of intramuscular pH probe in use.

plan to expand the time domains if differences remained in excess of 15 minutes. Discrete data were analyzed using the paired *t* test. Time series of IpH data were compared using a repeated measures correlation analysis.[48] The descriptive methods of Allmon et al[49] were used to characterize the location and extent of tibia involved in the fracture. The results were assessed as statistically significant if $P < 0.05$.

3. Results

A total of 16 subjects with tibial shaft fractures (OTA/AO type 42) were enrolled in this study (Table 1). Four of the 16 subjects (25%) sustained open injuries (2 of Gustilo–Anderson type 1, 2 type 2, 0 type 3). Zero subjects were diabetics, while 31% were active smokers and 13% active IV drug users. Fracture geometry largely clustered in the distal third of the shaft (63%) as opposed to the middle of the shaft (25%) or proximal third of the shaft (13%); the fibula was concomitantly injured in 88% of subjects. There were no subjects with extreme distal or extreme proximal fractures with no shaft involvement. On average, the fractures involved 23% of the length of the tibia (SD: 11%, max: 39%, min 5%). Observation of fracture morphology demonstrated 50% of patients with a simple fracture (single plane), 31% with comminution present, and 19% sustaining segmental injuries.

Acute compartment syndrome was diagnosed in one (1) subject preoperatively, and the subject was therefore excluded from this study as intramedullary nailing was not performed immediately after fasciotomy.

TABLE 1

Study Cohort Characteristics

Number of subjects	16
Mean age (range)	49.9 (19.7–81.7)
BMI, mean ± SD, kg/m^2	25.7 ± 4.4
% Male sex	62.5%
Time to surgery, mean ± SD, hours	35.0 ± 31.8
Acute compartment syndrome, n (%)	1*

* This subject is not included in the 16 subjects reflected herein.
BMI, body mass index; kg/m^2, kilograms per meter squared.

The average time from injury to surgery was 35.0 hours (SD, 31.8). IpH was acidic at both the start and end of surgical stabilization, with mean starting IpH of 6.64 (SD, 0.21) and mean ending IpH of 6.74 (SD, 0.17).

The mean reaming duration was 15 minutes. The mean IpH before, during, and after reaming was 6.72 ± 0.18, 6.73 ± 0.15, and 6.72 ± 0.16, respectively. There was no difference in mean IpH before, during, or after reaming ($P = 0.996$, using a 1-minute window; Table 2; Fig. 3A).

The conclusion that there was no difference in IpH was robust across the entire range of time domains analyzed, using averaging windows ranging in length from 30 seconds to 30 minutes. Across this range of time domains, the greatest difference in mean IpH between prereaming and postreaming was 0.02 units of pH, demonstrating that patterns of IpH were preserved across time domains that were both long and short relative to the duration of reaming (Fig. 3B).

There were no adverse events associated with the study protocol.

4. Discussion

We observed that in tibia fractures treated with reamed intramedullary nailing, IpH was not affected by the process of reaming the intramedullary canal. Previous studies have demonstrated transient increases in compartment pressures, giving rise to concern over potential adverse effect to adjacent soft tissues during reaming. By contrast, the current work suggests that local tissue acid–base physiology is not affected by reaming. These are new findings enabled by novel, investigational technology that

TABLE 2

Summary of IpH Data

	Median [Q1, Q3]	Mean ± SD	Min, Max
Before reaming	6.75 [6.68, 6.79]	6.72 ± 0.18	[6.19, 7.03]
During reaming	6.71 [6.68, 6.82]	6.73 ± 0.15	[6.34, 6.96]
After reaming	6.72 [6.63, 6.82]	6.72 ± 0.16	[6.37, 6.92]
P		0.996	

BMI, body mass index; kg/m^2, kilograms per meter squared; Q, quartile.

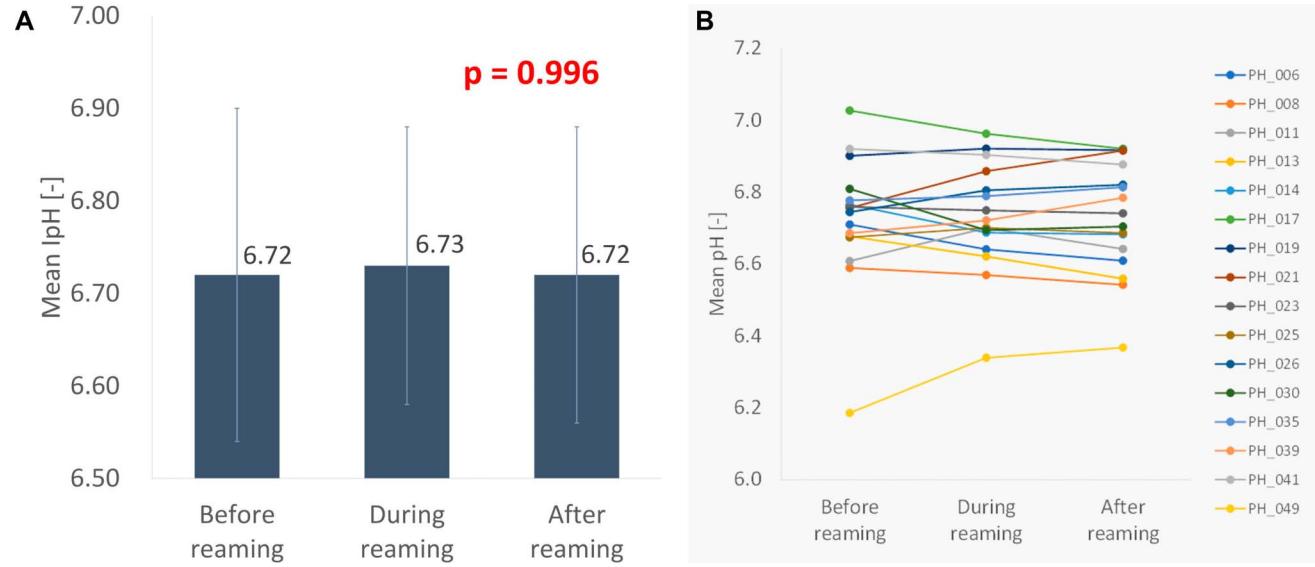

Figure 3. A, There is no change in mean IpH before, during, and after reaming of the intramedullary canal ($P = 0.996$). B, Individual patient intramuscular pH means: before, during, and after reaming.

allows in vivo measurement of soft tissue acid–base physiology in humans after musculoskeletal trauma.

Historically, muscular research has been confined to indirect measurements[44] or point-in-time biopsy measurements as the instrumentation required to measure pH in solution is large and difficult to introduce into tissues without invasive approaches. The measurement of tissue acid–base balance in vivo represents a substantial shift in our ability to investigate the consequences of trauma. This is meaningful because there is a commensurate push from the world of regenerative medicine and bioengineering to cease consideration of extremity bone and muscle as separate systems.[50] Instead, the model of *composite injury* hypothesizes that healing of bone and muscle is not merely adjacent but highly coordinated and codependent.[51,52]

To the best of our knowledge, no previous work has described in vivo acid–base physiology adjacent to tibial shaft fractures during surgical stabilization with reamed intramedullary nails. The findings described herein including the absence of any effect of reaming on IpH represent foundational advances in our understanding of tissue physiology adjacent to long bone fractures. Challa et al[44] established through indirect near-infrared spectroscopy that interruptions in blood flow indeed alter muscular pH, resulting in an acidotic state rescuable by reperfusion. This research was performed in healthy, uninjured subjects with a tourniquet and offers us little new knowledge about the state or fragility of muscle in the setting of traumatic injury. Tatman et al[45] established in an elegant ex vivo study that muscle fibers in a hypoxic environment lose contractile power and exhibit increases in markers of cellular injury and anerobic metabolism including increases in potassium and lactate concentrations. However, this research was unable to comment on changes in hydrogen ion concentration (pH) as a function of muscular ischemia because of limitations in the model (self-described: "nonphysiologic gaseous concentrations").

Given the emerging nature of this technology, the appropriate window over which to assess IpH has not been established. In the absence of guidance from prior work, we selected a timeframe in reference to the period of the intervention in question, using a maximum assessment period of double the time of reaming. While it is possible that this study selected a timeframe that was either too granular or too broad, the observation that our conclusion remains statistically significant across the broadest reasonable range of time scales (from 30 seconds to 30 minutes, against a reaming process averaging 15 minutes in duration) strengthens the validity of the claim, in our view.

Strengths of this work include the in vivo nature of the observations, which eliminate the challenges of transferring conclusions from animal models, where similar research has been conducted. The probe itself is unique; no other devices exist at this scale (pH laboratory catheters are usually on the size order of 1 cm in diameter rather than the 2-mm wide probe used in this study), allowing for direct measurement without disruption of, or iatrogenic injury to, the surrounding tissue. The probe is introduced percutaneously during a surgical procedure, although future work may involve probe placement in awake patients at the bedside.

Limitations of this work include the multifactorial nature of extremity acid–base physiology as well as the emerging nature of the technology. For example, while our study protocol required fluoroscopic confirmation that the IpH probe was placed within 5 cm of the fracture, this was predicated on data published with respect to intramuscular pressure.[47] Without any prior literature regarding in vivo measurement of IpH adjacent to fractures, it is not yet known whether this was an appropriate standard for this study. It may be, for example, that acid–base physiology is more (or less) locally specific, introducing either type I or type II error. Other limitations include the strict non–weight-bearing activity restriction and splinting to prevent ongoing muscular contractility during the data collection period. In our view, this was required to ensure that all variance in IpH measurement was related to fracture-related physiology and not physiologic response to exercise[53] or weight bearing.

This study reflects work in the early stages of translational research and highlights with clarity that intramedullary reaming is unlikely to cause, or exacerbate, acute muscular damage in the short term. Other similarly designed observations, including the association between local and systemic pH, are ongoing. The sample size is not yet of sufficient scale to draw conclusions with

respect to many parameters including, critically, whether IpH may have utility as a diagnostic modality for acute compartment syndrome. Further research in this area is both needed and ongoing to address these issues.

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