Fluid Lavage of Open Wounds (F.L.O.W.)
A Multi-center, Blinded, Factorial Trial Comparing Alternative Irrigating Solutions and Pressures in Patients with Open Fractures
An International Study
Kyle J. Jeray, MD
OTA, Phoenix AZ
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I have no potential conflicts with this presentation
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Objectives
- Background - Need for a Trial
- Irrigation Pressures
- Irrigation Fluids
- Pilot Study - Results
- Definitive Trial status
- Why International?
Open Fractures

- Estimated 250,000 open fractures occur annually in the US in the civilian population
- High risk of infection - up to 50%
- Infections can lead to nonunions, and wound and bone healing complications - re-operations
- Increased Health Care Costs!

International Impact

- 67% of admissions in Canada are orthopedic/fracture related
- Urbanization of China and India - vehicular accident every 3 minutes
- Traffic accidents major cause of fractures and top 3 for disability
- Increased Global Health Care Costs!

Military Implications

- Estimates that over 80% of war injuries are extremity related
- 70% involve orthopedic surgical care
- Global Issue!
Military Implications

- Procedure performed by military is I & D due to contaminated nature of combat wounds.
- Injuries caused by exploding bombs, artillery shell, mortar rounds, grenades or land mines - forces drive foreign material into soft tissue and bone.

Lin et al. JOT18:No8;supp2004

Have Surgeons Been Swayed by Experimental Data?
FLOW An International Survey of 984 Surgeons
50% response rate

<table>
<thead>
<tr>
<th>Method of Irrigation</th>
<th>High</th>
<th>Moderate</th>
<th>Low</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal saline</td>
<td>37%</td>
<td>20%</td>
<td>43%</td>
</tr>
<tr>
<td>Soap</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Chlorhexidine</td>
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</table>

37% High

20% Low

43% V. Low

FLOW Survey 2008

<table>
<thead>
<tr>
<th>Irrigation Solution</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal saline alone</td>
<td>66 (30.5%)</td>
</tr>
<tr>
<td>Normal saline with bacitracin</td>
<td>164 (16.8%)</td>
</tr>
<tr>
<td>Soap solution (equiv. detergent)</td>
<td>12 (1.3%)</td>
</tr>
<tr>
<td>Chlorhexidine</td>
<td>15 (1.6%)</td>
</tr>
<tr>
<td>Iodine based</td>
<td>55 (5.3%)</td>
</tr>
</tbody>
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70% Normal Saline
Only 1% Using Soap
What We Know in 2009

- Experimental evidence and opinion favors low pressure irrigation
  - Very Low Pressure is most common

- Clinical trial evidence suggests a benefit to detergent (soap) solution
  - Most still use Normal Saline

FLOW Pilot RCT

- 111 patients
- 9 participating sites - (US and Canada)
- 47% Type III, 75% Lower Extremity
- 86% follow up -1 year
- Compliance rates>90%

High (30 PSI) and Low (9 PSI) Irrigation Pressures

Irrigation device for all sites
- Stryker Surgilav
- Zimmer Pulsavac Plus
Irrigating Solutions - Soap

- Surfactant
- Forms micelles
- REMOVES bacteria

Pilot Results

- Soap versus Saline: Relative Risk: 1.24 (95% CI: 0.72-2.13), p=0.53
- Low versus High Pressure: Relative Risk: 0.68 (95% CI: 0.39-1.18), p=0.19
- Inconclusive need for large clinical trial

Pilot - Summary

- Need significant funding to run large clinical trial
- Need Level 1 Evidence to determine which pressure and solutions are best
- Power analysis estimates 2280 patients
- Need for additional arm - gravity flow
2x3 factorial design RCT to investigate whether irrigation solution and/or irrigation pressure will decrease the rate of re-operations for infection, wound healing or bone healing complications among patients with open fracture wounds.

**Fluid Lavage in Open Fracture Wounds:**

**Funding - International**

- US Department of Defense
  - Orthopaedic Trauma Research Program
  - Peer Reviewed Orthopaedic Research Program
- Canadian Institutes of Health Research
  - Fund most of Canadian sites
- AIOD
  - Fund international sites

**FLOW Pivotal**

Launched 2009 Summer

- Initially 2280 patients
- 3 x 2 factorial design (HP, LP, VLP)
- Aimed for 50 sites multi-national
Gravity Flow Arm

- Evidence to support very low flow
- Huge savings if pulsivac devices NOT necessary
- Requires additional patients

41 - Clinical Sites

- Canada – 14 sites
  - 14 sites
- U.S. – 15 sites
  - 15 sites
- Norway – 1 site
  - 1 site
- Australia – 1 site
  - 1 site
- India – 10 sites
  - 10 sites

Randomization Methods

- Randomize patients using random variable block sizes
- Using phone or Internet
- Patients stratified by:
  - Center
  - Type of Gustilo-Anderson open fracture
Fax System - Standardized forms and Electronic Data Collection

Enrollment of 2545 complete as of Sept. 30, 2013

Overall Loss to Follow-up just under 10%

Final results (rate or re-op at one year) pending 1 year F/U

Fluid Lavage in Open Fracture Wounds: Multi-Center RCT

This trial has the potential to:

- Resolve the current controversy on irrigation solutions and pressures for care of open fracture wounds
- Improve the current practices across emergency medicine, orthopaedics and plastic surgery
- Improve patient outcomes
- Potentially reduce health care costs
What Have We Learned?

- Site Selection Key!
- Need Physician Champion
- Need Dedicated Research Staff at each site

What Helped Us Succeed?

- Strong Methods Center
- Proven Data Collection System
- Dedicated Staff
  
  - Stryker
    - Donating 500 Surgilav irrigators for international sites (India)
  - Zimmer
    - Provided Pulsavac irrigators at a reduced rate
  - TRIAD
    - Donated first shipment of castile soap
  - Aplicare
    - New supplier of castile soap, provided at a reduced rate

Acknowledgment Support
Funding - Thank You

US Department of Defense
- Orthopaedic Trauma Research Program
- Peer Reviewed Orthopaedic Research Program

Canadian Institutes of Health Research
- Fund most of Canadian sites

AIOD
- Fund international sites

Collaborators - Thank You!

Canada
- Hamilton Health Sciences
- St. Michael's Hospital
- QE II Health Sciences Centre
- Ottawa Civic Hospital
- Vancouver General Hospital
- Hôpital du Saint-Cœur de Montréal
- McGill University Health Centre
- Royal Columbian Hospital – Burnaby
- Sunnybrook Health Sciences Centre
- Health Sciences Centre – Winnipeg
- Kingston General Hospital
- Université de Sherbrooke
- hôpital de l'Enfant-Jésus

US
- Greenville Health System
- Brooke Army Medical Center
- Duke University Medical Centre
- San Francisco General Hospital
- Orthopaedic Associates of Michigan
- University of Missouri Health Care
- Kerns Hospital
- Herrin Hospital
- St. Louis University
- Wright State University - Mayo Clinic
- University of Alabama at Birmingham
- University of California – Irvine
- Scottsdale Healthcare

International
- The Alfred
- Ullevål University Hospital
- Sancheti Institute for Ortho and Trauma
- Highway Hospital
- Lahey Clinic Medical Center
- University of Missouri Health Care
- University of Alabama at Birmingham
- Apollo Hospital Tondierpet
- Apollo Hospital Dreams Lane
- Apollo Hospital Toothaker
- RBL Hospital and Research Centre
- Popular Hospital
- Kolhapur Institute of Ortho and Trauma