Effectiveness of Amniotic Fluid Injection for Low Back Pain

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Disclosures

- Vivex donated product for our IRB-approved study of Epidural Amniotic Fluid Injections

- **Glenn R Buttermann, MD**
  - Consultant, Dio Medical
  - Licensing Agreement, FG Solco
- **Louis C Saeger**, MD
  - Travel expenses, Vivex
- **Matthew G. Thorson, MD**
  - None

Why is amniotic fluid (AF) of interest in the treatment of discogenic & radicular pain?

Current treatment options are limited:

- Tincture of time
- Manipulation
- Physical Therapy/Exercise
- Spinal steroid injections
- Surgical discectomy and/or fusion

Why is amniotic fluid (AF) attractive for treatment of discogenic & radicular pain?

Stated simply: Amniotic Fluid injections may have potent anti-inflammatory and regenerative properties ***without*** the risks of steroid-related side effects

Background Review

- Biochemical and physiological properties of AF
- Preliminary data from in vitro and animal studies
- Suggestive evidence from other clinical applications
- Anecdotal evidence for efficacy and safety in clinical use for epidural and intra-discal injection

Summary of Protein Milieu

- *Inflammatory proteins* to scavenge/digest trauma debris and initiate repair.
- *Anti-inflammatory proteins* to prevent scar and excessive fibrosis.
- *Growth factors* for continued optimal repair.

Commercially Available AF Contains Interesting Constituents

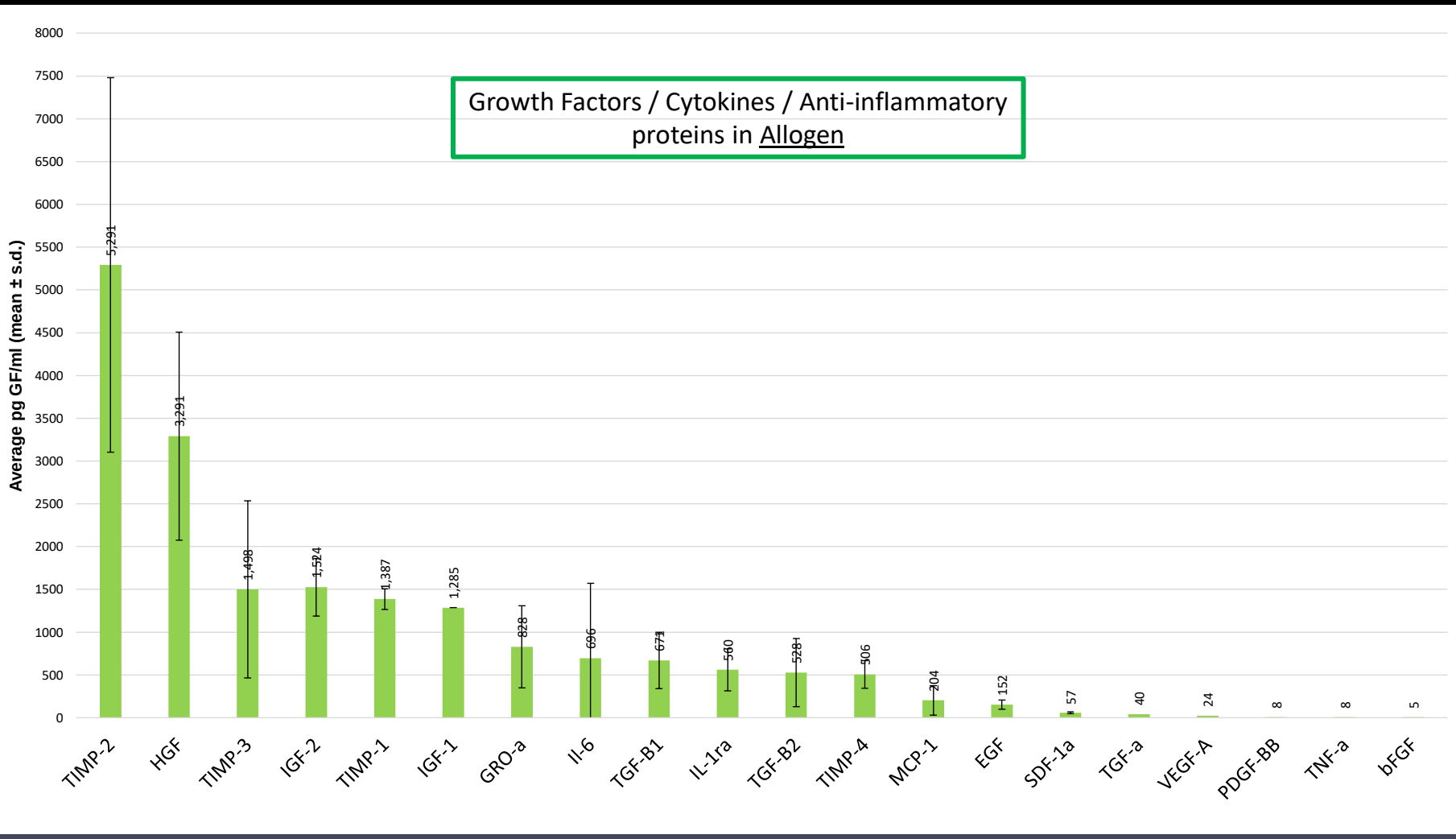
- AF preparations for the use under discussion is a chorion-free, cryopreserved allograft derived from amniotic membrane and fluid, but the preparations ***do not*** contain living mesenchymal stem cells.
- Contains: collagen substrates, growth factors, amino acids, carbohydrates, cytokines, TIMPs, hyaluronic acid, extra cellular matrix, micronized amniotic membrane and exosome products derived from multipotent amniotic cells.
- Components potentially promoting tissue regeneration, providing an anti-microbial environment, and anti-inflammatory characteristics with anti-adhesion and anti-fibrotic capabilities.

Biochemistry of AF

Amniotic epithelial cells produce potential regenerative substances :

- Transforming growth factor –a (TGF-a), and –b (TGF-b)
- Basic fibroblast growth factor (bFGF)
- Epidermal growth factor (EGF)
- Keratinocyte growth factor
- Hepatocyte growth factor
- Nerve growth factor(NGF)
- Brain-derived neurotrophic factor (BDNF), noggin, and activin have also been identified in the AM

AF contains anti-inflammatory proteins & growth factors



Rationale for use of AF as an alternative to steroids for epidural and intradiscal Injection

- Properties of AF confer potent effects, including suppression of inflammation, reduced neovascularization, fibrosis, and scarring without inhibition of healing, as well as potential regenerative effects
- Radicular pain associated with intervertebral disc disruption is primarily caused by inflammation
- Elements contributing to stenosis result from inflammatory changes
- Discogenic pain is assocaited with inflammatory endplate changes
- Annular disruption-related sensitization is inflammation-induced
- Degenerative changes may be at least partially reversible

Rationale behind our pilot study

- Epidural steroid injections are commonly used for degenerative spinal conditions
- Effectiveness of ESI varies for DDD, stenosis, and HNP
- ESI has risks: high blood glucose levels in diabetic patients, infection, adrenal suppression, stroke, cataracts, etc.
- Amniotic fluid injection is a potential alternative with a better safety profile

Amniotic Fluid Background

- AF has long history of demonstrated safety
- AF is obtained using sterile technique from volunteers at the time of C-section
- Mothers consent to donating AF
- Donated AF is filtered, concentrated, serologically tested by UMTB
- Stored frozen (with non-DMSO cryoprotectant, particulate-free, and acellular)

Study Purpose: Define Indications for epidural AF

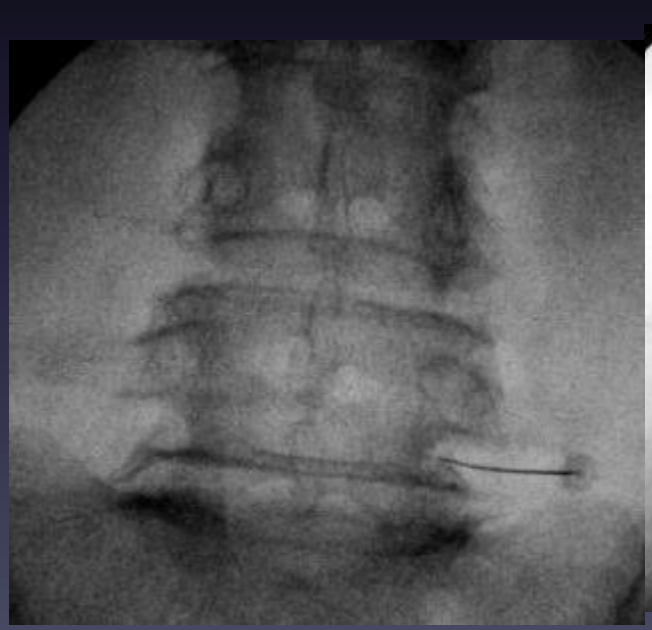
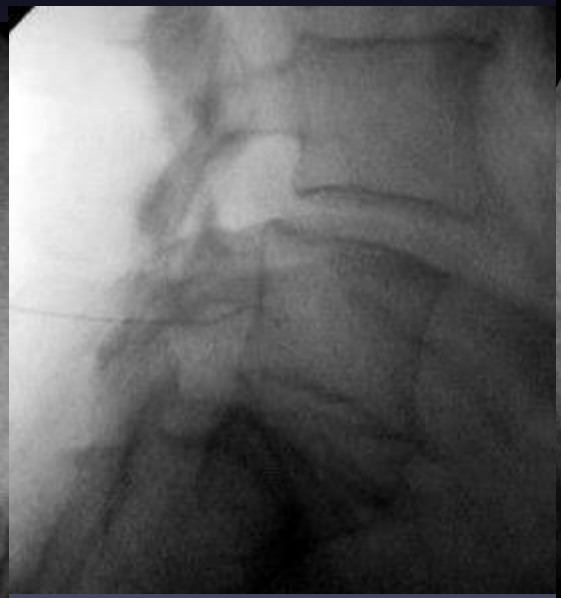
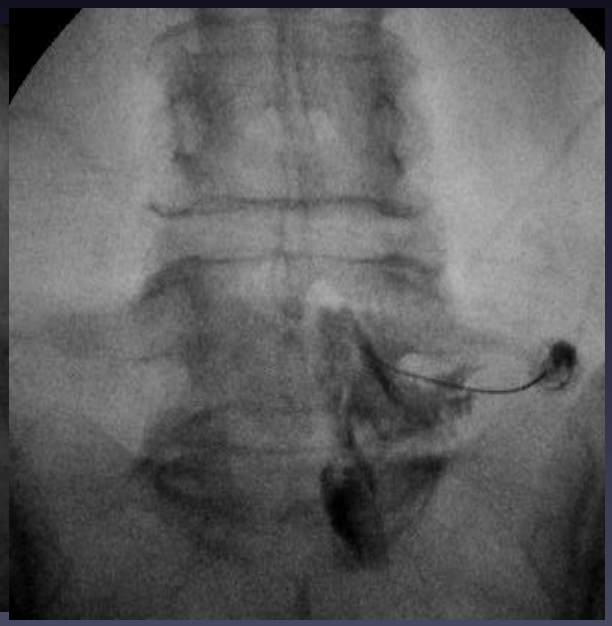
- **Question: Do epidural AF injections reduce pain and improve function in patients with low back & leg pain?**
- **IRB-approved for three cohorts:**
  - HNP
  - Stenosis
  - DDD
- **Inclusion criteria**:
  - >6 weeks symptoms, min LBP VAS 40/100
  - Failed conservative care (PT, chiro, meds)
  - MRI consistent with clinical Dx and exam

Methods

- Cohort Study, 15 patients in each group
- Symptoms > 6 weeks
- Prospective Outcomes:
  - LBP & leg VAS
  - Pain Drawing
  - ODI
  - PROMIS
  - pain meds
- Follow-up: 2-4 wk, 6-8 wk, 3-4m, 6-8m, and 1 yr

Methods

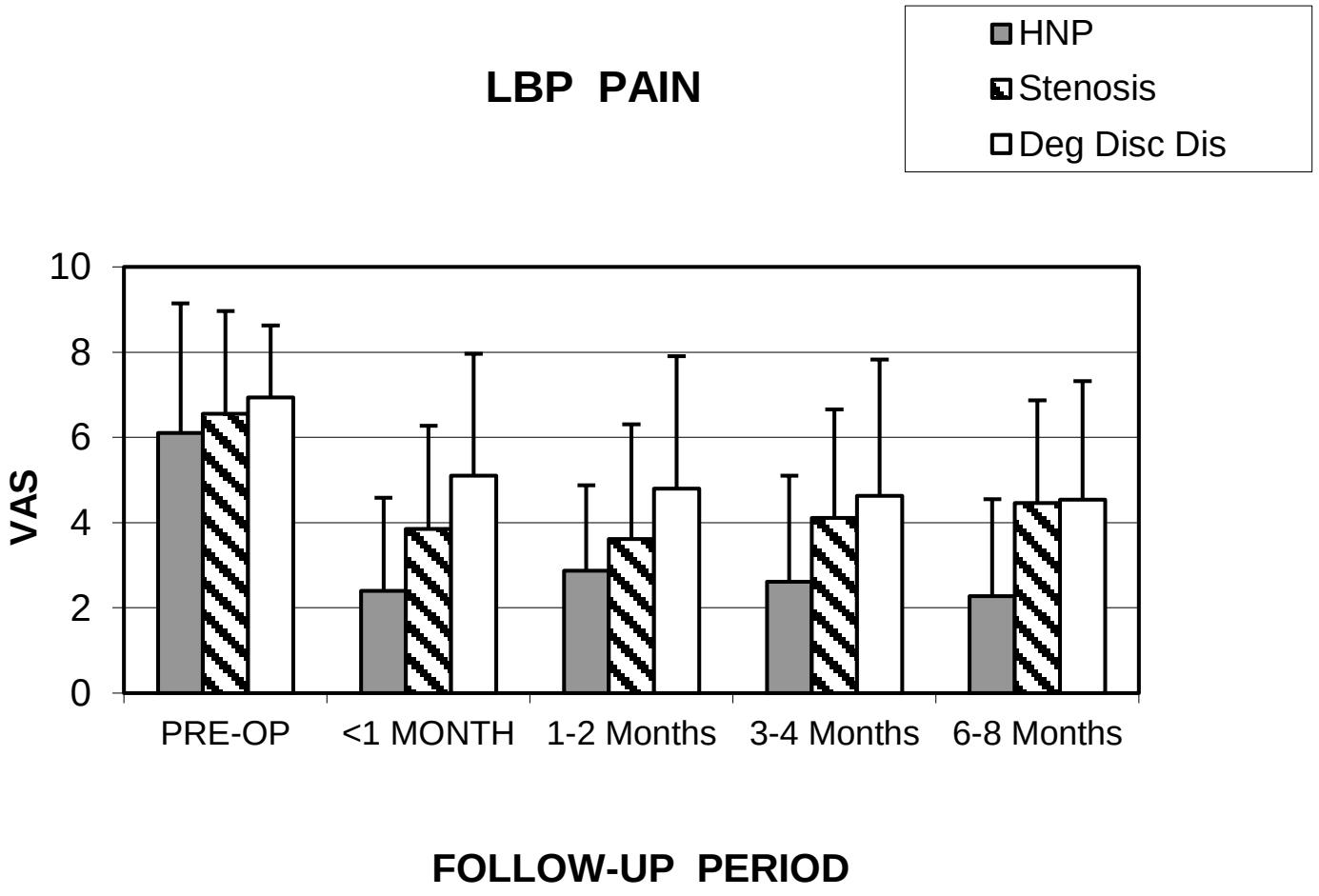
- 2 mls thawed AF with 1 ml 4% lidocaine
- Mild or no sedation, single injection
- Fluoroscopy in multiple planes
- Transforminal technique

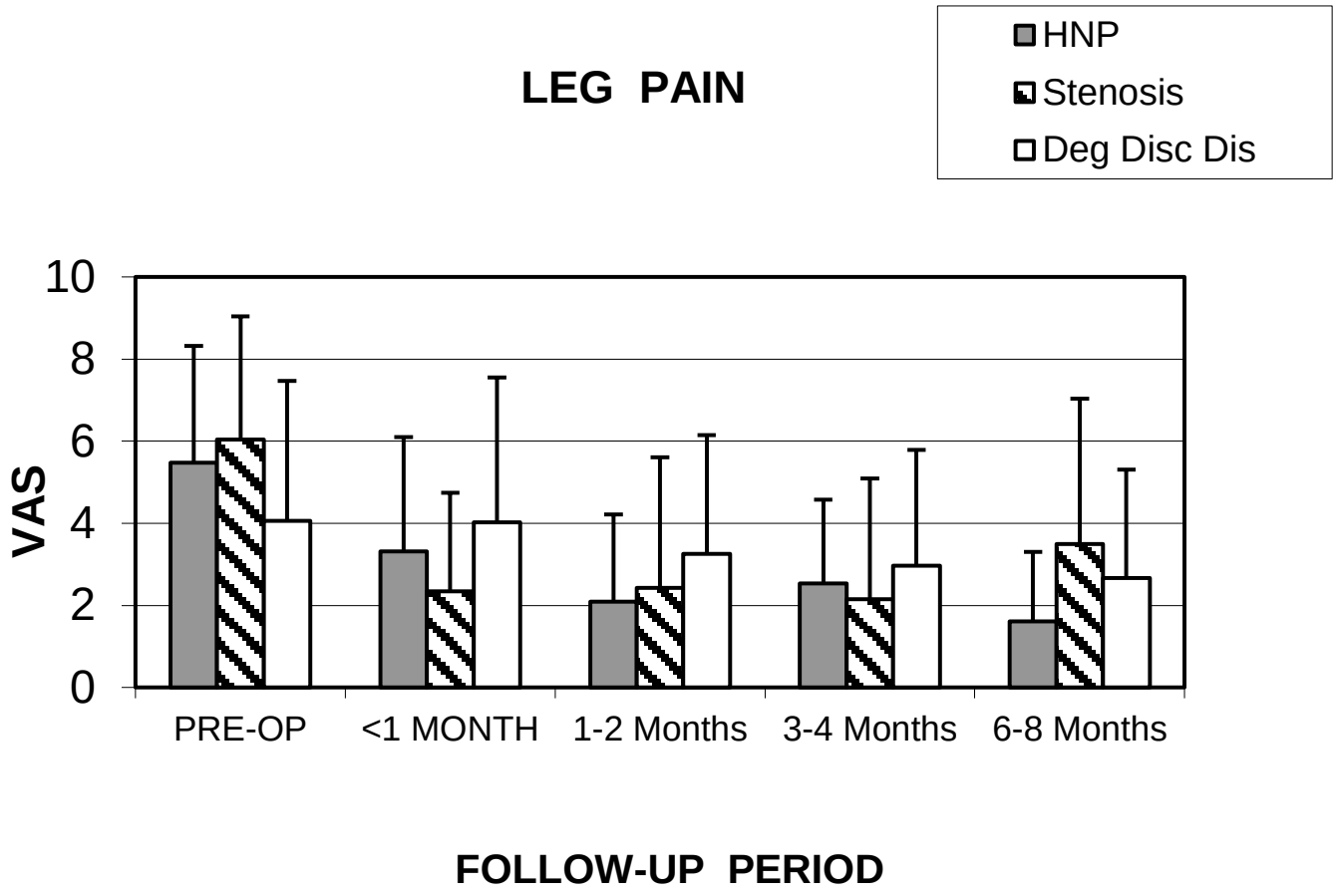
Results Regarding Safety

- Zero dural leaks
- Zero infections
- Zero transient radiculitis
- Zero allergic reactions

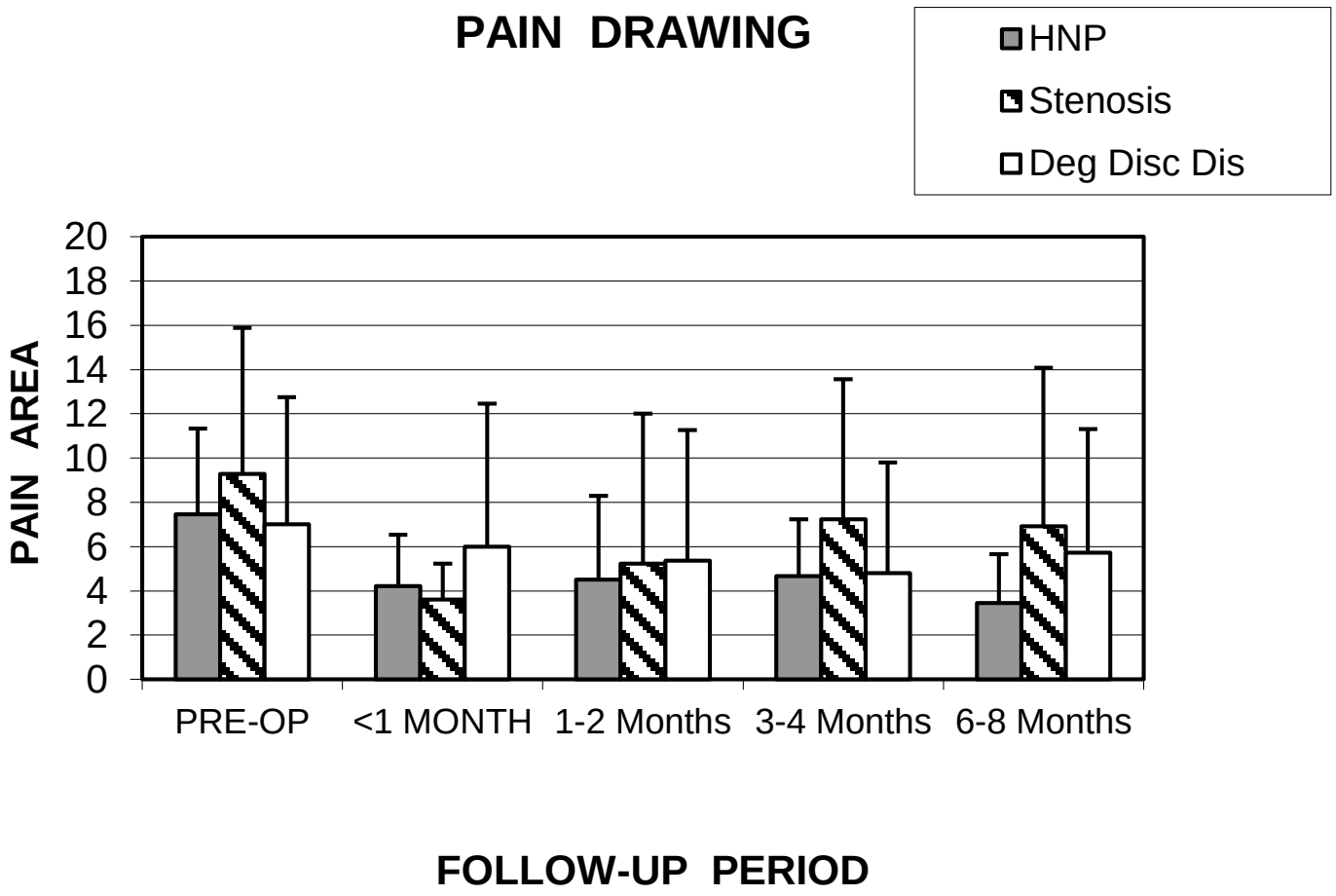
Low Back Pain Outcomes



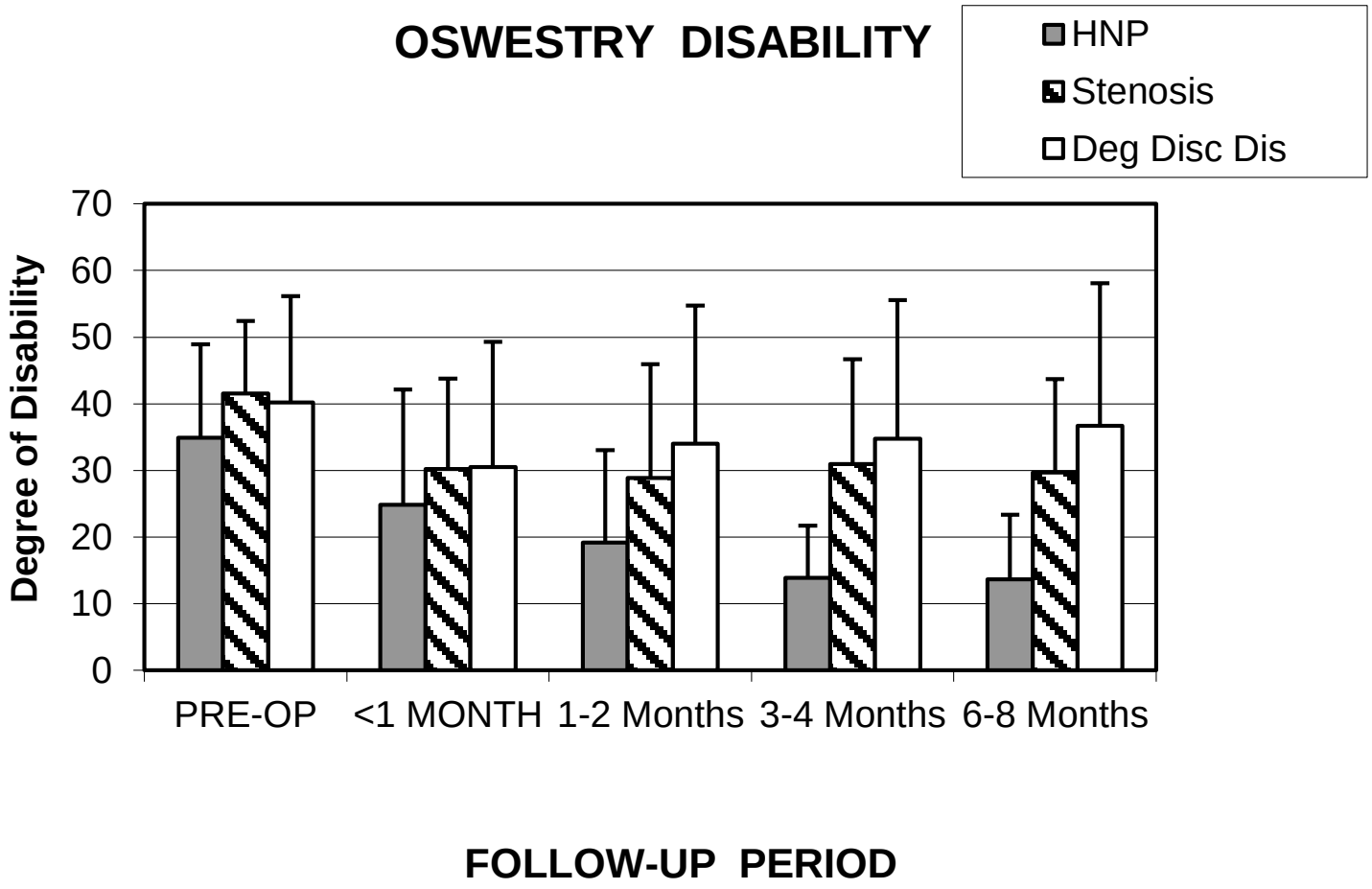
Leg Pain Outcomes



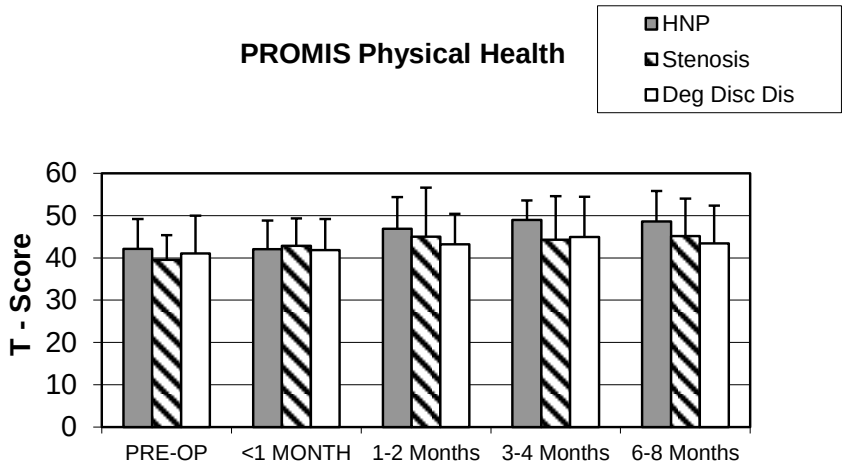
Pain Drawing Outcomes

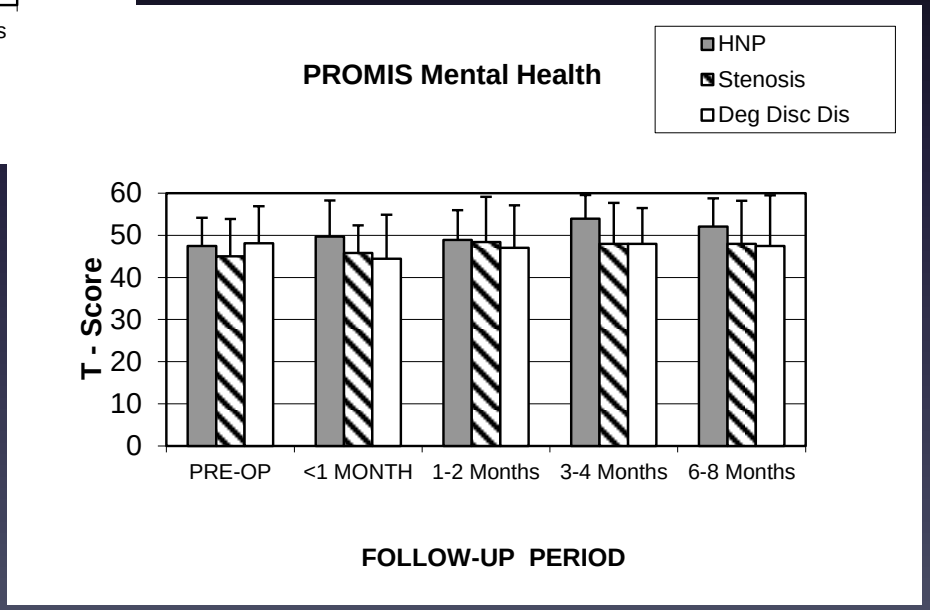


Disability Outcomes



PROMIS T-scores





Summary of Results

***Within* Groups**

- **HNP**: significant improvement @ all FU, VAS back & leg pain, Pain Diagram, ODI, PROMIS-Phys.
- **Stenosis**: significant improvement @ all FU, VAS back & leg pain, Pain Diagram, ODI, PROMIS-Phys.
- **DDD**: significant improvement at @ all FU, VAS back pain.

***Between* Groups**

- No difference in pre-treatment measures.
- **HNP**: significantly greater improvement in VAS back & leg pain, & ODI compared to **DDD**.
- **HNP** greater leg pain improvement compared to **Stenosis**.
- **Stenosis**: significantly greater improvement in VAS leg pain compared to **DDD**.

Is **PROMIS** useful for studies such as this?

- **PROMIS**® (Patient-Reported Outcomes Measurement Information System) is a set of person-centered measures that evaluates and monitors physical, mental, and social health. It can be used with the general population, and with individuals living with chronic conditions. **PROMIS** has been advocated for use in spinal fusion outcome studies.
- **PROMIS** T-scores showed that most of our study patients were below average ***at baseline*** (i.e., not doing very well).
- **PROMIS** outcomes in this cohort show limited treatment effect, despite significant changes in other measures, so it may not be a sensitive instrument in this study setting.

Treatment Success/Failure

HNP: 70% Success

2 patients → Other injections

2 patients → Discectomy

Stenosis: 58% Success

4 patients → Other injections

DDD: 53% Success

2 patients → Other injections

3 patients → Fusion/TDR

Study Limitations

- Small numbers
- New injuries
- Confounding effect of those patients with multi-level degeneration and other potential sources of LBP
- Variable opioid tolerance of subjects
- Repeat injections not studied

Discussion - Conclusions

- Epidural AF injections are safe.
- Epidural AF injections are most effective for patients with HNP.
- Epidural AF injections may be effective for stenosis.
- Epidural AF injections equivocal for DDD (study of intradiscal injection of AF is planned for DDD).
- Randomized epidural AF vs steroid study is planned with subanalysis for diabetic patients.