RECENT ADVANCES IN THE MANAGEMENT OF URINARY INCONTINENCE

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AUA STRESS URINARY INCONTINENCE GUIDELINE UPDATE
INDEX PATIENTS

- The otherwise healthy woman who has decided to seek surgical therapy for stress urinary incontinence.

- The otherwise healthy woman, who has decided to seek surgical therapy for stress urinary incontinence, and who also has concomitant pelvic organ prolapse.
INCLUSION CRITERIA

- Surgical therapy for adult female stress urinary incontinence.
- Minimum follow up of 12 months.
- Treatment available in the United States.
- English Literature only.

2005, American Urological Association Education & Research Inc.

METHODS

- 6801 articles indexed for years 1990 - 2004.
- 1205 articles were chosen for extraction.
- Number of patients reported in the extracted articles is 21,145.
- 1,008 entered
  - accepted = 288
  - rejected = 720

2005, American Urological Association Education & Research Inc.
RECOMMENDATIONS

- Consistency of diagnostic criteria.
- Standardized outcome measures.
- Minimum follow up > 12 months.
- Prospective randomized controlled trials.

2005, American Urological Association Education & Research Inc.

STRESS URINARY INCONTINENCE
THE PAST

- Kegel exercise
- Pharmacotherapy (Sudafed & Imipramine)
- Bulking agents (Teflon)
- Abdominal Urethropexy (MMK/Burch)
- Bladder neck suspension
  (Perreyra/Stamey/Raz/Gittes)
STRESS URINARY INCONTINENCE
THE PRESENT

- Kegel Exercise & Biofeedback
- Pharmacotherapy
- Bulking Agents
  (Contigen/Durasphere/Tegress)
- Transvaginal RF tissue ablation
- Sling (Vaginal wall/Rectus fascia/Fascia Lata/
  Bone Anchors/Cadaveric graft/Synthetic graft)

SLING MATERIAL

AUTOLOGUS GRAFT
VS
ALLOGRAFT & XENOGRAFT
VS
SYNTHETIC MESH
SLING MESH
Tissue Ingrowth Study: 3 months, rabbit

SLING MECHANISM

BLADDER NECK & URETHRA
VS
MID URETHRA
SLING TECHNIQUE

TVT
VS
TOT
**T.O.T HISTORY**

- N = 130
- Age: 59.22 (29-87) years
- Stress Incontinence (SUI): 90.69%
- Urge Incontinence (UI): 58.91%
- Parity: 2.47 (0-6)

**T.O.T RESULTS**

- Follow up: 13.11 (6-17) months
- Sling: 100%
- Pelvic prolapse: as indicated
- Hospital: 0.75 (0-3) days {77% Outpatient}
- Catheter: 1.24 (0-14) days {71% No catheter}
T.O.T RESULTS

- SUI : 10.07%
- UI : 17.05%
- De novo UI : 0.76%

T.O.T QOL RESULTS

<table>
<thead>
<tr>
<th>N=94 (72%)</th>
<th>Pre Op</th>
<th>Post Op</th>
<th>% Improved</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPD</td>
<td>3.01 (0-10)</td>
<td>0.20 (0-3)</td>
<td>93.35%</td>
</tr>
<tr>
<td>IIQ</td>
<td>13.82 (0-28)</td>
<td>1.67 (0-23)</td>
<td>87.91%</td>
</tr>
<tr>
<td>UDI</td>
<td>11.05 (0-18)</td>
<td>3.09 (0-14)</td>
<td>72.03%</td>
</tr>
<tr>
<td>GSS</td>
<td>1.14 (0-10)</td>
<td>8.14 (0-10)</td>
<td>85.99%</td>
</tr>
</tbody>
</table>
T.O.T
ALPP RESULTS

<table>
<thead>
<tr>
<th></th>
<th>ALPP &lt; 30 cm H20</th>
<th>ALPP &gt; 30 cm H20</th>
</tr>
</thead>
<tbody>
<tr>
<td>SUI</td>
<td>95.83%</td>
<td>96.88%</td>
</tr>
<tr>
<td>UI</td>
<td>88.24%</td>
<td>75.00%</td>
</tr>
<tr>
<td>PPD</td>
<td>97.11%</td>
<td>96.80%</td>
</tr>
<tr>
<td>IIQ</td>
<td>84.77%</td>
<td>85.56%</td>
</tr>
<tr>
<td>UDI</td>
<td>61.33%</td>
<td>69.49%</td>
</tr>
<tr>
<td>GSS</td>
<td>93.02%</td>
<td>85.12%</td>
</tr>
</tbody>
</table>

T.O.T
ADVERSE EVENTS

- Vaginal Extrusion: 2.17% (5/230)
- Bladder perforation: 0.87% (2/230)
- Urethral Obstruction: 0.87% (2/230)
- Vascular Injury: 0%
- Nerve Injury: 0%
- Urethral Erosion: 0%
CONCLUSIONS

- These results demonstrate the efficacy of the TOT at intermediate follow up. The ALPP does not appear to have a significant impact on outcome. The low incidence of de novo urgency suggests an advantage for the TOT over existing techniques. The risk of vaginal extrusion is low.

STRESS URINARY INCONTINENCE
THE FUTURE

- Pharmacotherapy
  - ?????
- Bulking agents
  - CA Hydroxyl apatite
  - Dextranomer / Hyaluronic acid (Zuidex)
- Transurethral RF tissue microremodeling
- Modified Transobturator sling
- Stem Cell Injection
**ZUIDEX**

- Dextranomer microspheres (80-250 micron) in sodium hyaluronan solution.
- Dextranomer:
  - Organic substance
  - Biodegradable
  - No migration
  - Non immunogenic
  - No malignant potential

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**ZUIDEX**

**Demographics**

- N = 42
- Age 52.7 (30-77) years
- BMI 23.8 (19-34.3)
- Menopause 52% (22)
- Provocative Test = 37.19gm (0-300)
- Incontinence episodes/24hr = 1.89 (0-24)

P. Van Kerrebrouck, Urology 64(2):276, 2004
Radiofrequency Energy

- **RF Ablation** results in gross thermal tissue destruction with or without gross tissue shrinkage:
  - BPH / joint & ligament injury / menorrhagia / SUI (RF bladder suspension)

- **RF Micro-remodeling** results in microscopic collagen denaturation without necrosis, leading to reduced dynamic tissue compliance:
  - gastroesophageal reflux disease / fecal incontinence
  - SUI (non-surgical, transurethral RF micro-remodeling)

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The Renessa System: Treatment

- sub-necrotic submucosal target temperature results in focal collagen denaturation

- no effect on overlying mucosa or deeper urethral wall tissues

- healed submucosal sites measure only ~200µ in diameter

- no luminal narrowing or stricture formation occurs
The Novasys Renessa™ System

U.S. Clinical Trial
- prospective, randomized, sham-controlled design
- 110 treatment and 63 sham treatment arm subjects, 12 month follow-up
Subjective Outcome Measure: ≥10 point I-QOL Score Improvement
- treated women with moderate-to-severe baseline SUI experienced greater incidence of at least 10 point I-QOL score improvement relative to sham treated women with baseline moderate-to-severe SUI ($p=0.03$)

Objective Outcome Measure: Valsalva Leak Point Pressure Elevation
- treated women experienced an elevation in mean VLPP, and sham treated women experienced a reduction in mean VLPP ($p=0.02$)
TOT
THE FUTURE

OVERACTIVE BLADDER
(OAB)
OVERACTIVE BLADDER
THE PAST

- Probanthine
- Oxybutinin (Ditropan)
- Levsin
- Subtrigonal injection of alcohol
- Denervation
- Augmentation

Economic Cost of Urinary
Incontinence & Overactive Bladder

- 17,000,000.00 (UI)
- $ 19,500,000,000.00 (UI)
- 34,000,000.00 (OAB)
- $ 12,600,000,000.00 (OAB)

TW Hu et al, Urology 63(3): 461-465, 2004
MOTOR NEUROTRANSMITTERS & RECEPTORS

Cholinergic Receptors
- Nicotinic
- Muscarinic
- $M_1$, $M_2$, $M_3$, $M_4$

Adrenergic Receptors
- $\alpha$-Adrenergic
- $\beta$-Adrenergic
- $\alpha_1$, $\alpha_2$, $\alpha_n$
- $\beta_1$, $\beta_2$, $\beta_n$


Distribution of Muscarinic Receptors in Target Organs

CNS (M4)
- Dizziness
- Somnolence
- Impaired Memory & Cognition

Iris/Ciliary Body = Blurred Vision
Lacrimal Gland = Dry Eyes (M3)
Salivary Glands = Dry Mouth (M3)
Heart = Tachycardia (M2)
Gall Bladder
Stomach = Dyspepsia
Colon = Constipation (M3)
Bladder (M2/M3)

OVERACTIVE BLADDER MANAGEMENT

- Behavioral Modification
- Pharmacotherapy
- Botox
- Neuromodulation
- Surgery (Augmentation)

Overactive Bladder Rx
BEHAVIORAL MODIFICATION

OVERACTIVE BLADDER
PHARMACOTHERAPY

- Uroreceptor selectivity (M2/M3)
- Alternate metabolic pathways (N-DEO)
- Alternate method of delivery (N-DEO)

OVERACTIVE BLADDER
PHARMACOTHERAPY

- ER Oxybutynin (Ditropan XL)
- Tolterodine (Detrol LA)
- TD Oxybutynin (Oxytrol)
- Tropsium (Sanctura)
- Solefenacin (Vesicare)
- Darifenacin (Enablex)
**BOTULINUM A TOXIN**
(BOTOX)

- Botulinum toxin A, B, C, D, E, F, G
- Block Ach @ NMJ & M receptors
- It does not cross the blood brain barrier
- Transurethral injection in the Detrusor
- Frequency & Urgency reduced 50%
- Average duration 3-4 months
- Dose: 20-30 injections sites (10 units/site)
- Safe & effective for refractory OAB

**NEUROMODULATION**
(INTERSTIM)

- N=34
- F/U 6 months
- Urgency improved 82%
- Frequency improved 64%
- Urge incontinence improved >50% in 76%
- Revision rate 32.5%
OVERACTIVE BLADDER
THE FUTURE

- IDIOPATHIC
  - SENSORY
  - MOTOR
- NEUROGENIC
  - CNS
  - PNS
- MYOGENIC
  - PRIMARY
  - SECONDARY
OVERACTIVE BLADDER
THE FUTURE

CENTRAL RECEPTOR TARGET
Opioid Receptor µ, δ, κ
Serotonin (5HT) receptor

PERIPHERAL RECEPTOR TARGET
Vanilloid receptors C-Fiber receptor (OAB)
α₁D & α₁A receptor (BOO)
B₃ adrenoreceptors (OAB)
P₂X₂ & P₂X₃ purinergic receptor (OAB)

OVERACTIVE BLADDER
THE FUTURE

- RECEPTOR SUPERSELECTIVITY
- ALTERNATE TARGET RECEPTORS
- NEUROMODULATION
- GENE THEARAPY