

## PREDICTIVE FACTORS FOR THE EFFICACY OF AUTOLOGOUS MUSCLE DERIVED CELL INJECTIONS IN WOMEN WITH STRESS URINARY INCONTINENCE

### Hypothesis / aims of study

Autologous muscle derived cells (AMDC) have the potential to restore muscle function, thus reconstructing the weakened urinary sphincter that causes stress urinary incontinence (SUI). A systematic review has suggested that AMDC injection in the urethral sphincter is promising due to its safety and potential effectiveness as a treatment modality for SUI (1-2). Autologous muscle cell therapy, which involves isolation of cells from skeletal muscle biopsies, *ex vivo* expansion, and subsequent injection into the urethral sphincter, may serve as a potential durable therapy. In animal studies, muscle derived cells have successfully integrated within tissue to improve sphincter function (3).

Despite promising results on continence in women, no predictive factors have been identified in order to more accurately select patients who could benefit from this therapy. Therefore, the objective of this study was to explore predictive factors for the efficacy of AMDC injections, defined as a reduction of incontinence episode frequency (IEF) at 12-months compared to baseline.

### Study design, materials and methods

This prospective study was conducted at a tertiary care center between February 2012 and January 2015. This is a secondary analysis from a larger randomized controlled trial (RCT) in which participants received either a placebo or a 150 x10<sup>6</sup> AMDC injection. Participants in the treatment group received either one or two injections (second treatment was approximately 6 months after the initial). Patients who received the placebo treatment were not included in this analysis. After obtaining informed consent and approval by the ethics committee, thirty-seven women with SUI received transurethral injections of AMDC that were derived and manufactured from a quadriceps muscle biopsy as part of the larger RCT. All subjects were evaluated at baseline and 12 months post-injection. A transperineal 3D ultrasound was performed at baseline and each of the follow-up visits. Data were collected, namely participant demographics, past surgical history, clinical hypermobility, valsalva leak point pressure and key ultrasound measurements (length of urethra, volume of rhabdosphincter, bladder neck caudal/dorsal/dorso-caudal displacement at valsalva). For this post-hoc analysis, women were considered to be responders when they demonstrated a reduction of 75% or more of IEF at 12 months compared to baseline. Predictive factors were evaluated by applying univariate

### Results

Thirty-seven (37) patients with a mean age of 47 years (SD 9; range 26-69) received transurethral injections of AMDC. All had a body mass index (BMI) of 34 or less (SD 4; range 19-34), with 15 (41%) having a normal BMI ranging from 19 to 24. Regarding previous treatment for UI, 1 (3%) had urethropexy, 2 (5%) had TVT/TOT and 30 (81%) had practiced pelvic floor muscle training. A total of 14 (37.8%) women were considered responders as they showed a reduction of 75% or more of IEF at 12 months. Univariate logistic regression revealed that the following variables were non-significantly associated with treatment success ( $p > 0.05$ ): age, body mass index, length of urethra, volume of rhabdosphincter, VLPP and clinical urethral hypermobility. However, as shown in Table 1, lower ultrasound bladder neck hypermobility at valsalva, defined as caudal displacement ( $p = 0.05$ ), and dorso-caudal displacement ( $p = 0.04$ ) were associated with greater success. Univariate logistic regression for bladder neck dorsal displacement showed a tendency towards statistical significance ( $p = 0.07$ ) (see Figure 1 for example of bladder neck position measurement at rest). It should be noted that the strong correlations between these variables (multicollinearity) prevented computing multivariate logistic regression. When defining responders as a reduction of 50% or more of IEF at 12 months, similar results were obtained from univariate logistic regression showing a tendency towards statistical significance for the following: bladder neck caudal ( $p = 0.06$ ) and dorso-caudal displacement ( $p = 0.06$ ).

### Interpretation of results

To our knowledge, this is the first study that explores predictive factors for the efficacy of AMDC injections in women with SUI. Results suggest that patients with limited bladder neck hypermobility at valsalva on ultrasound respond better to this treatment modality. These results corroborate with the principle that AMDC injections improve SUI by reducing intrinsic sphincter deficiency rather than reducing bladder neck hypermobility. These data may allow physicians to preoperatively identify women that may benefit from such treatment.

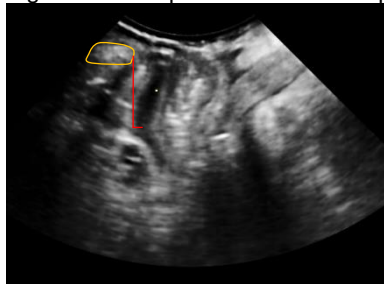
### Concluding message

Ultrasound bladder neck hypermobility was shown to be a predictive factor for the efficacy of AMDC injections in women with SUI. More precisely, this suggests that patients with limited bladder neck hypermobility at ultrasound respond better to this treatment. Studies focusing on the identification of predictive factors on a larger scale are much needed.

Table 1: Predictive factors for the success of AMDC injections based on univariate logistic regression

Variables	OR (95% CI)	p-value
Bladder neck Caudal displacement	0.35 (0.12-1.00)	p=0.05
Bladder neck Dorso-caudal displacement	0.38 (0.15-0.95)	p=0.04
Bladder neck Dorsal displacement	0.32 (0.09-1.12)	p=0.07

Figure 1: Example of bladder neck position measurement at rest



Legend: Orange line: pubic symphysis  
Red line: distance between pubic symphysis and bladder neck

#### References

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2. Carr LK., Steele D., Steele S., et al. 1-year follow-up of autologous muscle-derived stem cell injection pilot study to treat stress urinary incontinence. International urogynecology journal and pelvic floor dysfunction. 2008;19(6):881-883.
3. Praud C., Sebe P., Bierinx AS., Sebille A. Improvement of urethral sphincter deficiency in female rats following autologous skeletal muscle myoblasts grafting. Cell transplantation. 2007;16(7):741-749.

#### Disclosures

**Funding:** Cook MyoSite **Clinical Trial:** Yes **Registration Number:** ClinicalTrials.gov Autologous Muscle-derived Cells Female Stress Urinary Incontinence Clinical Study CT01382602 **RCT:** Yes **Subjects:** HUMAN **Ethics Committee:** Comité d'éthique de la recherche du Centre intégré universitaire de santé et de services sociaux de l'Estrie - Centre hospitalier universitaire de Sherbrooke **Helsinki:** Yes **Informed Consent:** Yes