Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix 1. Procedure for 1-hour Pad Test According to International Continence Society Instructions[1]

Participants were instructed to void 2 hours before the pad test. On arrival, they received a pre-weighed pad and were asked to sit and drink 500 ml sodium-free water in 15 minutes. Next, they were instructed to walk for 30 minutes, including going up and down 24 stairs. On returning to the clinic, the participants were instructed to perform several activities, including standing and sitting 10 times, coughing vigorously 10 times, running for 1 minute, picking up a coin from the floor 5 times, and putting their hands under water for 1 minute. After the activities were completed, the pad was reweighed to measure the amount of urinary leakage.

eAppendix 2. Multiple Imputation

For the amount of urine leakage measured by the 1-hour pad test (primary outcome), we had 18 cases with missing data (see eTable1). The “Missing Data Patterns” table lists distinct missing data patterns with corresponding frequencies in each group . Here, a “Pattern” means an unique missing pattern from the data set; values of “**√**” and “**×**” indicate that the variable is observed or missing, respectively, in the corresponding pattern. The table confirms a monotone missing pattern for these three time points. We assumed the data were missing at random missing at random, and regression-based multiple imputation with baseline the amount of urine leakage measured by the 1-hour pad test as covariate was used (SAS PROC MI).[2]

eTable 1. Missing Data Patterns

Pattern	Baseline	Week 2	Week 6	Electroacupuncture	Sham electroacupuncture	Total (%)
1	√	√	√	246	240	248(96.4)
2	√	√	×	0	6	6(1.2)
3	√	×	×	6	6	12(2.4)

√ = complete data. × = incomplete data.

Code:

```
proc mi data=ds1tran nimpute=200 seed=19850901 out=test_reg;
 var group col1 col2 col3;
 class group;
 monotone reg(col2 / details);
 monotone reg(col3 / details);
run;
```

eAppendix 3. Details for Results of Primary Analysis

Four sensitivity analyses (1 preplanned and three post hoc) were conducted for the primary outcome. The preplanned used control-based pattern model to evaluate sensitivity to missing data departure from the missing at random assumption. Three post hoc sensitivity analyses evaluated whether baseline imbalance in age, clinical site and a mixed-effect model with repeated measures could have diluted the estimates of treatment effect.

1.1 Sensitivity Analysis for Accounting for Center Effects Using Three Methods

In our multicenter trials, randomization is carried out using permuted blocks stratified by center. To account for center effects,[3] three methods were used to adjust for center effects in the analysis. 1) *without center effects*: ANOVA with change from baseline as response; 2) *fixed center effects*: ANCOVA with change from baseline as response variable, baseline the amount of urine leakage measured by the 1-hour pad test as a covariate, and treatment, site (dummy variable) and interaction between site and treatment as fixed effect; 3) *random center effects*: Mixed model with change from baseline as response variable, baseline the amount of urine leakage measured by the 1-hour pad test as a covariate, treatment as a fixed effect, site (dummy variable) and interaction between site and treatment as random effects. The results of unadjusted and adjusted for center effects showed stratified factor did not affect the treatment effects (eTable 2).

eTable 2. Different Analysis Model Accounting for Center Effects

Variables	Electroacupuncture (n=252)	Sham electroacupuncture (n=252)	Difference (95%CI)	*p* value
Change from baseline in amount of urine leakage measured by the 1-hour pad test, LS mean (95% CI), g				
Week 2 [a]				
ANOVA	-5.70 (-7.43 to -3.98)	-2.17 (-3.89 to -0.45)	3.53 (1.10 to 5.97)	<.001
ANCOVA	-5.81 (-7.22 to -4.40)	-2.07 (-3.47 to -0.67)	3.74 (1.75 to 5.72)	<.001
Mixed model	-5.80 (-8.06 to -3.55)	-2.07 (-4.33 to 0.19)	3.73 (1.71 to 5.76)	<.001
Week 6 [b]				
ANOVA	-9.80 (-11.65 to -7.96)	-2.69 (-4.54 to -0.84)	7.12 (4.50 to 9.73)	<.001
ANCOVA	-9.93 (-11.32 to -8.54)	-2.56 (-3.96 to -1.17)	7.37 (5.40 to 9.33)	<.001
Mixed model	-9.93 (-12.52 to -7.33)	-2.57 (-5.16 to 0.03)	7.36 (4.76 to 9.96)	<.001

Abbreviations: CI, confidence interval; ANOVA, analysis of variance; ANCOVA, analysis of covariance; LS, least squares.

[a] The number of participants with imputed data was 6 (2.4%) in the electroacupuncture group, and 6 (2.4%) in the sham electroacupuncture group at 2-week.

[b] The number of participants with imputed data was 6 (2.4%) in the electroacupuncture group, and 12 (4.8%) in the sham electroacupuncture group at 6-week.

1.2 Sensitivity analysis for departure from the assumption of missing at random with control-based pattern model

The sensitivity analysis with a control-based pattern imputation model,[4] assessed whether the change from baseline in the amount of urine leakage measured by the 1-hour pad test at week 6 was robust to departure from missing at random missing at random. More specifically, an imputation model for the missing observations in the electroacupuncture group was constructed from the observed data in the sham electroacupuncture group rather than the electroacupuncture group. Parallel to the primary analysis based on missing at random missing at random, we were used a similar method with such an imputed data set to show the robustness of the final results. SAS PROC MI with the missing not at random statement was used. The results were robust to departure from missing at random missing at random(Table 2 and eTable 3).

Code:

```
proc mi data=ds1tran seed=19850901 nimpute=200 out=test_MNAR;
    class group;
    monotone reg;
    mnar model( col2 /modelobs=(group='B'));
    mnar model( col3 /modelobs=(group='B'));
    var col1 col2 col3;
run;
```

eTable 3. Multiple Imputation Under Departures From the Missing at Random Assumption for the Change of Amount of Urine Leakage Measured by the 1-Hour Pad Test

	Electroacupuncture (n=252)	Sham electroacupuncture (n=252)	Difference (95% CI)	*p* value
Change from baseline in amount of urine leakage measured by the 1-hour pad test, LS mean (95% CI), g[a]				
Week 2	-5.64 (-7.87 to -3.42)	-2.08 (-4.30 to 0.14)	3.56 (1.54 to 5.58)	<.001
Week 6	-9.66 (-12.20 to -7.12)	-2.60 (-5.1 to -0.05)	7.06 (4.48 to 9.64)	<.001

Abbreviations: CI, confidence interval ; LS, least squares.

[a] Mixed model were used on the intention-to-treat population with control-based pattern imputation under the missing not at random assumption for 18 participants (6 in the electroacupuncture group and 12 in the sham electroacupuncture group).

1.3 Sensitivity Analysis for Adjustment of Baseline Imbalance in Age

The baseline age was imbalanced from table 1 between groups electroacupuncture and sham electroacupuncture (54.5 vs. 56.2, *P*=0.02). We believe that our randomization process worked correctly. However, because baseline age is an important prognostic factor, to assess the robustness of the primary analysis, a sensitivity analysis including the age factor as a covariate was performed. The results of unadjusted and adjusted for age showed baseline imbalance in age did not affect the treatment effects (Table 2 and eTable 4).

eTable 4. Estimated Values With Age Adjustment for Change in Amount of Urine Leakage Measured by the 1-Hour Pad Test[a]

	Electroacupuncture (n=252)	Sham electroacupuncture (n=252)	Difference (95% CI)	P value
Change from baseline in amount of urine leakage measured by the 1-hour pad test, LS mean (95% CI), g				
Week 2	-5.78 (-8.04 to -3.53)	-2.09 (-4.35 to 0.16)	3.69 (1.66 to 5.73)	<.001
Week 6	-9.97(-12.57 to -7.37)	-2.53 (-5.13 to 0.08)	7.44 (4.85 to 10.03)	<.001

Abbreviations: CI, confidence interval; LS, least squares.

[a] The number of participants with imputed data was 6 (2.4%) in the electroacupuncture group, and 12 (4.8%) in the sham electroacupuncture group.

1.4 Sensitivity Analysis Using Mixed-Effect Model with Repeated Measures Method

A sensitivity analysis also was performed using a mixed-effect model with repeated measures approach. The model included change from baseline to 6-week as response variables, fixed-effects factors for treatment, visit, treatment × visit interaction, and the amount of urine leakage measured by the 1-hour pad test baseline value, random-effects factors for participant, site, and site × treatment interaction. The model did not impute missing data points. An unstructured correlation matrix was used to model the within participant errors. Parameters were estimated using the maximum likelihood. The results from both week 2 and week 6 were robust to use the mixed-effect model with repeated measures method (Table 2 and eTable 5).

Code:

```
proc mixed data=test_reg2    METHOD=ML;
        class group(ref="A") center visit subjid ;
        model col1=baseline group|visit/solution;
        repeated /type=un sub=subjid;
        random center center*group subjid;
        lsmeans group*visit /diff cl;
        ods output DIFFS=lsmdiffs lsmeans=lsmeans_ds(drop=effect) SOLUTIONF=parms;
run;
quit;
```

eTable 5. Estimated Values Using Mixed-Effect Model With Repeated Measures

	Electroacupuncture	Sham electroacupuncture	Difference (95% CI)	p value
Change from baseline in amount of urine leakage measured by the 1-hour pad test, LS mean (95% CI), g				
Week 2	-5.81 (-8.22 to -3.41)	-2.04 (-4.45 to 0.37)	3.77 (1.75 to 5.80)	<.001
Week 6	-9.88(-12.29 to -7.47)	-2.60 (-5.01 to -0.19)	7.28 (5.25 to 9.31)	<.001

Abbreviations: CI, confidence interval; LS, least squares.

eTable 6. Adverse Events Unrelated to Treatment

Adverse events [a]	Electroacupuncture (n=247)[b]	Sham electroacupuncture (n=249)[b]
	Participant, No. (%)	Participant, No. (%)
Total	71 (28.74)	67 (26.91)
Common cold	59 (23.89)	52 (20.88)
Chronic bronchitis	4 (1.62)	3 (1.20)
Cough	1 (0.40)	4 (1.61)
Pharyngitis	1 (0.40)	4 (1.61)
Climacteric syndrome	1 (0.40)	3 (1.20)
Rhinitis	2 (0.81)	0 (0.00)
Acute Bronchitis	1 (0.40)	0 (0.00)
Cervical Spondylosis	0 (0.00)	1 (0.40)
Fever	0 (0.00)	1 (0.40)
Knee Osteoarthritis	1 (0.40)	0 (0.00)
Lumbar surgery	0 (0.00)	1 (0.40)
Pneumonia	1 (0.40)	0 (0.00)
Uterine Fibroids	1 (0.40)	0 (0.00)

[a] Adverse events were analyzed in all participants who received treatment and counted by type rather than frequency in the same participant. Adverse events with different types occurring in one participant were defined as independent adverse events; an adverse event with multiple occurrences in one participant was defined as one adverse event.

[b] 5 participants in the electroacupuncture group and 3 in the sham electroacupuncture group did not receive treatment.

eTable 7. Participant-Blinding Assessment Results

	Treatment guess No. (%)	Electro-acupuncture (n=42)	Sham electroacupuncture (n=42)	Kappa Coefficient (95%CI)	*p* value[c]
Week 3[a]	'Electroacupuncture'	31 (75.6)	29 (69.0)	.07 (-0.13 to 0.26)	.63
	'Sham Electroacupuncture'	10 (24.4)	13 (31.0)		
Week 6[b]	'Electroacupuncture'	32 (78.0)	25 (64.1)	.14 (-0.06 to 0.34)	.22
	'Sham Electroacupuncture'	9 (22.0)	14 (35.9)		

[a] One participant in the electroacupuncture group was not recorded at week 3.

[b] One participant in the electroacupuncture group and 3 participants in the sham electroacupuncture group were not recorded at week 6.

[c] P was calculated from a kappa analysis.

eFigure. Forest Plot of Subgroup Analysis per Stress Urinary incontinence Severity at Baseline by Mixed Effects Model

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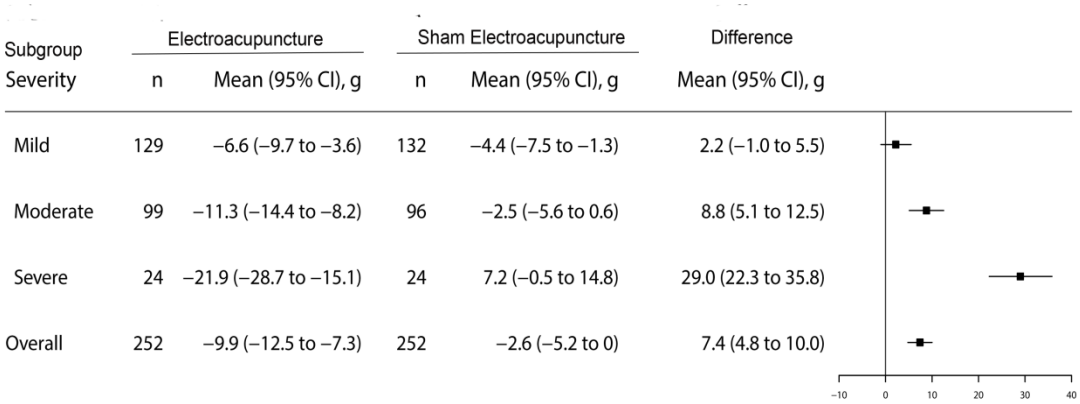

Abbreviations: CI, confidence intervals. The estimated mean values were change from baseline to week 6. A post-hoc subgroup analysis for stress urinary incontinence severity based on the baseline amount of urine leakage measured by the 1-hour pad test was conducted by adding an interaction term of the stress urinary incontinence severity rated × treatment into the primary analysis. The mixed effects model showed that the interaction between severity of incontinence and treatment was statistically significant (*P*<.001). Stress urinary incontinence severity was based on baseline amount of urine leakage measured by the 1-hour pad test as follows: 1.1-9.9 g, mild; 10-49.9 g, moderate; ≥ 50 g, severe.

eReferences

1. Abrams P, Blaivas JG, Stanton SL, Andersen JT. The standardisation of terminology of lower urinary tract function. The International Continence Society Committee on Standardisation of Terminology. *Scand J Urol Nephrol Suppl*. 1988;114:5-19.

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3. Kahan BC, Morris TP. Analysis of multicentre trials with continuous outcomes: when and how should we account for centre effects. *Stat Med*. 2013;32(7):1136-1149.

4. Ratitch B, O'Kelly M. Implementation of pattern-mixture models using standard SAS/STAT procedures. 2011. http://pharmasug.org/proceedings/2011/SP/PharmaSUG-2011-SP04.pdf. Accessed July 25,2012.