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PREDICTORS FOR POOR RECOVERY IN WOMEN WITH STRESS URINARY INCONTINENCE FOLLOWING PHYSIOTHERAPY INTERVENTION

Hypothesis / aims of study
During the last decades many studies have been published considering the efficacy of conservative therapies with 'cure/improvement' rates ranging from 50% to 97%. However, definitions of 'cure' or 'improvement' are highly variable as well as the populations studied. Caution must be taken in interpreting these outcomes because there are still gaps in our knowledge, specifically on prognosis.

Up until now, little research has been done on risk factors associated with the evolution of (stress) UI but being modifiable by conservative intervention. The identification of risk factors, which can be modified in women who are at risk for developing (longstanding) stress UI symptoms, may facilitate the selection of patients who will most likely benefit from conservative (or physiotherapy) intervention. To our knowledge, no study has examined risk factors as predictors of success or failure following physiotherapy intervention.

The objective of this prospective cohort study is to identify predictors for poor recovery in women with primary or recurrent stress UI episodes at 12 weeks of follow-up.

Study design, materials and methods
Inclusion in our prospective cohort study was restricted to women of 18 years or older with a diagnosis of urodynamically proven stress UI or stress UI at history and physical examination and who had stress UI for at least six months. Primary outcomes were the 5-item PRAFAB-Q (measuring UI leakage severity and its perceived impact) and the 7-point Global Rating Scale (GRS) of patient's perceived benefit of the intervention ranging from very much better to very much worse. The leakage severity scale includes the items protection, amount and frequency and per item four points can be earned (min-max = 3-12). Multiple logistic-regression analysis with specified candidate predictor variables was constructed to predict two binary outcomes: (1) Leakage severity (LS) of the PRAFAB-Q in which recovery was defined as a minimum score of three points]) and (2) the GRS, in which recovery was defined as moderately to very much better. The main follow-up moment for the analyses was set at 12 weeks. The candidate predictors were grouped in six distinct categories: [1] socio-demographic characteristics, [2] clinical history, [3] obstetric characteristics, [4] previous urogynaecological surgeries, [5] general health characteristics (self-assessed psychological distress, physical health, obesity and selected co morbidities by physician-diagnosis). The number of selected candidate predictors was restricted in the analysis of smaller subsets of patients to make sure that the two models contained at least 15 events on the primary outcome measures per predictor. All 14-candidate predictors were forced in a full multivariate logistic-regression model to control for confounding or intercorrelations between predictors to calculate mutually adjusted odd ratios (OR [95% CI]) for both binary outcomes of recovery. The models were evaluated by addressing three aspects of predictive performance: (1) calibration (agreement between predicted and observed frequencies), (2) discrimination (ability of the model to distinguish patients with different outcomes) and (3) classification (ability of the model to correctly classify patients given a certain threshold value).

Results
Two hundred and seventy-nine women enrolled in the study of which 12 were excluded from the analyses because they were classified by the PRAFAB-Q as having mild UI (< 8 points on the total PRAFAB-Q score). About 44% (n=117) were considered recovered by the LS and 59% (n=158) when defined by the GRS. Ten of the 14-candidate predictors were significant (p-value <0.05) predictors of a poor outcome on the LS and included women with severe UI leakage scores at baseline, low education, peri-menopausal status, a BMI greater than 30 kg/m^2, mixed UI, a poor outcome following physiotherapy intervention for a previous UI episode, a severe pelvic organ prolaps (POP), a prolonged second stage of labour (> one hour), a poor physical health, a high psychological distress score and co-morbidity. The predictive power of the predictors in the most parsimonious model ($P_{out} \geq 0.10$) was high: the percentage of patients correctly classified was 88.0% with an explained variance of 55.6%. The accuracy of the final model was excellent with a ROC AUC of 0.89 (95% CI: 0.85; 0.93) and good calibration and model fit (Hosmer and Lemeshow test; p=0.44). The odds ratios were ranging from 0.10 (95% CI: 0.04; 0.22) for severe baseline UI leakage scores and 0.40 (0.04; 0.64) for mixed (but predominantly) stress UI. Predictors associated with the second binary outcome resulted in eight predictors, of which all but one (parity $\geq$ 3) was also included in the first model.

Interpretation of results
Identifying hardly or even non-modifiable risk factors associated with a poor outcome for stress UI is crucial for clinical practice as well as research. Further research for clinical practice is needed to evaluate different and specific treatment strategies related to these risk factors and strong predictors for poor recovery in women with stress UI, such as life style, behavioural or psychological interventions, better supervised pelvic floor muscle training programmes (and for longer periods of time with higher intensities) but with more emphasise on the improvement of the general physical health status.

However, this study also shows that physiotherapy intervention years after incontinence and prolaps surgery, may restore and strengthen the pelvic floor muscles with very satisfying short-term results that should be considered as general practice, which also could prevent recurrences at the long term.

The results of this study might also explain the highly variable 'cure/improvement' rates as shown in systematic reviews. Future research that aims to evaluate the efficacy or cost-effectiveness of (physiotherapy) interventions must take into account the impact of these predictors for poor recovery.

Concluding message
We have developed a practical model for predicting the probability of (poor) recovery at 12 weeks of follow-up in women with stress UI. This study provides robust evidence of clinical relevant predictors associated with a poor outcome at 12 weeks of follow-up in women with stress UI following physiotherapy intervention. However, future studies are needed to replicate these findings and further model validation in different populations and types of interventions.

To improve the model's predictions for future similar patient populations, we will estimate the final model's regression coefficients by using penalized maximum likelihood procedures to adjust for over-optimism. The penalty factor will be determined by optimizing Akaike information criterion using Harrell's Design library and S-PLUS software, version 6.0 (Insightful Inc., Seattle, Washington) for external validation in a new set of data.