Evaluation of the factors contributing to success of pelvic floor muscle training in stress urinary incontinence

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Abstract

Pelvic Floor Muscle Training (PFMT) is an effective, non-invasive, and cost-effective treatment for Stress Urinary Incontinence (SUI). However, its success rate varies. We evaluated the factors predicting success in PFMT, such as age, initial urinary leakage, initial pelvic floor muscle contraction strength, urethral hypermobility, and myostatin level. A nested case-control study was conducted at Dr. Cipto Mangunkusumo hospital between February and October 2021. We evaluated demographic characteristics, UDI-6 and IIQ-7 questionnaire scores, physical exam, pad weight test, urethral hypermobility ultrasound, perineometry, myostatin level, and we instructed the subjects in PFMT according to a guidebook. After 12 weeks of PFMT, we evaluated therapy success, defined as less than 3g on the pad weight test. The study involved 58 women: 5 subjects dropped out, 47 subjects reached treatment success, and 6 subjects did not reach treatment success. Following bivariate analysis, we found that initial pad weight was the only variable that was significantly associated with treatment success (p=0.001, 95% CI: 1.02 – 2.25). The PFMT success rate was 88.68%, and initial urine leakage lower than 6.5g predicts PMFT success with 80.9% sensitivity and 83.3% specificity (p=0.001, 95% CI1.02–2.25).

Introduction

Stress Urinary Incontinence (SUI) is the involuntary leakage of urine during physical activity (e.g., exercise) or coughing/sneezing.[1] SUI is reported in 13.9% of males and 51.1% of females.[2] Among the three types of urinary incontinence, SUI is the most prominent: 49% SUI, 21% urge urinary incontinence, and 29% mixed urinary incontinence.[3] Therapy for SUI can be non-surgical or surgical; Pelvic Floor Muscle Training (PFMT) is the first non-surgical treatment of choice. The mechanism of PFMT action in SUI treatment is to improve the strength of pelvic floor supporting structures, especially pelvic floor muscles.[4]

Surgical treatment can include mid-urethral sling placement or retropubic urethropexy. The success of the Burch and Marshall-Marchetti-Krantz procedure for SUI treatment was reported to be 85–90%, transvaginal tape was 88%, and trans-obturator tape was 84%.[5] However, such surgical procedures can lead to an increased risk of voiding dysfunction.[5] Urinary incontinence is an economic burden. In Dr. Cipto Mangunkusumo hospital, a midurethral sling procedure costs 42,861,389.55 IDR despite the 17,138.,500.00–37,922,600.00 IDR National Health Coverage limits.[6] Nonsurgical treatment, such as PFMT, is an effective and affordable alternative to SUI treatment. Rehabilitation costs in outpatient clinics are 234,000.00 IDR,[6] with lower PFMT costs per unit. However, the success rate of PFMT varies; Nystrom's study in 2018 reported a success rate of 61.4%,[7] and another study reported >84%.[8] This variation in success rate indicates that there are various factors that determine the success of PFMT; therefore, those determining factors should be evaluated. By doing so, we will be able to predict the success of PFMT treatment for each patient, thus helping clinical decision-making in daily practice.

Age,[9,10] disease severity (initial urine leakage weight),[11,12] urethral hypermobility,[1] and myostatin level[13] were reported as probable predicting factors for PFMT success. Myostatin, or *growth differentiation factor* 8 (GDF8), is one of the myokines (*i.e.*, cytokines or peptides secreted by myocytes in response to contraction) of striated muscle. Myostatin acts as an inhibitor of striated muscle myogenesis through muscle cell growth and differentiation.[13,14] Radziminska, in 2018, reported a reduction of myostatin level associated with improvement of SUI severity in women treated with PFMT.[13] Therefore, myostatin is considered a success predictor. To our knowledge, there are no previous studies predicting PFMT success using these factors.

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Informed consent: Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

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Material and Methods

This study is part of the *Kegel Guide Book Role on Stress Urinary Incontinence Woman in Success Improvement Through Adherence Improvement* study (in progress), which was a randomised-controlled trial comparing treatment success among an intervention group who used the Kegel guide book and a control group who did not use the book. The *Evaluation of the Factors Contributing to Success of Pelvic Floor Muscle Training in Stress Urinary Incontinence* study (in progress) is a nested.case control study, evaluating the success of PFMT in the group of Kegel guidebook users. In the main study, the PFMT regimen included 50 minimal contractions/week for 12 weeks, including slow-twitch and fast-twitch contractions and monthly evaluation by a physician. The guidebook provided knowledge of SUI, a PFMT technical guide, and exercise monitoring. Among the population we evaluated, initial urine leakage weight, age, initial levator ani muscle contraction strength, urethral hypermobility, and myostatin blood level were potential predictors of PFMT success in SUI treatment.

Our inclusion criteria were women >20 years old who underwent PFMT for SUI treatment and were able to perform PFMT correctly. Our exclusion criteria were those who were unable to complete the questionnaire (either medically or cognitively unable), had undergone continence surgery or other pelvic floor surgery, were receiving other treatment for urinary incontinence, had levator ani avulsion, stage 3 or 4 pelvic organ prolapse according to the Pelvic Organ Prolapse-Quantification (POP-Q) system, had neurological or muscular disease preventing PFMT practice, had a history of malignancy/pelvic radiation/pelvic injury, urinary tract infection, chronic cough, chronic constipation, or systemic collagenous disease. Drop-out criteria were determined with the main study criteria, which was twice in a row loss to follow-up (follow-up every 2 weeks), exercise frequency at each follow-up less than 100 contractions twice in a row, or refusal to continue participation in the research. The urinary leakage weight was evaluated via 1-hour pad test, urethral hypermobility was evaluated via ultrasound exam in litotomy position comparing rest and valsava [either Bladder Neck Descent (BND) of 20.8 mm,[15] shifting of the Retrovesical Angle (RVA) >141.5°,[16] or rotational angle (RoU) of 45°][17] using a Mindray Resona 7® machine with smart pelvic® application, levator ani contraction strength was evalu-

Table 1. Subject characteristics.

Subject characteristic	53 Subjects Frequency	%	Subject characteristic	53 Subjects Mean	SD	Median	Range
Age category			Age (years)	46.04	9.90		
20–40 years	14	26.4					
41–68 years	39	73.6					
Body Mass Index (BMI) (kg/m^2)			Largest baby's birthweight (g)			3,300.00	1,675–4,200
<18.5	1	1.9					
18.5–22.9	4	7.5					
23–24.9	8	15.1					
25–29.9	27	50.9					
>30.0	13	24.5					
Educational Level			First baby's birthweight (g)			3,000.00	1,675–4,000
Lower than university	12	22.6					
University	41	77.4					
Menopausal status			Initial urinary leakage weight (g)			4.00	3–90
Pre-menopause	33	62.3					
Post-menopause	20	37.7					
Spontaneous vaginal delivery			Myostatin level (pg/mL)	2,333.02	1,133.78		
0	6	11.3					
1	14	26.4					
2	12	22.6					
3	14	26.4					
4	5	9.4					
5	3.8						
History of vacuum extraction			Initial UDI-6 Score	38.99	14.23		
None	51	96.2					
Yes	2	3.8					
History of forceps extraction			Initial IIQ-7 Score	45.00	16.86		
None	52	98.1					
Yes	1	1.9					
History of caesarean section			Initial pelvic floor muscle contraction strength (cmH$_2$O)	23.10	9.28		
None	38	71,7					
Once	11	20.8					
More than once	4	7.6					
Initial urinary leakage severity							
3–10g	43	81.1					
11–50g	8	15.1					
>50g	2	3.8					
Urethral hypermobility							
No hypermobility	22	41.5					
Hypermobility	31	58.5					

ated using a Peritron® perineometer, and myostatin level was evaluated using ELISA of a morning venous blood sample after >12 hours night-time fasting at Laboratorium Terpadu Faculty of Medicine Universitas Indonesia. Our study was conducted in the outpatient clinic of Dr. Cipto Mangunkusumo Hospital Jakarta between February and October 2021. We received ethical permission from the Ethical Commission of the Faculty of Medicine Universitas Indonesia (number: KET-912/UN2.F1/ETIK/PPM.00.02/2020). After 12 weeks of treatment, we defined treatment success as pad test weight less than 3g.

We analysed our data using the Statistical Package for Social Sciences (SPSS) for Windows, version 20. We evaluated the association of each of initial urinary leakage weight, initial levator ani contraction strength, and myostatin level with treatment success using the Mann–Whitney U test,[18] and urethral hypermobility and age with treatment success using the Fischer test.[18] Variables with a p-value <0.25 were analysed in a logistic regression test, and variables with a final p-value <0.05 were included in the treatment success prediction formula. When our bivariate analysis produced only one variable associated with treatment success, the multivariate analysis was not needed.

Results

Of the 59 women being evaluated, 1 had bilateral levator ani avulsion. Among the 58 study subjects, 5 dropped out. We analysed 47 subjects who achieved treatment success and 6 subjects who did not achieve treatment success. The population characteristics are presented in Table 1.

After 12 weeks of PFMT, the mean Incontinence Impact Questionnaire - Short Form (IIQ-7) score improved from 43.97 to 22.56, the mean Urogenital Distress Inventory – Short Form (UDI-6) score improved from 38.22 to 21.46, the mean urinary leakage weight improved from 4 g to 0.8 g, and the mean levator ani contraction strength improved from 23.17 to 36.73 cm H_2O. We had 47 subjects (88.68%) achieve treatment success; the characteristics of the subjects according to treatment success are listed in Table 2. Bivariate anal-

Table 2. Subject characteristics according to treatment success.

Variable	12-Week PFMT Evaluation				Variable	12-Week PFMT Evaluation	
	No treatment success		Achieved treatment success			No treatment success (%)	Achieved treatment success (%)
	X/Med	SD/Range	X/Med	SD/Range			
Age (years)	52.50	13.16	45.21	9.27	Age category		
					20–40 years	1	13
					41–68 years	5	34
Myostatin level (pg/mL)	2,260.94	863.52	2,342.22	1,171.03	Urethral hypermobility		
					No hypermobility	2	20
					Hypermobility	4	27
Initial pelvic floor muscle contraction strength (cmH_2O)	19.52	10.24	23.56	9.18	Educational level		
					Lower than university	2	10
					University	4	37
Initial urinary leakage weight (g)	27.83	31.78	7.53	11.62	Menopausal status		
					Pre-menopause	2	31
					Post-menopause	4	16
Body mass index (kg/m2)	28.88	2.32	27.58	4.98	Body mass index		
					<18,9	0	1
					19–22,9	0	4
					23–24,9	0	8
					25–29,9	4	23
					>30	2	11
Number of spontaneous deliveries	3.00	1.095	1.96	1.301			
Largest baby's birthweight (g)	3,548.33	226.311	3,196.38	501.830			
First baby's birthweight (g)	3,331.67	256.94	3,038.51	499.99			
Initial UDI-6 score	43.75	10.79	38.39	14.59			
Initial IIQ-7 score	61.29	47.14–70.71	33.00	14.14–51.86			

Table 3. Bivariate analysis teratment success determinants.

Variable	P (95% CI)	Variable	P (95% CI)
Age	0.35*	Urethral hypermobility	1.00***
		No hypermobility	
		Hypermobility	
Myostatin level	0.84*		
Initial pelvic floor muscle contraction strength	0.51*		
Initial urinary leakage weight	0.01**		

*Unpaired t test, **Mann–Whitney U test *** Fischer's test ysis of the independent variables is presented in Table 3.

We found that initial urinary leakage weight was the only factor that was significantly associated with PFMT treatment success in SUI. We evaluated the cut-off point of initial urinary leakage weight and found the cut-off to be 6.5 with 80.9% sensitivity and 83.3% specificity (p=0.001, 95% CI 1.02–2.25). The ROC curve is described in Figure 1.

We had six subjects who failed. The characters of those six subjects are summarised in Table 4.

Discussion

The success rate of PFMT in our study was 88.68%; this was similar to a previous study.[8] Furthermore, we found that 12 weeks of PFMT intervention improved the UDI-6 score, IIQ-7 score, and levator ani contraction strength. This finding is in line with the exercise benefit of PFMT on the levator ani, increasing muscle mass and strength, thereby improving the supporting structure and preventing urinary leakage. As the leakage resolved, the symptoms were relieved and quality of life improved, as represented by the UDI-6 and IIQ-7 scores.

To predict treatment success, we used initial urinary leakage weight to represent the severity of SUI. Most of our population had mild SUI. We found that subjects with less severe disease, represented by a smaller urinary leakage weight, achieved better treatment success. Brooks *et al.* reported that disease severity, represented by the International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form (ICIQ-UI-SF) questionnaire, was a predicting factor of treatment success.[19] Similar to our study, Obloza *et al.* reported that patients with milder symptoms achieved greater treatment success. However, the study reported symptom

Table 4. Characteristics of subject who did not succeed.

Variable	Subjects who did not succeed 1	2	3	4	5	6	Note
Age (years)	67	67	49	50	32	50	Mostly 41–68 years old
Myostatin Level (pg/mL)	2,216.16	1,102.34	3,239.48	2,288.78	1,520.89	3,197.96	66.67% had a myostatin level lower than the mean of the study population
Initial pelvic floor muscle contraction strength (cmH_2O)	14.70	24.40	11.00	17.00	12.00	38.00	66.67% had initial strength 22.5–35.24 cmH_2O
Initial urinary leakage weight (g)	90	7	15	5	30	20	66.67% had moderate-severe SUI, with most above 6.5 g
Urethral hypermobility	Hypermobility	Hypermobility	Hypermobility	No hypermobility	Hypermobility	No hypermobility	66.67% had hypermobility
Educational level	University	Less than university	University	University	University	University	Most had university education
Menopausal status	Menopause	Menopause	Menopause	Pre-menopause	Pre-menopause	Menopause	66.67% were menopause
Body mass index (kg/m^2)	27.34	31.24	32.03	26.84	26.67	29.14	All subjects were obese
Number of spontaneous deliveries	4	3	4	3	1	3	Mostly multiparous
Largest baby's birthweight (g)	3,600	3,900	3,200	3,600	3,490	3,500	No macrosomia
First baby's birthweight (g)	3,600	3,300	3,200	2,900	3,490	3,500	No macrosomia
Initial UDI-6 Score	54.17	45.83	41.67	25.00	54.17	41.67	Most had higher scores than the mean score of the study population
Initial IIQ-7 Score	61.29	70.71	56.57	47.14	61.29	70.71	All had higher scores than the mean score of the study population

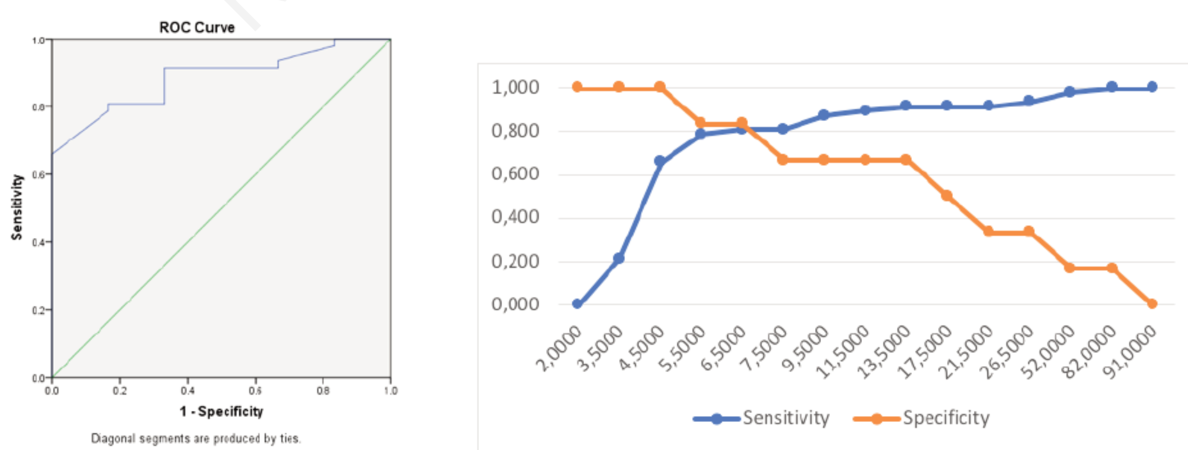

Figure 1. ROC (AUC = 88.7%) and cut-off point of initial urinary leakage weight.

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severity as incontinence episodes, not as urinary leakage weight.[20] Singh *et al.* reported severe SUI as a poor prognostic factor for PFMT treatment success.[21] In contrast to our findings, Hung *et al.* reported that patients with more severe SUI achieved better symptom improvement after PFMT than patients with less severe SUI.[12] The disease severity parameter varied in other studies. Dumolin *et al.* and Labrie *et al.* reported symptom severity as urinary leakage episodes within 24 hours,[22,23] while Yoo *et al.* reported it as severity index.[24]

Our study found that less than 6.5g initial urinary leakage weight was associated with PFMT treatment success. This finding is expected to aid in clinical management, helping clinicians and patients consider which cases will reach a post-PFMT treatment dry pad test, and which cases should be considered for second line treatment if the PFMT outcome is not favourable.

Our study population had a mean age of 46.04 years, and 73.6% of the patients were more than 40 years old. And we did not find a significant association between age and PFMT treatment success. Lindh *et al.* reported that treatment success was predicted by older age. However, in his study, the mean age was 50.3±10.1 years, and 22% of the population used topical oestrogen, which was not used in our population.[9] Another study by Labrie *et al.* evaluated the need for surgical treatment after PFMT treatment by combining age <55 years, severe SUI, and UDI scores. He found that subjects younger than 55 years of age were prone to fail PFMT.[23] However, his study population was 49.9±8.3 years old, with moderate-to-severe SUI, which was in contrast to our study.

Our population's mean initial strength was 23.10±9.20 cmH_2O. This mean strength corresponded to moderate strength (Moegni and Ocsilia Wengkang reported that 22.5–35.24 cmH_2O corresponded to modified Oxford scale 3 or 'moderate strength'),[25] and we expected that the muscle could respond optimally to PFMT. However, initial pelvic floor muscle contraction strength was not found to be significantly associated with PFMT treatment success. Our findings were similar to those of Brooks *et al.*, who evaluated initial pelvic floor contraction strength on the Oxford scale.[19] Furthermore, Yoo *et al.* reported that initial pelvic floor muscle contraction strength was not predictive of treatment success.[26]

In our study, myostatin mean level was 2,333.02 pg/mL. Radzminiska reported a median myostatin level of 142.74 ng/mL (142,740 pg/mL) in an older population (>60 years old, with a median age of 69.50 years).[13] Myostatin level can be influenced by sarcopenia in the elderly; however, myostatin levels are also increased in obesity and insulin resistance,[27] and our population was dominated by obese women. Moreover, disease severity can influence myostatin level. Both studies populations were dominated by mild SUI; however, they used the Revised Urinary Incontinence Scale (RUIS) to represent disease severity, and their population was Caucasian while ours was Asian/Malay. Racial differences might account for differences in myostatin level; however, we have not found a base line level of myostatin in Asian/Malay women with SUI. Our study could contribute to filling the information gap. Moreover, physical activity also influences myostatin level. Louis *et al.* reported that myostatin levels decreased 3.6-fold 8–12 hours after acute physical exercise.[28] Kabak *et al.* reported that myostatin levels increased immediately following high-intensity physical exercise and decreased back to baseline after 3 hours in a population of male kickboxer athletes.[29] In our study, there was no history of high-intensity physical exercise in our subjects. However, we did not evaluate in-depth the physical activity of our subjects, and this might represent one of the weaknesses of our study.

We found that myostatin level was not correlated with treatment success, which was in contrast to Radzminiska's report.[13] Yuan *et al.* reported increased myogenesis in vitro and in vivo in myostatin-gen-suppressed rats.[30] Akita *et al.* reported that myostatin inhibited human rhabdosphincter cell proliferation.[31] Our finding of no correlation of initial myostatin level with treatment success indicates that myostatin might not act as a single biological predictor of PFMT success; its role as a multiple biological marker still needs further study. Akita *et al.* reported that myostatin inhibited other myokines.[31,32] Calvani *et al.* reported that, to evaluate sarcopenia, a group of biological markers was needed, including myostatin.[32,33] We realised that, in addition to insufficient evaluation of the metabolic condition and physical activity of our subjects, which could have influenced myostatin level, only evaluating a single biomarker was another weakness of our study.

Urethral hypermobility, as one of the major pathophysiological pathways to SUI, correlated with pelvic floor support weakness; therefore, PFMT was expected to improve it. However, our study found no significant association between urethral hypermobility and PFMT success. Kalejaye *et al.* reported a wide spectrum of urethral hypermobility and intrinsic sphincter deficiency, indicating an overlap between urethral hypermobility and intrinsic sphincter deficiencies.[34] This observation might explain why urethral hypermobility could not predict PFMT success in our study as we did not evaluate the intrinsic urethral sphincter function. We acknowledge that this is another study weakness. Another report by Brooks *et al.* suggested that bladder neck distance in resting-standing position was predictive of PFMT success.[19] In our study, we evaluated urethral mobility in lithotomy position, comparing its position and movement at rest and during Valsalva.

Among the failed subjects, we found that the their age was mostly above 40 years; 66.67% had an initial contraction strength of 22.5–35.24 cmH_2O, which corresponded to modified Oxford scale 3 (moderate strength).[25] Therefore, it was expected that the muscles could contract quite well. Most of the subjects had moderate-to-severe SUI, and we know that more severe SUI is associated with PFMT treatment failure. Most of the subjects had hypermobility, and this was expected to benefit from PFMT; however, our statistical analysis found no association between urethral hypermobility and PFMT success. Most subjects had a university education, and they were expected to have better understanding and correctly practice PFMT, leading to better treatment success. Another factor to consider in addition to correctness is the compliance of training; this compliance factor will be evaluated deeper in the ongoing main study, *Kegel Guidebook Role on Stress Urinary Incontinence Woman in Success Improvement Through Adherence Improvement*.

Most of the subjects had menopause, which might have been associated with a lack of oestrogenic effect on the pelvic floor muscle to improve the positive impact of physical exercise. All the subjects were obese. Hittel *et al.* reported that myostatin secretion increased in women with obesity and insulin resistance.[27] Higher myostatin levels are detrimental to muscular proliferation and differentiation.[13,14,31] Interestingly, the subjects who did not have success had lower levels of myostatin. Again, further study on the biomarker is needed. However, our statistical analysis found no association between myostatin level and PFMT success. Most of the subjects were multiparous (3–4 deliveries), with no history of macrosomia. The initial UDI-6 and IIQ-7 scores were mostly higher than the mean score of the study population. Those higher scores were correlated with a more severe SUI. Therefore, from the unsuccessful PFMT subject characteristics, the characteristic that was most associated with their lack of success was initial urinary leakage weight. This was consistent with our finding that initial urinary leakage over 6.5 g was associated with PFMT treatment failure.

Conclusions

In our study, the success rate of PFMT in SUI was 88.68%. Success of PFMT (pad test weight <3g) in SUI can be predicted by initial urinary leakage weight. The cut-off point of initial urinary leakage weight was 6.5g.

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