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ORIGINAL ARTICLE

External validation of de novo stress urinary incontinence prediction model after vaginal prolapse surgery

Jordi Sabadell[1] · Sabina Salicrú[1] · Anabel Montero-Armengol[1] · Núria Rodriguez-Mias[1] · Antonio Gil-Moreno[1] · Jose L. Poza[1]

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Abstract

Introduction and hypothesis Stress urinary incontinence (SUI) may appear after the correction of pelvic organ prolapse (POP). The aim of this study was to externally validate a described predictive model for de novo SUI and to assess its clinical performance when used as a diagnostic test.

Methods This was a retrospective descriptive study on a cohort of consecutive women treated in our institution. The main outcome used to validate the model was the presence of objective or subjective SUI 1 year after surgery. A receiver operating characteristic curve was generated from our population to evaluate the predictive accuracy and to compare it with the original model. A cutoff point of ≥50% was used to evaluate its clinical performance as a diagnostic test.

Results Of the full cohort, 169 women were suitable for analysis. The rate of de novo SUI was 11.8%. The predictive accuracy of the model in our population was similar to the original [area under the curve (AUC) = 0.69; 95% confidence interval (CI) = 0.58–0.80). However, its performance measures when evaluated as a diagnostic test were low: positive likelihood ratio = 2.71 and negative likelihood ratio = 0.86. Only 15 women presented a positive test result.

Conclusions External validation of the model found a global predictive accuracy similar to that of the original model. Despite the study being underpowered to give firm conclusions, the test did not show a good clinical performance when applied to our population with low de novo SUI prevalence. A larger sample size is needed to validate the model conclusively.

Keywords Pelvic organ prolapse · Stress urinary incontinence · De novo incontinence · Predictive model · External validation · Model performance

Introduction

Pelvic organ prolapse (POP) is a common condition affecting up to 50% of parous women. Of them, between 6 and 20% will require surgical correction [1]. Continent women may develop stress urinary incontinence (SUI) after POP surgery. The prevalence of de novo SUI is estimated to be 22–61% [2–4]. Although the association of an incontinence procedure with POP surgery can reduce the risk of postoperative SUI, it has been calculated that the number of women needed to treat to avoid subsequent SUI surgery is 6–20 [2, 3, 5–7]. Moreover, the combination of POP vaginal surgery with a midurethral sling (MUS) procedure is associated with an increased risk of adverse events such as bladder and urethral perforations, bleeding, sling erosion, pain, and long-term voiding dysfunction [3, 7, 8]. For those reasons, a one-step approach to all women who will undergo surgery for vaginal prolapse seems inappropriate.

Identifying women at higher risk of developing de novo SUI would allow surgeons to tailor the surgical approach to each individual. With this purpose in mind, a model for predicting the risk of de novo SUI after POP surgery was developed based on data from the Outcomes Following Vaginal Prolapse Repair and Mid Urethral Sling (OPUS) trial [9]. In that trial, previously continent women who underwent

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✉ Jordi Sabadell
jsabadell@vhebron.net

[1] Urogynecology and Pelvic Floor Unit, Department of Obstetrics and Gynecology, Hospital Universitari Vall d'Hebron, Vall d'Hebron Barcelona Hospital Campus, Universitat Autònoma de Barcelona, Passeig Vall d'Hebron 119-129, E-08035 Barcelona, Spain

vaginal prolapse surgery were randomized to a concomitant MUS placement. The incidence of urinary incontinence (UI) at 3 and 12 months after surgery was evaluated. This study involved women being considered for an apical and/or anterior vaginal prolapse repair (POP stage ≥2), allowing native tissue repairs, use of synthetic or biological grafts, and occlusive techniques [2].

The aim of our study was to externally validate this predictive model and assess its clinical performance when used as a diagnostic test in our population.

Materials and methods

The research protocol was approved by the Ethics Committee of the Vall d'Hebron University Hospital. This retrospective descriptive study was performed by reviewing the medical charts of all consecutive women who underwent POP surgical correction in our center between January 2013 and December 2014. Women with a vaginal surgical correction for prolapse of the anterior and/or apical compartment and a minimum follow-up of 10 months were suitable for the analysis. Both native tissue surgery and vaginal mesh repair were included, analogously to the OPUS trial design [2]. Exclusion criteria were clinical SUI prior to surgery, previous incontinence surgery with MUS, and diagnosis of a neoplasm in the surgical specimen that required an additional surgical procedure and/or radiotherapy.

Preoperative evaluation included detailed history, interview following a questionnaire signs and symptoms of lower urinary tract dysfunction based on the terminology recommended by the International Continence Society (ICS) [10], physical examination including cough test (with and without prolapse reduction), and urinalysis and urine culture if indicated. Staging was done using the POP Quantification (POP-Q) system. Women with occult SUI underwent a concomitant MUS procedure according to surgeon and patient consensual decision.

Postoperative follow-up visits were performed at 1 and 12 months. Annual follow-up was done at the hospital or a specialized primary care setting and included physical examination with a cough stress test, interview about symptoms of UI and POP, use of urinary protection, and micturition difficulties. The primary outcome for validating the predictive model was presence of SUI 12 months (± 2 months) after surgery or the need of SUI surgical correction before (this 12 months after surgery). The presence of postoperative SUI was defined as an affirmative response to the direct question: "Do you usually experience urine leakage related to sneezing, coughing, laughing, or any other physical effort?" or by objectifying it during physical examination. Severity of SUI was defined according to the Sandvik score validated for the Spanish language that categorizes incontinence into four groups [11].

Data were analyzed using the software SPSS® version 18.0 for Windows. The probability of SUI at 1 year was calculated using the logistic regression equation provided with the original model [9]. Variables needed to calculate the risk of de novo SUI were age at surgery, parity, body mass index (BMI), preoperative stress test, presence of urge UI (UUI), and association with an MUS procedure. Women without any of these variables or their primary outcome explicitly recorded in charts were excluded. In the descriptive analysis, the prevalence of SUI in different subgroups was compared using Fisher's exact test. A receiver operating characteristic (ROC) curve was generated to calculate predictive accuracy using the area under the curve (AUC) and compared with the original model; 95% CIs were calculated. To clinically evaluate the model as a predictive test, a probability cutoff point of ≥50% was established, as previously suggested [9]. The predictive accuracy of the test was evaluated using sensitivity (Se), specificity (Sp), and likelihood ratios (LHR). As predictive values depend greatly on disease prevalence, potential predictive values in hypothetical populations with different prevalence of de novo SUI were calculated applying the Bayes' theorem. For this purpose, we used Se and Sp values obtained in our population, as this information was not provided in the original study.

Results

A total of 338 women underwent surgery for POP during the above-mentioned period. Of them, 169 were suitable for the final analysis (Fig. 1). Patient characteristics and surgery type are detailed in Table 1. The rate of de novo SUI 1 year after surgery was 11.8% ($n = 20$; 95% CI = 7.8–17.6) in the whole cohort and 12.8% in women who did not receive a MUS. In the first months after surgery, seven additional women complained of SUI, which resolved spontaneously in less than 1 year. When SUI was present, severity at 1 year was mainly slight to moderate, with a median Sandvik score 3.5 [interquartile range (IQR) = 2–4]; one woman (5%) required a second surgery for SUI.

The descriptive analysis of subgroups showed that, on the one hand, the rate of de novo SUI in women with occult incontinence was 0% if they underwent a concomitant MUS and 23.7% if not ($p = 0.09$). On the other hand, women who had their prolapse corrected using a vaginal mesh experienced de novo SUI more frequently than those operated with native tissue repair (41.7% vs. 9.5%; $p = 0.006$).

The global predictive accuracy of the model in our population was similar to the original (AUC = 0.69; 95% CI = 0.58–0.80), with shrinkage of only 4% (Fig. 2). However, when assessed as a diagnostic test using the cutoff point of ≥50%, it showed a low capacity to identify adequately women who would develop SUI. Only 15 women obtained a positive test result under the defined criterion. Performance measures were as follows: Se = 20.0% (95% CI = 8.1–41.6), Sp =

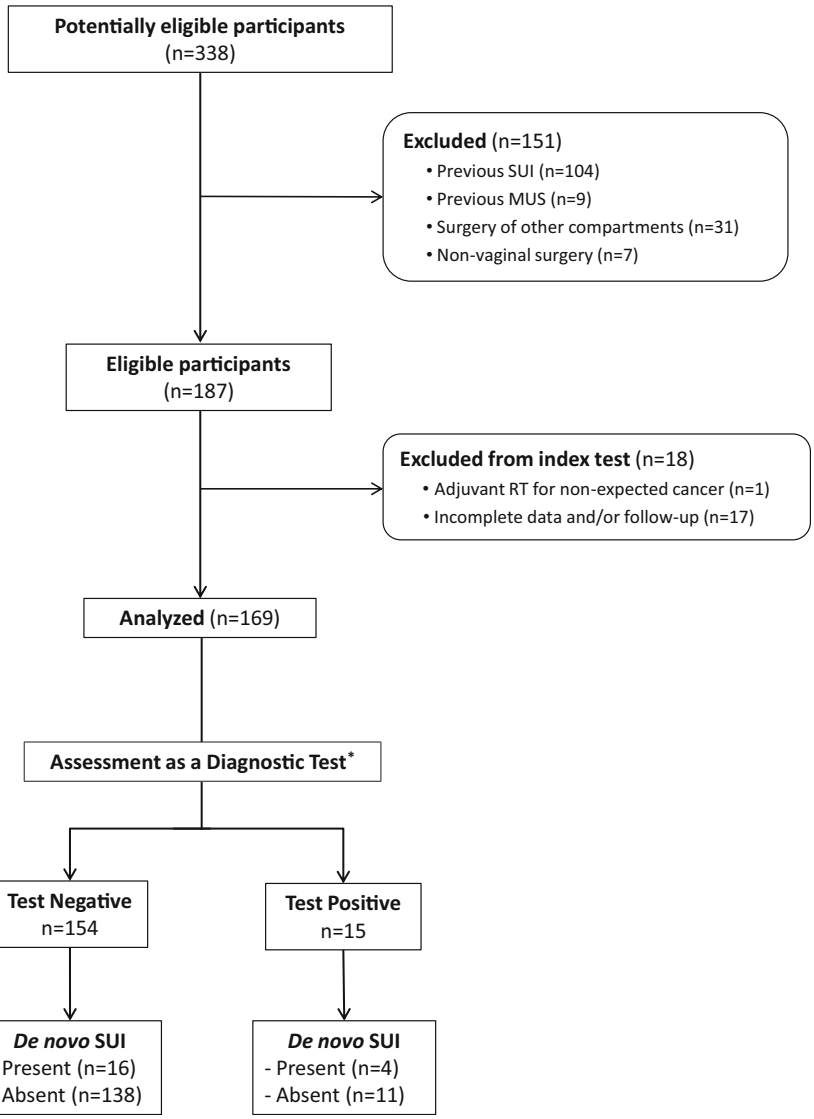

Fig. 1 Study design: *cutoff point, ≥50% probability. *SUI* stress urinary incontinence

92.6% (95% CI = 87.3%–95.8%), positive LHR = 2.71 (95% CI = 0.95–7.70) and negative LHR =0.86 (0.69–1.08).

When it was clinically evaluated in our specific cohort with low prevalence of de novo SUI, using the above-mentioned threshold, the test did not predict appropriately those women who actually developed SUI after a positive result (Fig. 1): Positive predictive value (PPV) = 26.7% (95% CI = 10.9%–51.9%), Negative predictive value = 89.6% (95% CI = 83.8–93.5). After having evaluated the test in different hypothetical scenarios, we calculated that the PPV would be clinically relevant in populations with de novo SUI prevalence close to 50% (see Table 2).

Discussion

SUI may appear after vaginal surgery for POP. Its development decreases patient satisfaction with the procedure and their quality of life. The prevalence of de novo SUI varies substantially depending on the study [2–4]. In addition, MUS surgery is not free from potential serious adverse events [7, 8]. Therefore, their systematic association seems inappropriate. In this context, it would be useful to have a tool to identify women who will benefit from combined surgery.

A predictive model for de novo SUI after vaginal POP surgery was developed based on the OPUS trial [9]. We externally validated that model in a consecutive cohort and found the global predictive accuracy was similar to the original model. Differently from the original model, and due to its clinical relevance, we chose the presence of SUI at 1 year as the primary outcome point rather than the presence of SUI symptoms at any follow-up point during the first year. In fact, we observed that some women developed self-limiting SUI soon after surgery. That could be one reason the prevalence of de novo SUI at 1 year in our population differs greatly from that reported in the study by Jelovsek et al. [9], which used a

Table 1 Preoperative characteristics and surgery type

Patient characteristics	
Age at surgery (years)	67 [61–72]
Body mass index (kg/m^2)	27.5 [25.2–30.4]
Parity	2 [2–3]
Vaginal deliveries	2 [2–3]
Postmenopausal	157 (92.9)
Smoking status	
Nonsmoker	154 (92.8)
Former smoker	9 (5.4)
Current smoker	3 (1.8)
Prior pelvic surgery	27 (16.1)
Diabetes	24 (14.2)
Preoperative urge urinary incontinence	49 (29.0)
Positive stress test[a]	52 (30.8)
Type of surgery	
Anterior repair	53 (31.4)
Anterior repair with mesh	5 (3.0)
Manchester procedure	25 (14.8)
Vaginal hysterectomy	5 (3.0)
Vaginal hysterectomy + anterior repair	64 (37.9)
Vaginal hysterectomy + anterior and posterior repair	9 (5.3)
Anterior and posterior repair	3 (1.8)
Colpocleisis	5 (3.0)
Associated midurethral sling	14 (8.3)

Data expressed in median [interquartile range] or *n* (%)

[a] After having the prolapse reduced

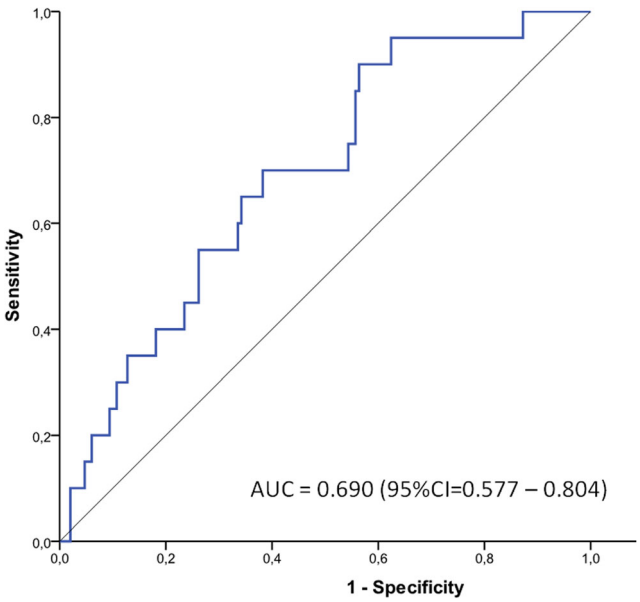

Fig. 2 Receiver operating characteristic curve of the model in our population. AUC: area under the curve

cumulative definition. Although women with posterior prolapse corrections alone could also develop de novo SUI, we chose not to include them in the analysis in order to validate the model in a cohort similar to the derivation one.

Accuracy of a predictive model and a concrete value predictive of an event are, however, difficult to translate into clinical practice. For that reason, we evaluated its clinical performance as a diagnostic test. Although the authors of the

Table 2 Potential predictive values according to the prevalence of de novo stress urinary incontinence (SUI)

SUI prevalence (%)	Bayes' theorem	
	PPV (%)	NPV (%)
10	23.1	91.2
20	40.3	82.3
30	53.7	73.0
40	64.3	63.5
50	73.0	53.7
60	80.3	43.6

PPV positive predictive value, *NPV* negative predictive value

original model did not report a formal analysis of an ideal cutoff point, they suggested a probability value ≥50% at which most clinicians will likely offer a prophylactic continence procedure [9]. Using that threshold, the test does not seem to show satisfactory predictive accuracy measures. Both the LHR+ and LHR− seem to indicate that the test would not change any clinical decision after applying it. However, our study is clearly underpowered to give firm conclusions; there were only 20 cases of de novo SUI. Nonetheless, a recent simulation study found that >100 cases were necessary to perform a conclusive validation of a prognostic model [12]. The lack of power in our study could also be seen when analyzing the CI for accuracy measures.

In our scenario, with a low prevalence of de novo SUI, we found the diagnostic test has a poor ability to identify women who will actually develop SUI. It is important to emphasize that predictive values are directly related to disease prevalence. For that reason, we performed an exploratory analysis and found that PPV would be of clinical interest in populations with a high prevalence of de novo SUI close to 50%. This may be one reason another study found no differences regarding patient satisfaction when using the predictive model [13].

A possible criticism of the model is that both native-tissue and vaginal-mesh surgeries were included, with no distinction made between them. Although no conclusions could be drawn from our study in this regard due to the small number of patients in the subgroups, it seems that native-tissue repair and vaginal-mesh surgery behave as two different populations regarding the development of de novo SUI. This hypothesis is plausible owing to differences between procedures: while native-tissue repair attempts to fix anatomical defects, vaginal mesh does not restore the anatomy but creates a fibrotic layer that decreases vaginal elasticity, thus impairing the dynamic continence mechanisms.

The main limitation of our study is the sample size, which limits its statistical power. In light of our results, a larger cohort with more cases of de novo SUI is needed to attain strong results on the model's validation. Another limitation is its retrospective design. In this respect, the database used is subject to a potential source of information bias that may slightly underestimate the outcome. This potential bias was also limited by calculating probabilities of the model automatically once all clinical data and outcomes were collected. These potential variations would surely not affect the clinical interpretation of results.

In summary, clinical validation of a predictive model is desirable to evaluate the clinical relevance of its prognostic information. In our specific population with very low prevalence of de novo SUI, the described model does not seem to have a good clinical performance. However, the study was underpowered to reach conclusive results. Although results of the estimated predictive values may vary when analyzed using Se and Sp values from the original data, it seems the model could be of clinical interest in populations with high prevalence of de novo SUI. We therefore believe this predictive model should first be evaluated in each population before its clinical application and that a validation study with a larger cohort is needed to provide a more precise evaluation.

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