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MIXED INCONTINENCE: COMPARING DEFINITIONS IN WOMEN HAVING STRESS INCONTINENCE SURGERY

Hypothesis / aims of study:
Mixed urinary incontinence is a common condition and represents a clinically important diagnosis. It is well-recognized that post-operative urge incontinence is associated with both objective and patient perceived surgical failure. In order to better counsel women on outcomes after surgical treatment for stress incontinence it would be helpful to have a scientifically-derived preoperative definition of mixed incontinence or an urge symptom threshold beyond which the risk of persistent urge incontinence is clinically problematic. Unfortunately, a scientific definition for mixed incontinence has not yet been operationalized. We report our attempt to determine a scientifically sound, clinically useful definition of mixed urinary incontinence in a surgical population.

Study design, materials and methods:
The Urinary Incontinence Treatment Network (UITN) recently completed randomized surgical trial comparing the fascial sling to the Burch colposuspension for treatment of stress incontinence. The methods and primary outcomes of the trial have been previously reported [1]. Inclusion criteria for participants required a Medical, Epidemiologic and Social Aspects of Aging (MESA) stress subscale score higher than that of the MESA urge subscale score. [2] In addition to the MESA scale, standardized baseline measures included the Urogenital Distress Inventory (UDI)[2], a three-day urinary diary, and standardized urodynamic studies. The three-day diaries and standardized urodynamic tests (using ICS diagnostic definitions) were completed at baseline and at the two-year primary end point
A variety of definitions for mixed incontinence were explored using these baseline measures. First, using the MESA instrument, the "higher threshold" definition was defined as: any answer ≥2 for each subscale question (responses of sometimes, quite a bit). The "intermediate threshold" MESA definition was defined as: score total > 2 for each subscale and the "lower threshold" definition was defined as any answer ≥ 1 on both the MESA stress and urge subscale (any response of "rarely", "sometimes" or "quite a bit"). Separate definitions were created based on a "ratio" using the MESA subscale score converted to a percentage based on the number of items meeting each definition criteria in an attempt to account for the predominance of each incontinence subtype. Urge and Stress Indexes were calculated by taking the MESA urge or stress subscale score and dividing it by the total possible subscale score Three ratios were tested: pure stress incontinence (Urge index = 0), stress predominant MUI (0 < Urge index < ½ stress index) and MUI (½ stress index <= Urge index < Stress index). Given the inclusion criteria for this trial, evaluation of the MUI urge predominant definition was not feasible.
Secondly, we used UDI responses which question whether the patient is currently experiencing urine leakage related to the feeling of urgency and stress symptoms and whether there is an element of bother associated with these symptoms. Similar to the MESA definitions, we created definitions based on the amount of bother for patients experiencing this symptom based on this question. Using bother, we defined "low threshold" as any response greater than "not at all". The UDI "intermediate threshold" UDI definition was defined as UDI urgency or irritative symptom scale > 20. The UDI ratio was based on two UDI subscales: Irritative (UDI-i) and Stress (UDI-s): pure stress incontinence (UDI Irritative symptom scale = 0), stress predominant MUI (0 < UDI-i < ½ UDI-s) and MUI (the rest of the cases).
A third definition of MUI was based on the results of urodynamic evaluation, where the presence of MUI required the presence of urodynamic stress incontinence and detrusor overactivity incontinence.
We also tested these definitions against the clinical outcome. The composite outcome criteria was divided into stress success (standardized stress test, SUI re-treatment and MESA stress symptoms) and overall success (stress criteria plus diary and pad test). We previously reported that diary failure was more common than pad test failure in more women who did not meet overall success criteria. Therefore, we used the diary as a proxy measure for "non-stress" failures, presumably due to urge incontinence episodes. Threshold-oriented definitions for the UDI and MESA were determined using received operator curves (ROC) with diary failure and overall failures.
All analyses were carried out using the personal computer version of SAS statistical software (SAS Institute, Inc, Cary, NC. Version 9.1). Statistical significance was defined by a p-value < 0.05. Logistic regression analysis was used to estimate the association between the study outcomes and different definition of MUI.

Results:
In the 655 women randomized to rectus fascial sling or Burch colposuspension for treatment of SUI, the proportion of women with MUI varied substantially according to the definition of MUI used (Tables 1 and 2).
Table 1: Definition of "mixed incontinence" based on baseline MESA in study population

MESA	Stress (N, %)	MUI (N, %)
Low threshold MUI definition: any answer ≥1 on urge subscale (rarely, sometimes, quite a bit)	Pure Stress 44 (6.7%)	611 (93.3%)
Intermediate threshold MUI definition: Total urge score>2 (Urge index > 11%):	Stress predominant 116 (17.7%)	539 (82.3%)
High threshold MUI definition: any answer ≥2 (Sometimes, quite a bit)	Stress predominant 134 (20.5%)	521 (79.5%)

Ratio (score converted to a percentage based on the number of items)	Pure stress 44 (6.7%) Stress predominant 281 (42.9%)	Mixed 330 (50.4%)

Table 2. Definition of "mixed incontinence" based on participants who reported baseline urge incontinence (N=452, 70.1%).

UDI (required response of "yes" to question 2), definition based on question 3 bother response	Stress (N, %)	MUI (N, %)
Low threshold MUI definition: Any response >"not at all"	Pure Stress 16 (3.5%)	436 (96.5%)
Intermediate MUI definition: UDI Irritative Symptom Scale>20	Stress predominant 114 (17.5%)	Mixed 538 (82.5%)
Ratio (score converted to a percentage based on the number of items)	Pure stress 29 (4.5%) Stress predominant 182 (28%)	Mixed 438 (67.5%)

The definition based on urodynamic testing resulted in the lowest proportion of participants diagnosed with MUI (8.3%) and a low threshold UDI definition resulted in the highest proportion categorized as MUI (96.5%). None of the tested baseline measures had clear "cut" points utilizing ROC analyses to support a scientific definition of MUI. When these definitions were tested against incontinence severity using diary data, the MESA ratio, UDI intermediate, and UDI ratio were all associated with severity as measured by the frequency of incontinence episodes; however very little of the variability was explained by any definition. No strict cut-off value for these baseline measures was useful in predicting clinical outcomes.

Interpretation of results:
Mixed incontinence definitions as currently defined, do not adequately categorize clinically relevant UI subgroups, with both the UDI and MESA categorizing nearly all participants of this trial into the mixed category.

Concluding message:
Researchers who study women with mixed urinary incontinence should consider characterizing and reporting the details of incontinence subtype rather than using the term "mixed".

References

1. Urology 2005;66:1213-1217.
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Is this a clinical trial?	**Yes**
Is this study registered in a public clinical trials registry?	**Yes**
Specify Name of Public Registry, Registration Number	**Clinicaltrials.gov NCT00064662**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**All nine clinical sites and the biostatistical coordinating center the Urinary Incontinence Treatment Network had approval by the relevant Institutional Review Boards and all participants in both trials provided written consent for research participation.**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**