639

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MIXED EFFECTS MODEL FOR ANALYSIS OF LONG-TERM DATA IN FEMALE PELVIC MEDICINE AND RECONSTRUCTIVE SURGERY (FPMRS)

Hypothesis / aims of study

The mixed effects model (MEM) can account for the variability in measures that change over time (e.g. data collected in longitudinal studies). One of the MEM strengths is that the time at which data is collected can be treated as a continuous variable, so does not have to lose precision by being split up into value at year 1, value at year 2, etc. MEM also allows for inequality in the frequency of observations per patient. This is especially important when one considers that in a clinical setting, some patients will visit regularly, others sporadically or only once or twice. The only caveat is that the data must be missing at random in regards to the covariates. With the exception of independence, the typical parametric assumptions apply to the MEM: 1) A linear relationship exists between the response variable and the covariates; 2) the data is normally distributed across all combinations of levels of the covariates; and 3) the error (the difference between the actual response level and the model's estimated response level for each observation) is uniformly distributed.

Study design, materials and methods

Following IRB approval, 3 groups of women with various FPMRS conditions were prospectively studied using MEM: 1) vaginal repair of stress urinary incontinence secondary to urethral hypermobility, with associated early stage anterior compartment prolapse (stage ≤ 2); 2) vaginal repair of >stage 2 anterior compartment prolapse; and 3) long- term objective collagen injection results documented by 3D vaginal ultrasound (3D US). Women with neurogenic bladder were excluded. Data acquisition included Urogenital Distress Inventory (UDI-6), QoL based on a visual analog scale, examination findings (POP-Q/Aa and Ba Points), ultrasound volume of collagen, and median with interquartile range (IQR) for duration of follow-up as well as total numbers of clinical visits. All statistical analyses were completed using SAS 9.3 (SAS Institute Inc., Cary, NC).

Results

In Group 1, 213 patients were followed for a median of 3.1 years (IQR: 1.5-6.2). Ba point was found to be stable over time whereas Aa point and UDI-6 Q3 (SUI) very slightly worsened (p=0.440, p=0.0008). The Aa point change of 0.01/year was not found to be clinically significant. For patients who had a baseline Aa of -1.0, the mean Aa point was -2.8 at both 1 year and 3 years. Group 2 had a median follow-up of 2.7 years (IQR: 1.4-5.1) for 169 patients. Aa and Ba points raised slightly over time (p=0.0019, p=0.0003), but none of the questionnaire values did. In Group 3 (n=67), followed for a median of 2.9 years (IQR: 2.0-4.6), the 3D US volume was found to significantly decrease by 0.11cm^3 per year (p=0.0014). For patients with a single injection, 1 year and 3 year mean volume was 2.5 and 2.3cm^3, while for patients with multiple injections, 1 year and 3 year mean volume was 3.3 and 3.1cm^3.

Interpretation of results

Typical data analysis includes baseline versus post-operative data comparison, and Kaplan-Meier curves (time to failure). We explored a statistical tool seldom used so far in FPMRS to work with large datasets from prospective studies when the data points were acquired in non-standardized interval times. Because of correlated data, we made an assumption about how one observation relates to the other observations from the same patient in place of the assumption of independence. This method was found useful to highlight trends in several FPMRS-related outcome measures over time.

Concluding message

This study confirms that MEM applied to selected FPMRS procedures can trend data points collected at various interval times and irregular frequency, so that data collected in prospective databases in real life practice can be used to their fullest.

Table 1. Summary of results for the three groups

	n	# of visits (average)	Mean Value				*p*
			Baseline	1 year	3 years	Change/year (95% CI)	
Group 1*							
Aa point (-3,+3)	213	744 (3.5)	-1.0	-2.8	-2.8	0.01 (0.0004, 0.03)	.0440
Ba point (-3, +8)	213	744 (3.5)	-0.9	-2.8	-2.7	0.01 (-0.003, 0.03)	.1158
UDI6 Total (0-18)	122	409 (3.4)	8.2	3.9	4.3	0.24 (0.10, 0.39)	.0013
UDI6 Q2 - UUI (0-3)	122	409 (3.4)	1.6	0.8	1.0	0.08 (0.02, 0.14)	.0059
UDI6 Q3 - SUI (0-3)	122	409 (3.4)	1.7	0.6	0.7	0.06 (0.03, 0.09)	.0008
UDI6 Q5 - Empty (0-3)	122	409 (3.4)	1.0	0.4	0.5	0.02 (-0.01, 0.05)	.2206
QoL Score (0-10)	120	400 (3.3)	6.2	2.1	2.4	0.16 (0.05, 0.26)	.0045
Group 2*							
Aa point (-3,+3)	169	594 (3.5)	0.1	-2.7	-2.6	0.04 (0.02, 0.07)	.0019
Ba point (-3, +8)	169	594 (3.5)	0.2	-2.6	-2.5	0.06 (0.03, 0.09)	.0003
UDI6 Total (0-18)	97	324 (3.3)	7.9	4.0	4.2	0.11 (-0.06, 0.27)	.1950
UDI6 Q2 - UUI (0-3)	97	324 (3.3)	1.6	0.8	0.9	0.03 (-0.01, 0.08)	.1317
UDI6 Q3 - SUI (0-3)	97	324 (3.3)	1.2	0.7	0.7	0.02 (-0.03, 0.06)	.4844
UDI6 Q5 - Empty (0-3)	97	324 (3.3)	1.2	0.4	0.5	0.03 (-0.003, 0.07)	.0739
QoL Score (0-10)	98	335 (3.4)	6.1	1.9	2.1	0.09 (-0.03, 0.21)	.1248
Group 3†							
3D US Volume	66	263 (4.0)		2.5/3.3	2.3/3.1	-0.11 (-0.18, -0.04)	.0014

*Baseline value is controlled for in the mixed model. 1 year and 3 year mean values were calculated based on the mean at baseline.
†Number of injections is controlled for in the mixed model. 1 year and 3 year mean values were calculated for single injection/multiple injections.

References
1. Laird NM, Ware JH. Biometrics. 1982, 38(4):963-974.

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