Original article

Collagen contents variations between different stages of anterior vaginal wall prolapse

ANDRÉS MARAMBIO[1], CÉSAR SANDOVAL[1], RAÚL VALDEVENITO[1], MICHEL NASER[1], VALENTÍN MANRÍQUEZ[1], RODRIGO GUZMÁN[1], JORGE LECANNELIER[1], JAIME JANS[1], AMALIA AGUILERA[1], GUILLERMO DÍAZ[2]

[1] Female Pelvic Floor Unit, Obstetric and Gynecology Service, University of Chile Clinical Hospital
[2] Pharmacological and Toxicological Department, Chemistry and Pharmacy Faculty, University of Chile

Abstract: Objective: Vaginal prolapse is a common disease, whose etiology is not well understood. Many studies have focused on alterations in the levels of collagen would present these patients, yielding conflicting results. Aim of the study: To measure the amount of types I and III collagen found in the connective tissue lining the vagina among patients with anterior vaginal wall prolapse and compare it with patients without prolapse and between different clinical stages of prolapse. *Materials and Methods:* Cross-sectional study. Statistical analysis was carried out considering a statistical power of 80% and an alpha level of 5%. Results: A total of 84 patients in different stages as per natural distribution were recruited. The mean patient age was 53,9 ± 11 years (32-78). We didn´t find significant differences in the levels of type I and type III collagen, between the various stages of prolapse or when comparing with the control group. *Conclusion:* Our histological findings in the endopelvic fascia reveal that there would be no changes in the levels of type I and type III collagen between the different stages of genital prolapse, so it would not meet an etiological role in the development of this pathology.

Key words: Pelvic Organ Prolapse; Vaginal Prolapse; Pelvic Floor; Type I and III Collagen.

INTRODUCTION

To date, although risk factors are well known, the reason why some women suffer vaginal wall prolapse remains unclear. Several research lines have emerged as an attempt to unveil the susceptibility of some patients to suffer this. Research has focused on connective tissue findings and comparison with those women without prolapse. Research work has studied alteration in collagen amount and structure, measuring various collagen subtypes, mainly types I and III collagen.[1-12] Moreover, variations in a series of other molecules participating of collagen metabolism such as metalloproteinases[1,7,10,13,14] and their inhibitors[10,14] and cathepsin,[1] as well as the metabolism of elastin,[1,6,8,11] smooth muscle[15,16] and extracellular matrix glycoproteins[4,11] have been studied in patients with and without the pathology. Unfortunately, results have been contradictory impeding the unscrambling of the proposed objectives. This might be the result of a lack of uniformity seen in published work regarding patient selection, prolapse type (many times not even specified), staging methods, use of small sample size, different biopsy sites and standardization of this, indirect measurement of collagen, etc. Nevertheless, it's possible to note that most of the results point towards a decrease in collagen amounts in the vaginal support structures of such patients, controlling by other variables that also have an effect on this such as age and hormonal status.

The aim of this study is to perform a cross-sectional study, measuring the amounts of types I and III collagen in the connective tissue that surrounds the vaginal wall in patients with different stages of anterior vaginal wall prolapse and without such condition. Although the vast majority of studies have been carried out on uterine prolapse with analysis of level I suspension, the present study has been designed to be carried out on patients with anterior wall prolapse and analysis of level II, since it`s the most common site[17] and thus the mostly addressed for treatment. Based on the literature, the proposed work hypothesis is that in patients with anterior vaginal wall prolapse the contents of types I and III collagen in the connective tissue that overlays the vagina are decreased, and such decrease would be proportional to the prolapse stage clinically diagnosed as per POP-Q.

PATIENTS AND METHODS

A cross-sectional and analytic study was carried out. Patients with anterior vaginal wall defects with indication for surgery were included. Patients admitted to surgery for other benign gynecological pathologies were included as the control group (stage 0). All the patients were informed of the nature of the study and provided their authorization for admission with an informed consent. The study was previously approved by the hospital Ethics Committee (dated January 10th, 2008; certificate of approval No. 5). Design consists of an initial assessment including medical history, physical examination, and documentation of age, occupation, symptoms, history other pathological conditions, obstetric formula, type of delivery (vaginal, cesarean or forceps delivery), history of macrosomy (defined as birthweight > 4.000 gr.), presence of menopause, smoking habit, family history, weight, height, body mass index, POP-Q and associated urinary incontinence. Exclusion criteria were: prior history of pelvic surgery, cancer of any origin, radiation therapy, neuromuscular o connective tissue disorders, pelvic inflammatory process, endometriosis, current pregnancy or presence of adhesion or scar at the biopsy site.

A sample was obtained during surgery from the connective tissue adjacent to the anterior vaginal wall at the Ba point, because it`s the zone where cystocele usually recur[18]. For this reason prolapse staging classification was based on the maximum extension according to that point. Efforts were made to obtain sufficient tissue for the analysis required (at least 2 x 2 cm.) and dissecting the sample to obtain only single fascia tissue, separating the vaginal wall (epithelium and muscular wall) or any other structure which does not correspond to connective tissue. Once obtained, samples were immediately stored in liquid nitrogen at –80 °c until completion the adequate number of patients per group. Then, were analyzed with an immunowestern

blot technique, which consists roughly of: a) initial homogenization of samples with a tissue lysis buffer solution in the presence of enzymatic inhibitors (RIPA buffer), in a dounce glass homogenizer, with subsequent sonication of the specimen during 7 minutes, and re-homogenization to ensure a total distribution and finally centrifugation at 10.000 rpm at 4 ºc during 10 minutes to extract the supernatant containing the protein of interest; b) quantification of extracted proteins with the Lowry method; c) electrophoretic separation of proteins (as per molecular weight), on a acrylamide/polyacrylamide gel (8%); d) electrotransference of the proteins to a nitrocellulose membrane; e) incubating with a specific antibody targeted to the protein of interest (an antibody recognizing human type I collagen, CN: AB758 and an antibody recognizing human type III collagen, CN: MAB3392, Chemicon, Millipore, US), and subsequently with a second horseradish peroxidase conjugated antibody and finally, chemiluminiscense immunodetection and subsequent detection with autoradiography films; f) quantification of such final product (the bands on the film) with the appropriate software that shows the results as total pixels per band to be quantified. Thus we obtained a quantitative variable and comparable between different samples, since the method standardized by the unit of tissue, regardless of the initial size of the biopsy. Samples were analyzed, interpreted and reported by professionals blind to the different analysis groups.

To carry out this study we decided not to consider stage IV prolapse because its low frequency of presentation, so that the sample size was composed of 96 patients distributed in 72 patients with prolapse (stages I, II and III) and 24 patients in stage 0 (control group). Calculation of sample size was estimated considering a prevalence of prolapse of 30% in the general population[19,20] on a universe of 2.000 patients attending at our Female Pelvic Floor Unit per year, an estimation error of 9%, a statistical power of 80% and an alpha level of 5%. All data concerning the preoperative record and the measured collagen values were concomitantly entered into an Excel database. Statistical analysis was carried out with the Stata 8.1 software (Stata Corp., Lakeway Drive, TX, USA). The following statistical tests were used: Mann Whitney, Student´s T, Kruskal Wallis, chi-square, ANOVA and multiple regression analysis. A $p \leq 0,05$ was considered as statistically significant.

TABLE 1. – Mean age of patients per prolapse stage.

Stage	Patients Mean Age
0	49.2±9
I	48±8
II	55.1±1
III	61±9

TABLE 2. – Association between different variables and the presence of prolapse.

Variable	**Number**	**P**
Gestations	357	0.19
Deliveries	296	0.11
Vaginal	226	0.007
Cesarean	49	0.02
Forceps	22	0.06
Miscarriage	61	0.84
Child > 4000 gr.	21	0.07
Menopause	43	0.45
HRT[a]	14	0.53
Smoking	21	0.61
Constipation	26	0.49
Family history	14	0.7
Obesity	34	0.09

[a:] Hormone Replacement Therapy

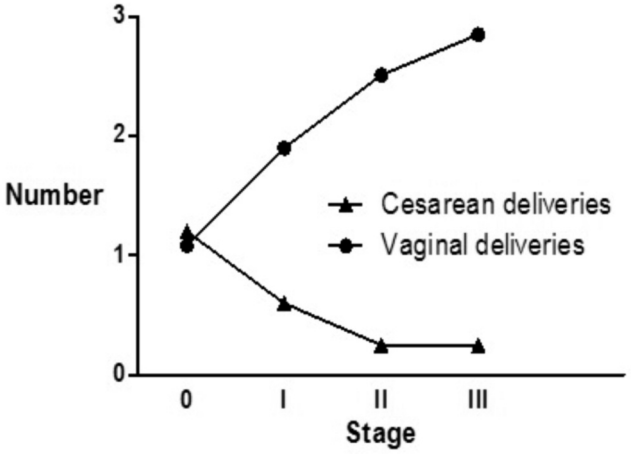

Figure 1. – Distribution of vaginal / cesarean deliveries per prolapse stage.

RESULTS

The study was conducted between September 2007 and March 2010. A total of 84 patients were recruited, without attaining the estimated study sample for stage 0 (12 patients), by the refusal of this patients to be exposed to a vaginal biopsy. Mean age was 53,9±11 (32 - 78). Patient age increased significantly ($p<0,001$) as they had a higher prolapsed stage (Table 1). The vast majority of patients were housewives (49,4%), followed by administrative (15,1%) and commerce activities (11,1%). Occupation of the rest of patients included various activities. Main clinical onset form was stress urinary incontinence (SUI), observed in 37 patients. In the total group, 67,8% of the patients had SUI, and it`s presence was significantly associated to the presence of prolapse ($p=0,007$) and increased significantly ($p=0,024$) with higher prolapse stages. Upon analysis of the various pre-operative variables, there were statistically significant differences between the different groups in terms of vaginal ($p=0,006$) and cesarean deliveries ($p=0,02$), while the rest of the analyzed variables did not relate to the presence of prolapse and did not differ between the various study groups (Figure 1 and Table 2).

At the molecular analysis, there were no significant differences in type I collagen levels neither between patients with and without prolapse ($p=0,82$) nor between the different prolapse stages ($p=0,68$). However, there was a tendency towards an increase in type I collagen levels as the prolapse stage increased (Figure 2). As for type III collagen, again there were neither significant differences between patients with and without prolapse ($p=0,41$) nor between the different prolapse stages ($p=0,47$), however, there was a tendency towards a decrease in such levels as the degree of prolapse increased (Figure 3). When carrying out the multiple regression analysis, with age and type of delivery being used as control variables (only variables statistically different between groups), there were no statistically significant differences in type I collagen levels between patients with and without prolapse ($F^{3,89}=1,08$; $p=0,36$) and between different prolapse stages ($F^{5,87}=1,26$; $p=0,28$). The same findings were evidenced for type III collagen levels when comparing patients with and without prolapse ($F^{3,91}=0,68$; $p=0,56$) and different prolapse stages ($F^{5,89}=0,65$; $p=0,66$). As for the type I collagen / type III collagen ratio

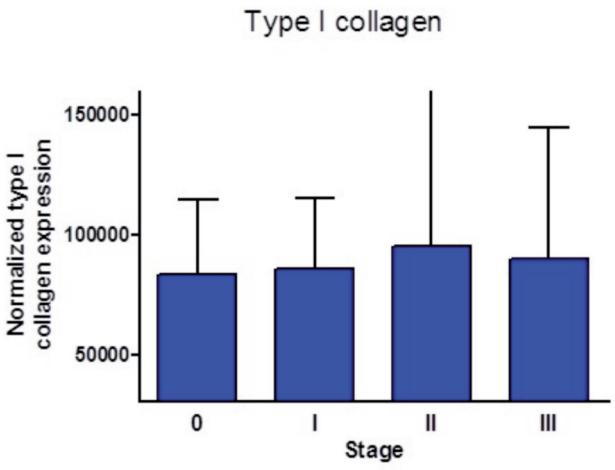

Figure 2. – Type I collagen levels per prolapse stage.

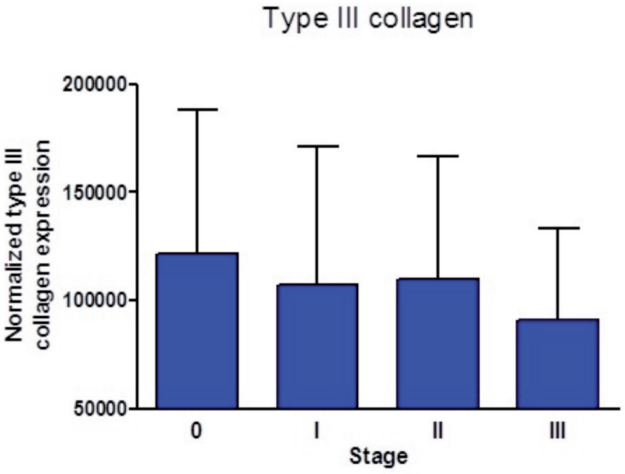

Figure 3. – Type III collagen levels per prolapse stage.

there were no significant differences between patients with and without prolapse (p=0,56) nor between the different prolapse stages (p=0,75), however, there was a tendency towards an increase in the ratio as the degree of prolapse was higher (Figure 4). When analyzing collagen levels in patients with SUI, they evidenced a significantly higher content of type I collagen than patients without SUI (p=0,03), and there were no differences in type III collagen levels (p=0,4). Finally, upon analyzing the various patient variables available (Table 2), including age, there were no statistically significant differences neither in type I and III collagen levels nor in type I collagen / type III collagen ratio.

DISCUSSION

In view of the discordant published literature on the field, the aim of the present work has been to shed light into what`s really happening with collagen in pelvic connective tissue of patients with prolapse. Although the study group includes patients of different ages, it has been shown that prolapse affects mainly woman in the fifth, sixth and seventh decades of life, with highest incidence between fifty and sixty years. This is the reason why most of our patients are already housewives without a current labor occupation. Prolapse onset includes classically a sensation of heaviness or vaginal bulging, however here has evidenced that presence of SUI is significantly associated to this condition, with an increase in it`s incidence as the prolapse stage progresses. Because SUI is a more disabling disease, it has become the main onset form or concern upon consultation. Both, patient age and type of delivery (vaginal or cesarean) are two prolapse risk factors that have been widely documented. In the present study there were the only two factors associated to the presence of prolapse, and have directly correlated to stage.

Several studies have addressed genital prolapse in search for anomalies in collagen and other extracellular matrix structures metabolism, trying to find the cause or the first physiopathologic changes involved in such disease, to explain the pathology and therefore enable the early identification of susceptible patients. Literature reports concerning types I and III collagen have been diverse and contradictory. Most of these works indicate that physiopathology of prolapse would involve a decrease in total collagen and types I, III and VI collagen at least, in the connective tissue surrounding the vagina.[1-5,10,11] Moreover, there would be an increased activity of certain metalloproteinases at the vaginal epithelium of patients with prolapsed.[1] It's from this information that the main hypothesis has emerged and has prevailed to date, indicating that the decrease of types I and III collagen specifically, in support tissues, would represent a key event in the subsequent development of pelvic organ prolapse, an event that doubtlessly will be associated to various other factors that would facilitate such process. On the other hand, various studies point to an increase at least in types III and V collagen levels, in association to a tissue-remodeling environment resulting from a greater metalloproteinase activity.[6-9] These works refer to the fact that a greater amount of a more lax collagen, such as type III, would favor the development of prolapse. The results of the present work do not support such theories, because it can be seen that in this series, the largest presented so far in the study of this matter, neither of both types of collagen present significant variations in the different groups to be compared, both for patients without prolapse when compared with the rest of the patients, as well as between the different stages of prolapse. Likewise, upon carrying out the multiple regression analysis, with the confounding variables (age and vaginal deliveries) present as control variables, statistical significance was not attained between patients with and without prolapse or between the various stages. When observing the numbers, it was possible to see that there are certain tendencies as the disease worsens. For example, type I collagen has a tendency to increase in higher prolapse stages and inversely, type III collagen tends towards a decrease, thus reflecting accurately a progressive increase of the type I / type III collagen ratio. This could be related to a post-trauma cicatricial tissue, in which a firm scar is progressively generated over time, as collagen III is decreasing and finally replaced for type I collagen, all once injury and descent have occurred.[21] Some of these changes have already been reported and previously described in connective tissue as secondary to injury and repair processes.[22] In this sense, it is worth noting that patients with SUI presented a significantly greater amount of type I collagen than patients without SUI, something that could represent a greater initial injury with a larger associated tissue response, the latter being in accordance with clinical reports of one of the aforementioned works.[3]

However, all of these trends can't be interpreted and the final analysis show no differences between the levels of type I and III collagen in the connective tissue surrounding the vagina in woman with and without prolapse or the different stages. Limitation of this study was the lack of sample size of our control group which can be a source of bias, nevertheless, the others groups were complete and showed no changes related to our initial hypothesis.

In conclusion, patients with pelvic organ prolapse do not

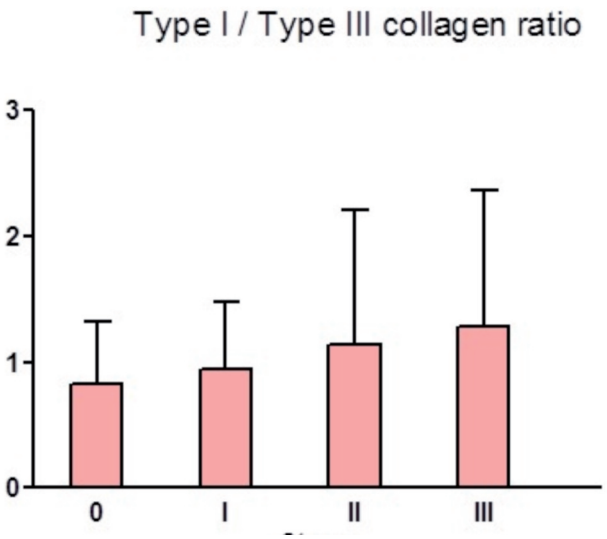

Figure 4. – Type I / type III collagen ratio per prolapse stage.

differ in levels of type I and type III collagen measured in the fascia surrounding the vagina, when compared with control patients or between different stages of prolapse. Based on this finding, levels of type I and type III collagen are not important in the study of the pathogenesis of this disease, so future histological studies should be focused on other types of molecules or tissues looking for changes that explain the development of this disorder.

ACKNOWLEDGEMENTS

This investigation was conducted in the Female Pelvic Floor Unit of the University of Chile Clinical Hospital. We want to thank to all the people that works there and especially to Pamela Contreras for the laboratory work at the Chemistry and Pharmacy Faculty and Alvaro Reyes (M.Biostat.) for the statistical analysis at the Bureau for Clinical Research Support of the University of Chile Clinical Hospital.

CONFLICTS OF INTEREST STATEMENT

None of the researchers has conflicts of interest to declare. The present study was financed by funding granted by the “2007 Clinical and Basic Clinical Research Contest” of the Bureau for Clinical Research Support from the University of Chile Clinical Hospital.

REFERENCES

1. Jackson SR, Avery NC, Tarlton JF, Eckford SD, Abrams P, Bailey AJ. Changes in metabolism of collagen in genitourinary prolapse. Lancet. 1996; 347:1658-61.
2. Takano CC, Girão JB, Sartori MG, Castro RA, Arruda RM, Simões MJ et al. Analysis of collagen in parametrium and vaginal apex of women with and without uterine prolapse. Int Urogynecol J. 2002; 13:342-5.
3. Liapis A, Bakas P, Pafiti A, Frangos-Plemenos M, Arnoyannaki N, Creatsas G. Changes of collagen type III in female patients with genuine stress incontinence and pelvic floor prolapse. Eur J Obstet Gynecol Reprod Biol. 2001; 97:76-9.
4. Goepel C, Hefler L, Methfessel HD, Koelbl H. Periurethral connective tissue status of postmenopausal women with genital prolapse with and without stress incontinence. Acta Obstet Gynecol Scand. 2003; 82:659-64.
5. Söderberg MW, Falconer C, Byström B, Malmström A, Ekman G. Young women with genital prolapse have a low collagen concentration. Acta Obstet Gynecol Scand. 2004; 83:1193-8.
6. Kökçü A, Yanik F, Çetinkaya M, Alper T, Kandemir B, Malatyalioglu E. Histopathological evaluation of the connective tissue of the vaginal fascia and the uterine ligaments in women with and without pelvic relaxation. Arch Gynecol Obstet. 2002; 266:75-8.
7. Moalli PA, Shand SH, Zyczynski HM, Gordy SC, Meyn LA. Remodeling of vaginal connective tissue in patients with prolapse. Obstet Gynecol. 2005; 160:953-63.
8. Ewies AA, Al-Azzawi F, Thompson J. Changes in extracellular matrix proteins in the cardinal ligaments of post-menopausal women with or without prolapse: a computerized immunohistomorphometric analysis. Hum Reprod. 2003; 19:2189-95.
9. Gabriel B, Denschlag D, Göbel H, Fittkow C, Werner M, Gitsch G et al. Uterosacral ligament in postmenopausal women with or without pelvic organ prolapse. Int Urogynecol J. 2005; 16:475-9.
10. Chen BH, Wen Y, Li H, Polan ML. Collagen metabolism and turnover in women with stress urinary incontinence and pelvic prolapse. Int Urogynecol J. 2002; 13:80-7.
11. Lin SY, Tee YT, Ng SC, Chang H, Lin P, Chen GD. Changes in the extracellular matrix in the anterior vagina of women with or without prolapse. Int Urogynecol J. 2007; 18:43-8.
12. Wong MY, Harmanli OH, Agar M, Dandolu V, Grody MH. Collagen content of nonsupport tissue in pelvic organ prolapse and stress urinary incontinence. Am J Obstet Gynecol. 2003; 189:1597-1600.
13. Gabriel B, Watermann D, Hancke K, Gitsch G, Werner M, Tempfer C et al. Increased expression of matrix metalloproteinase 2 in uterosacral ligaments is associated with pelvic organ prolapse. Int Urogynecol J. 2006; 17:478-82.
14. Phillips CH, Anthony F, Benyon C, Monga AK. Collagen metabolism in the uterosacral ligaments and vaginal skin of women with uterine prolapse. BJOG. 2006; 113:39-46.
15. Boreham MK, Wai CY, Miller RT, Schaffer JI, Word RA. Morphometric analysis of smooth muscle in the anterior vaginal wall of women with pelvic organ prolapse. Am J Obstet Gynecol. 2002; 187:56-63.
16. Badiou W, Granier G, Bousquet PJ, Monrozies X, Mares P, de Tayrac R. Comparative histological analysis of anterior vaginal wall in women with pelvic organ prolapse or control subjects. A pilot study. Int Urogynecol J. 2008; 19:723-9.
17. Olsen AL, Smith VJ, Bergstrom JO, Colling JC, Clark AL. Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. Obstet Gynecol. 1997; 89:501-6.
18. Shull BL, Benn SJ, Kuehl TJ. Surgical management of prolapse of the anterior vaginal segment: an analysis of support defects, operative morbidity, and anatomic outcome. Am J Obstet Gynecol. 1994; 171:1429-39.
19. Samuelsson EC, Victor FT, Tibblin G, Svärdsudd KF. Signs of genital prolapse in a Sweedish population of women 20 to 59 years of age and possible related factors. Am J Obstet Gynecol. 1999; 180:299-305.
20. Hendrix SL, Clark A, Nygaard I, Aragaki A, Barnabei V, McTiernan A. Pelvic organ prolapse in the women´s health initiative: gravity and gravidity. Am J Obstet Gynecol. 2002; 186:1160-6.
21. Robson MC, Steed DL, Franz MG. Wound healing: biologic features and approaches to maximize healing trajectories. Curr Probl Surg. 2001; 38:72-140.
22. Norton PA. Pelvic floor disorders: the role of fascia and ligaments. Clin Obstet Gynecol. 1993; 36:926-38.

Correspondence to:

amarambio@med.uchile.cl

Multidisciplinary Uro-Gyne-Procto Editorial Comment

To improve the integration among the three segments of the pelvic floor, some of the articles published in **Pelviperineology** are commented on by **Urologists**, **Gynecologists** and **Proctologists/Colo Rectal Surgeons** with their critical opinion and a teaching purpose. Differences, similarities and possible relationships between the data presented and what is known in the three fields of competence are stressed, or the absence of any analogy is indicated. The discussion is not a peer review, it concerns concepts, ideas, theories, not the methodology of the presentation.

Uro… Marambio et al. investigate in their study 84 patients with different stages of prolapse and compare the collagen I and III content in the connective tissue lining the vagina. In their study they were not able to find significant correlations of collagen contents and prolapse degree. There is still discordant evidence in the literature regarding this matter. Possible reasons could be: 1. The sampling sites are heterogenous or inadequate. 2. The parameters measuring connective tissue metabolism are inadequate. 3. The etiology is truly different.

In response to 1. Marambio took care to sample a defined anatomical mark in the vagina. Nevertheless heterogeneity is still a matter as it cannot be ruled out. In response to 2. The authors investigated collagen I and III by quantitative, molecular analysis. This is certainly an advantage, however many other parameters and molecules could still influence connective tissue quality. In response to 3. This cannot be answered by this study, as other etiological factors were not investigated. There is however a large evidence that connective tissue (lax ligaments) play a major role in pelvic floor disorders (Petros P, Integral theory).

From the urological, clinical point of view, the etiology is certainly important, as different therapeutical approaches have been developed over the years, including tissue substitution by alloplastic material. Evidence from surgical studies using connective tissue substitutions support also the fact, that deficient connective tissue serves as a major causative factor.

In conclusion, although in their study Marambio et al. could not identify significant differences between vaginal collagen I and III content comparing patients with and without prolapse, the etiology that lax vaginal ligaments are causative for pelvic floor disorders is not ruled out, due to multiple complicating and confounding factors possibly present.

FLORIAN WAGENLEHNER
Klinik für Urologie, Kinderurologie und Andrologie, Universitätsklinikum Gießen Germany
wagenlehner@aol.com

Gyne… I congratulate the authors on an excellent and important study. The findings of this article, no significant changes in collagen I&III in patients with pelvic organ prolapse (POP), are consistent with the statement of the Integral Theory[1] that it is the laxity of ligaments caused by altered collagen/ elastin which is the major cause of POP, bladder and bowel dysfunctions. Altered collagen/elastin does not necessarily mean diminished collagen content. It is possible to look at the pathogenesis of vaginal or ligament laxity as follows:

connective tissue in the area of the urogenital organs is sensitive to hormones. During pregnancy, collagen is depolymerized by placental hormones, and the ratios of the glycosaminoglycans change. The vagina and ligaments weaken. This explains the uterovaginal prolapse so often seen during pregnancy. Laxity in the hammock may remove the elastic closure force, causing urine loss on effort. This condition is described as stress incontinence. Loss of membranous support may cause gravity to stimulate the nerve endings (N) at the bladder base, so causing premature activation of the micturition reflex, expressed as symptoms of 'bladder instability'. This condition is perceived by the pregnant patient as frequency, urgency and nocturia. Laxity may also cause pelvic pain, due to loss of structural support for the unmyelinated nerve fibres contained in the posterior ligaments. The action of gravity on these nerves causes a 'dragging' pain. Immediately prior to delivery, the collagen fibrils of the cervix depolymerize further, losing 95% of their strength.[2] This allows the massive stretching of tissues required for delivery. Removal of the placenta restores connective tissue integrity and the symptoms rapidly disappear in a large percentage of patients. However, if the collagen fibres have been stretched extensively at delivery re-polymerize in an extended position, the vagina and ligaments may now be much looser than previously, causing POP, bladder and bowel dysfunction. The collagen content may remain the same. It is ligament laxity which diminishes the strength of the directional muscle forces controlling the musculoelastic elastic functions of the pelvic floor, not collagen content.

1. Petros PE & Ulmsten U. An Integral Theory of female urinary incontinence. Acta Obst Gyn Scand, Supp 153, 69, (1990), 1-79.
2. Rechberger T, Uldbjerg N & Oxlund H. Connective tissue changes in the cervix during normal pregnancy and pregnancy complicated by a cervical incompetence Obstets & Gynecol.(1988), 71:563-567.

PETER EP PETROS
Hon. Professor, University of NSW, Academic Dept of Surgery St Vincent's Hospital, Sydney
pp@kvinno.com

Procto… In the pathogenesis of genital prolapse the role of type I-III collagen is debated and in Marambio's study it does not appear to be consistent. In the proctologic literature, focusing on the rectal prolapse, a similar approach is lacking without relevant studies on the para-rectal tissues support. There are many theories describing different causes of the rectal prolapse but none of them seems to settle the matter once and for all.[1] The anatomical basis for rectal prolapse is a deficient pelvic floor allowing the rectum falling out of the anus. An interesting hypothesis argues that there is a significant difference in joint mobility between patients undergone to surgery for rectal prolapse and a control group, suggesting a role of the connective tissue disorder in the development of the prolapse.[2] Moschcowitz in 1912[3] described a redundant sigmoid colon within a deep pelvic cul de sac, the patient's excessive straining exiting in the prolapse. Other authors proposed that the complete rectal prolapse is the evolution of a rectal intussusception. This theory does not consider the extremely low percentage of patients in which the internal prolapse becomes external, as confirmed by defecography studies. Injuries to the pudendal nerves, due to stretching of the pelvic floor, may also play a role.[4] A laxity of the lateral ligaments of the rectum, or a loose sacral fixation to the sacrum combined with a supposed underlying connective tissue disorder (still hypothesis) and a colonic dysmotility have been also considered responsible of the rectal prolapse, a condition whose ethiology still needs a lot of attention and research.[1]

1. Gourgiotis S, Baratsis S. Rectal prolapse. Int J Colorectal Dis 2007; 22:231-243.
2. Wijffels NA, Collinson R, Cunningham C, Lindsey I. What is the natural history of internal rectal prolapse? Colorectal Dis 2010; 12:822-30.
3. Moschcowitz AV. The pathogenesis, anatomy and cure of prolapse of the rectum. Surg Gynecol Obstet 1912; 15:7-21.
4. Richelle J. F. Felt-Bersma and Miguel A. Cuesta. Rectal prolapse, rectal intussusception, rectocele, and solitary rectal ulcer syndrome. Gastroenterology Clinics of North America 2001; 30:199-222.

ALVISE FRASSON
Department of Surgery, University of Padova, Italy
alvise.frasson@unipd.it