gineco
+eu

review articles

The importance of the pathophysiology of the pelvic organ prolapse in understanding the symptoms of the pelvic floor disorders

Abstract

The prolapse of the pelvic organs (POP), defined as the inferior displacement of one or more of the pelvic organs, is a common pathology whose prevalence is difficult to estimate due to the inhomogeneity of the reported data between the studies. The aim of this review is to present the current literature on the mechanism of the pelvic floor disorders with focus on the importance of the quality of the pelvic conjunctive tissue. In Medline and Pubmed we have introduced the keywords "pelvic organ prolapse" combined with "pelvic organ prolapse and pathophysiology" and "pelvic organ prolapse and risk factors" selecting the articles published until October 2017 in the german and english languages. We have included the systematic reviews, case control studies and metanalyses which have examined the causes of the pelvic floor disorders in the view of the integral theory. The grade of the POP has been defined using the Pelvic Organ Prolapse Quantitation system recommended by the International Society of Continence and the American Society of the Urogynecology. After introducing the above mentioned selection criteria we have chosen 42 articles on primary and secondary POP. In both cases, the main cause of the POP was the deterioration of the pelvic conjunctive tissue as a result of genetic anomalies, pregnancy and parturition or advanced age. Understanding the structure and functions of the pelvic conjunctive tissue will allow a global approach of the pelvic floor by defining the pelvic suspensory ligaments, the consequences that results after weakening the pelvic support structures and the risk factors for a poor quality of the conjunctive tissue.
Keywords: *pelvic organ prolapse, conjunctive tissue, ligaments, fascia*

Olivia-Cătălina Ionescu[1], Nicolae Bacalbaşa[2,3], Nahedd Saba[4], Gabriel Bănceanu[3,4]

1. Department of Obstetrics and Gynecology, Breast Center. Fichtelgebirge Klinikum, Makrtredwitz, Bayern, Germany
2. Department of Obstetrics and Gynecology, „Ion Cantacuzino" Clinical Hospital, Bucharest, Romania
3. "Carol Davila University of Medicine and Pharmacy, Bucharest, Romania
4. "Department of Obstetrics and Gynecology, "Polizu" Clinical Hospital. "Alessandrescu-Rusescu" National Institute of Mother and Child Health, Bucharest, Romania

Correspondence:
Dr. Olivia-Cătălina Ionescu
e-mail: olivia_ionescu@yahoo.com

Introduction

The pelvic organ prolapse (POP) represents the herniation of the pelvic structures until or beyond the vaginal introitus although the definition does not specify the anatomical localization of the pelvic disorder[1].

For a more specific description of the female genital prolapse currently are used the terms: anterior or posterior compartment prolapse which involve the herniation of the anterior or posterior vaginal walls and are commonly associated with the descent of the bladder (i.e. cystocele) or the rectum (i.e. rectocele) respectively[2].

Uterine and vaginal vault prolapse refer to the descent of the uterus and cervix, cervix alone or vaginal vault (after hysterectomy) until or beyond the vaginal introitus and is known as the apical compartment prolapse[3]. The division of the vagina into compartments is mostly arbitrary made because the vagina is a continuous organ which cannot be segmented and often defects of the compartments are associated between them[4].

Pelvic floor disorders have reported to have a significant impact on the life quality with symptoms that impair the daily activities, the sexuality and the body image[5].

Moreover, they require enormous medical resources as the annual cost of the treatment has been estimated to be in the United States of America almost 300 million dollars[6].

Although there have been registered more women more than 60 years old with POP, the prevalence remains difficult to estimate mainly because the epidemiological studies do not differentiate between symptomatic and asymptomatic POP without specifying how many symptomatic POPs do not seek medical care[7].

Furthermore, there is now standardization regarding the classification system of POP so that the severity of the pelvic disorders differs from one study to another[8].

A cross sectional study of Nygaard and coworkers[9] has investigated 1961 women aged 20-80 years old with symptomatic POP defined as a "pelvic pressure", or "the sensation that something falls out of the vagina". The reported rate of prevalence in the study group was 2.9%. In other two population-based surveys[10,11], 6%-8% of female who have completed only a questionnaire have described symptoms of "vaginal bulge".

The questionnaire are generally more sensible in identifying advance genital prolapse while the incipient stages (I or II) are better diagnosed at the clinical examination. Generally, the number of POPs cases resulting from the questionnaires of evaluation do not correlate with the number of POPs identified after the clinical examination[12].

With regard to the asymptomatic POP, there have been estimated high rates of prevalence especially for stages I and II. The cases distribution of the Pelvic Organ Prolapse Quantitation (POP-Q) stages among 491 women who have been ambulatory assessed for POP symptoms showed the following rates of prevalence: 6.4% for stage 0; 43.3% for stage 1; 47.7% for stage 2; 2.6% for stage 3 and 0% in stage 4[13].

Among 27342 women aged more than 60 years with or without hysterectomy, the reported prevalence for uterine and cervical prolapse were 41% and 38% respectively[14].

Anterior, posterior and apical compartment prolapse have been identified in 34%, 18% and 14% of cases respectively[14]. Between 20 and 59 years the prevalence of POP was estimated to be about 30.8% for POP-Q stages I and II, 1.6% for POP-Q stage III and lower than 1% for POP-Q stage IV[15].

A direct relation between the age of the patients and the prevalence of the POP has been demonstrated. The surgical intervention is mandatory in 11.1% of cases[16] although the recurrence rate remains very high-almost 20%[17].

Thus, a global approach of the pelvic floor with focus on the repair of the suspension structured which contains conjunctive tissue is very important in choosing the optimal surgical method.

The aim of this article is to present the current data on the pathophysiology of the pelvic floor disorders focusing on the role of the conjunctive tissue whose deterioration results in specific lesion at different levels.

The Central Role of the Conjunctive Tissue

The integral theory of Petros and Goeschen[18] centers on the quality of the conjunctive tissue which can be found in the pelvic ligaments, fascias and membranes[18]. These contain intact colagen, elastine and proteoglicans which confer the firmness and elasticity of the pelvic structures thus allowing them to return to their normal form when the traction on the pelvic muscle is ended[18,19].

When the structure is overextended, the force is maintained at a constant intensity by the elastic fibers thus the form of the colagen fibers do not deform (or disrupt)[20]. When the collagen fibers are deteriorated (e.g during pregnancy, birth, menopause, or trauma) they lose their mechanical properties (i.e. transformation from a „S" shape to an „I" shape when applying a pressure defined as force to the surface area ratio) and consequently their vaginal support thus explaining the urinary and defecatory symptoms and the bulge or pressure symptoms[17,19].

In the perspective of the histopathology of the altered conjunctive fibers, there is evidence of a modified report between different subtypes of collagen fibers as well as the modifications in the homeostase of the elastic fibers[21].

However, there are not sufficient articles which focus on the morphologic characteristic of the conjunctive tissue and their implication in pelvic floor disorders[22]. The absence of the mutation in the gene that codifies fibulin-5 (known as Fbln5$^{-/-}$) would be involved in what is defined as „elastinopathy" that implies: pulmonary emphysema, lax skin, tortuous and enlarged vessels and genital prolapse with the herniation of the pelvic structure until or beyond the vaginal walls[23,24]. Studies on mice with mutation of the Fbln5$^{-/-}$ have demonstrated a prevalence of POP up to 91% as well as an increase of the rate with the age of the mice[25]. A higher number of parturitions is a risk factor for advanced POP as a result of the absence of elastic fibers through the Fbln5$^{-/-}$ mutation[21,25].

The absence of the genetic mutation Fbln5$^{-/-}$ as well as the increased sensibility of the conjunctive tissue at progesteron, prostaglandin and relaxant modify the structure of the collagen and elastic fibers inducing their depolimerization thus increasing their diameter and extensibility up to 3-fold[26].

Studies on pregnant mice have also demonstrated a reduced stiffness, decreased maximal pressure and an increased extensibility of the vaginal walls[24,26]. On the other side, an increased elasticity of the vaginal walls will lower the required tensions that sustain the ligaments and fascias which can split during the expulsive phase of the labor as they cannot support the increased forced applied on them due to different factors, e.g: cephalopelvic disproportion, obstetrical manoveurs or prolonged expulsive phase of labor.

There are four levels in which lesions can appear during parturition - anterior vaginal wall in the external infralevatory part, the middle infralevatory level, the internal supralevatory level and the posterior vaginal wall nearby the recto-vaginalis septum and external anal sphincter - each of them being associated with typical symptoms[27].

The implication of the morphological modifications of the collagen and elastic fibers in parturition has been presented by Lowder and coworkers[28] who showed that the vagina, the paravaginal tissues, the utero-sacral ligaments and the perineal membrane are more lax in pregnancy while the extension of the conjunctive fibers progressively increases during pregnancy and achieves its maximum during labor.

The structural modifications of the fibers and the compensatory mechanism during labor have been initially showed by a study on 38 pregnant mice at different gestational ages[29]. During pregnancy the authors reported an increase in the vaginal length up to 60% and in the vaginal weight up to 100%[24,29]. At the moment of delivery, the diameter of the vagina was 2 fold greater than in nonpregnant mice. Moreover, the tension of the conjunctive fiber decreases 3 to 4 folds, the maximal overload on ligaments decreases while the extensibility of the vaginal walls raises. With the increase of the number of birth, the extracellular matrix degrades causing a lower tension in the vaginal walls[29,30].

The anisotrope properties of the vagina will determine pelvic disorders depending on the direction of loading with different lesions and symptoms[31]. The pelvic muscles together with the ligaments and fascias form an elastic and muscular unit whose integrity and function are assured through peripheric neurological and mechanical coordination as well as a good quality of the conjunctive fibers[31].

A decrease in the intensity of the muscular contraction does not directly induce a pelvic disorder but lowers the quality of the elastic and collagen fibers which weakens the ligaments thus producing the symptoms. Therefore, the muscular contraction will not be sufficiently strong to allow the ligaments and fascias to fix and sustain the pelvic structures[32].

The severity of the conjunctive tissue alteration does not appear to be associate with the severity of symptoms or the grade of prolapse, an advanced POP does not produce severe symptoms[24].

In pre-or post-menopause a similar mechanism implying the alteration of the conjunctive tissue during an overextension as a result of a maximal load appear to produce POP although in the menopause there is no evidence of a hormonal influence on the collagen and elastic fibers[33-35].

The histopathologic examination of the vaginal tissues has showed the above presented deterioration of the fibers which became stiff and inextensible[24]. The maximal force which causes the disruption of the fibers is appreciated to be around 60 mg/mm^2[17]. After the age of 25 years there is a physiological decrease in the amount of elastic fibers while the collagen becomes rigid as a result of the increase in the number of intermolecular connections. They cannot respond properly to overtension and consequently they will atrophyed and get destroyed[17,24].

Although the majority of reports pledge for the biomechanical properties of the conjunctive tissue as the major determinatn of POP there is a high variability between studies mainly with regard to the methods used for the histopathological examinations of the samples.

The result can be influenced by the difference in the amount of epithelial and muscular tissue that can be examined. Other mechanism invoked in the pathophysiology of the POP refer to the increased activity of the enzyme matrix-metalloprotease from the extracellular matrix which digest the normal collagen fibers while the rest of collagen will distort the normal biomechanical properties of the pelvic supporting fibers consequently causing POP manifestations[36].

The Secondary Role of Other Factors

Overweight and obesity increase the risk of POP. A meta-analysis of 22 studies on the influence of overweight on the development of POP has revealed a risk of 50% for women with body mass index more between 25 and 29 kg/m^2 as well as more than 30 kg/m^2 compared with normal women[37].

The mechanism through which overweight and obesity induces pelvic floor disorders are unknown and weight loos does not appear to be associated with a lower risk of developing POP[38].

However, some data suggest that the bariatric surgery may reduce the risk of recurrence after surgical interventions for POP[39].

Surgical interventions which involve the complete removal of the uterus disrupt the normal anatomy of the pelvic floor as the absence of cervix implies the loose of the point of insertion for the suspension ligaments. Therefore the traction will be now directly transmitted to the vaginal walls[17].

Consequently the collagen fibers will progressively deteriorate; the ligaments will not have enough tension which will results in the development of vaginal prolapse.

The total hysterectomy generally increases the risk of apical compartment prolapse depending on the age of the patient and the performed surgical route[40].

Although not so often mentioned, among the African-American race the prevalence of POP is 4 to 5 times lower compared to the white race[41]. Other studies have not revealed the existence of an association between race or ethnicity and the risk of POP[9].

Other factors which may be implied in the pathophysiology of POP are: the constant increase of the abdominal pressure, genetic structural anomalies, Ehlers-Danlos syndrome, and the family history of POP which appears to increase the risk with about 2.5 folds[42].

Conclusions

Functional anomalies of the elastic fiber, the influence of the hormones during pregnancy, age more than 25-30 years are invoked in the process of deteriorating the conjunctive tissues of the fascia and ligaments which results in a weakening of the vaginal walls.

The pathophysiology of the female genital prolapse is important for the localization and diagnosis of the pelvic floor disorders as well as for the understanding of the symptoms associated with these lesions. Once identified, it is essential to start with the restoration of the support structures basing on the integral theory which states that the normalization of a function involved the reestablishment of the form. ∎

References

1. Bump RC, Mattiason A, Bo K, Brubaker LP, DeLancey JO, Klarskov P, Shull B, Smith AR The standardization of the terminology of the female pelvic organ prolapse and pelvic floor disfunction. Am Obstet Gynecol 1996, 175, 10-17.
2. Lippert Lehrbuch Anatomie. 6. Auflage 2006, 196-199, 419-21.
3. Hirsch, Käser, Ikle Atlas der Gynäkologischen Operationen.6. Auflage: 112-115, 1999, 286-7.
4. Kenton K, Shott S, Brubaker L. Vaginal topography does not correlate well with visceral position in women with pelvic organ prolapse. Int Urogynecol J Pelvic Floor Dysfunct 1997, 8, 336.
5. Lowder JL, Ghetti C, Nikolajski C. et al. Body image perceptions in women with pelvic organ prolapse: a qualitative study. Am J Obstet Gynecol 2011, 204, 441.
6. Sung VW, Washington B, Raker CA. Costs of ambulatory care related to female pelvic floor disorders in the United States. Am J Obstet Gynecol 2010, 202, 483.
7. Wu JM, Hundley AF, Fulton RG, Myers ER. Forecastingthe prevalence of pelvic floor disorders in U.S. Women: 2010 to 2050.Obstet Gynecol 2009, 114(6), 1278-83.
8. Bump RC, Norton PA. Epidemiology and natural history of pelvic floor dysfunction. Obstet Gynecol Clin N Am 1998, 25(4), 723-46.
9. Nygaard I, Barber MD, Burgio KL. et al. Prevalence of symptomatic pelvic floor disorders in US women. JAMA 2008, 300, 1311.
10. Rortveit G, Brown JS, Thom DH. et al. Symptomatic pelvic organ prolapse: prevalence and risk factors in a population-based, racially diverse cohort. Obstet Gynecol 2007, 109, 1396.
11. Tegerstedt G, Maehle-Schmidt M, Nyrén O, Hammarström M. Prevalence of symptomatic pelvic organ prolapse in a Swedish population. Int Urogynecol J Pelvic Floor Dysfunct 2005, 16, 497.
12. Strauber, Weyerstahl Gynäkologie und Geburtshilfe : 2005: 2. Auflage, 339.
13. Swift SE. The distribution of pelvic organ support in a population of female subjects seen for routine gynecologic health care. Am J Obstet Gynecol 2000, 183, 277.
14. Hendrix SL, Clark A, Nygaard I. et al. Pelvic organ prolapse in the Women's Health Initiative: gravity and gravidity. Am J Obstet Gynecol 2002, 186, 1160.
15. Samuelsson EC, Victor FT, Tibblin G, Svärdsudd KF. Signs of genital prolapse in a Swedish population of women 20 to 59 years of age and possible related factors. Am J Obstet Gynecol 1999, 180, 299.
16. Olsen AL, Smith VJ, Bergstrom JO, Colling JC, Clark AL. Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. Obstet Gynecol 1997, 89(4), 501-6.
17. Goeschen K, Petros P, Müller Funogea A, Brătilă E, Brătilă P, Cîrstoiu MM. Planșeul pelvic la femeie. Anatomia funcțională, diagnostic și tratament în acord cu teoria integrativă. Editura Universitară „Carol Davila", 2016, 8-110.
18. Goeschen K, Petros PE. Die Integral-Theorie: Ein neuer Weg des Verstehens-Teil 1, Gynecology 2003a, 8, 86-109.
19. Goeschen K, Petros PE. Die Integral-Theorie: Ein neuer Weg des Verstehens-Teil 2, Gynecology 2003b, 8, 162-9.
20. Goeschen K, Petros PE. Die Integral-Theorie: Ein neuer Weg des Verstehens-Teil 2, Gynecology 2003c, 8, 246-66.
21. Drewes PG, Yanagisawa H, Starcher B, Hornstra IK, Csiszar K, Marinis SI, et al. Pelvic organ prolapse in Fibulin-5 knockout mice: pregnancy changes in elastic fiber homeostasis in mouse vagina. Am J Pathol 2007, 170, 578-89.
22. 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, 1597-9.
23. Patel DA, Xu X, Thomason AD, Ransom SB, Ivy JS, DeLancey JO. Childbirth and pelvic floor dysfunction: an epidemiologic approach to the assessment of prevention opportunities at delivery. Am J Obstet Gynecol 2006, 195, 23-8.
24. Rahn DD, Ruff1 MD, Brown SA, Tibbals HF, Word RA. Biomechanical Properties of The Vaginal Wall: Effect of Pregnancy, Elastic Fiber Deficiency, and Pelvic Organ Prolapse. Am J Obstet Gynecol 2008, 198(5), 590, e1-590.
25. Wieslander CK, Acevedo JF, Drewes PG, Yanagisawa HK, Word RA. Pelvic organ prolapse severity increases with age in Fibulin-5 knockock mice. Int Urogynecol J 2006, 17, S371-2.
26. Riss P Ursachen,Symptomatik und Diagnostik von Senkungszuständen des weiblichen Genitales in: Klinik der Frauenheilkunde und Geburtshilfe, Band 9, Gutartige gynäkologische Erkrankungen II, Hrsg. H. G. Bender (1998) 3. Auflage, München Wien Baltimore.
27. Peschers U, Jundt K, Tunn R Fortschritte in der Diagnostik und Therapie der weiblichen Harnkontinenz, Dtsch Ärztebl 100, 2003, 3322-5.
28. Lowder JL, Debes KM, Moon DK, Howden N, Abramowitch SD, Moalli PA. Biomechanical adaptations of the rat vagina and supportive tissues in pregnancy to accommodate delivery. Obstet Gynecol 2007, 109, 136-43.
29. Rundgren A. Physical properties of connective tissue as influenced by single and repeated pregnancies in the rat. Acta Physiol Scand Suppl 1974, 417, 1-138.
30. Peschers U, Buczkowski M Möglichkeiten und Grenzen der konservativen Therapie der Harninkontinenz. Zentralblatt für Gynäkologie 2001, 123, 685-8.
31. Riss P Ursachen, Symptomatik und Diagnostik von Senkungszuständen des weiblichen Genitales in: Klinik der Frauenheilkunde und Geburtshilfe, Band 9, Gutartige gynäkologische Erkrankungen II, Hrsg. H. G. Bender. Auflage, München Wien Baltimore, 1998.
32. Hoffmann R, Wagner U. Inkontinenz und Deszensuschirurgie der Frau. Springer Medizin Verlag Heidelberg 2009, 9-13.
33. Lei L, Song Y, Chen R. Biomechanical properties of prolapsed vaginal tissue in pre- and postmenopausal women. Int Urogynecol J Pelvic Floor Dysfunct 2007, 18, 603-7.
34. Fritsch H, Kühnel W, Stelzner F. Entwicklung und klinische Anatomie der Adventitia recti. Langenbecks Arch Chir 1996, 381, 237-43.
35. Fritsch H. Gliederung des Bindegewebes im weiblichen Becken: Neue Konzeption morphologisch-embryologischer Untersuchungen. Pathologe 2006, 26, 273-5.
36. Fritsch H, Lienemann A, Brenner E, Ludwikowski B. Clinical anatomy of the pelvic floor. Adv Anat Embryol Cell Biol 2004, 175, 1-64.
37. Giri A, Hartmann KE, Hellwege JN. et al. Obesity and pelvic organ prolapse: a systematic review and meta-analysis of observational studies. Am J Obstet Gynecol 2017, 217(1), 11-26.e3.
38. Kudish BI, Iglesia CB, Sokol RJ. et al. Effect of weight change on natural history of pelvic organ prolapse. Obstet Gynecol 2009, 113, 81.
39. Daucher JA, Ellison RE, Lowder JL. Pelvic support and urinary function improve in women after surgically induced weight reduction. Female Pelv Med & Reconstr Surg 2010, 16, 263.
40. Walters MD. Abklärung der Inkontinenz: Anamnese, körperliche Untersuchung und weiterführende Diagnostik. In: Walters MD, K arram MM (Hrsg.) Gynäkologische Urologie. Berlin: Ullstein Mosby; S. 1997, 59-74.
41. Sears CL, Wright J, O'Brien J. et al. The racial distribution of female pelvic floor disorders in an equal access health care system. J Urol 2009, 181, 187.
42. Ward RM, Velez Edwards DR, Edwards T. et al. Genetic epidemiology of pelvic organ prolapse: a systematic review. Am J Obstet Gynecol 2014, 211, 326.