Apical defect — the essence of cystocele pathogenesis?

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Apical defect — the essence of cystocele pathogenesis?

[Short title: The role of apical defect in cystocele formation]

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ABSTRACT

Objectives: Lack of standardization causes misunderstandings in planning of cystocele treatment and the evaluation of surgical method effectiveness. The POP-Q System and DeLancey’s three levels of pelvic support do not account for the phenomenon of cystocele caused by an apical defect. We aimed to evaluate the impact of level I defect on the formation of cystocele.

Material and methods: Women reporting complaints related to bladder prolapse (cystocele)
were subjected to a urogynecological examination. For this purpose, a simple and standardized method was used, based on the POP-Q System and DeLancey's three levels of pelvic support. Furthermore, it was expanded by evaluating the impact of level I defect (apical defect) on prolapse at level II of the anterior compartment.

**Results:** In total, contribution of an apical defect to the pathogenesis of cystocele was founded in 72.2% of 302 female patients included in this study. In 30.8% the cystocele was caused exclusively by an apical defect. In turn, in 41.4% of patients, it resulted from concomitant apical and level II defect of the anterior compartment (lateral or central).

**Conclusions:** The results of this study indicate that an apical defect may play a significant role in the development of a cystocele. Hence, it could be essential to take the influence of an apical defect on level II in anterior compartment into account when planning a surgical procedure. The authors suggest that lack of such procedures potentially exposes some cystocele patients to ineffective treatment.

**Key words:** apical defect; central defect; lateral defect; cystocele; pelvic organ prolapse

**INTRODUCTION**

Cystocele, defined as a bulging of the bladder and anterior vaginal wall, is the most common form of pelvic organ prolapse [1]. This type of defect is also associated with the highest recurrence rate after surgical treatment [2]. The severity of pelvic organ prolapse is most often described in literature using the Pelvic Organ Prolapse Quantification System (POP-Q) [3], which distinguishes the following stages of prolapse extension:

- **Stage 0:** No prolapse is present.
- **Stage I:** The leading portion of the prolapse is located more than 1 cm cranially from the hymen level.
- **Stage II:** The leading portion of the prolapse is situated between 1 cm cranially or caudally from the hymen.
- **Stage III:** The leading portion of the prolapse is situated more than 1 cm caudally from the plane of the hymen but is everted at least 2 cm less than the total length of the vagina.
- **Stage IV:** The eversion is equal to the total length of the vagina.
While POP-Q is the most used scale in scientific research and literature on pelvic organ prolapse, its most popular basic form only describes their severity without indicating the type of a defect. Hence, for practical reasons, DeLancey’s three levels of pelvic support are more often used in surgical treatment planning. This scale classifies the following types of defects in the pelvis:

- Level I: Defects of the uterosacral ligaments, which may cause prolapse of the uterus, cervix, or vaginal vault, as well as potentially result in enterocele formation.
- Level II: Defects of the vesical or rectovaginal fascia, potentially resulting in cysto- or rectocele formation.
- Level III: Pubourethral ligament defects, potentially resulting in urethrocele formation, leading to stress urinary incontinence and defects of the posterior compartment perineum.

Level II defects in the anterior compartment are further divided into two groups: central and lateral defects. Central defects of the vesical fascia present as a cystocele with smooth vaginal mucosa, whereas in lateral defects, the vaginal rugae are preserved [3].

Qualification for surgical treatment should consider both the severity of the defect (POP-Q scale in its basic form) and its location (clinical classification of three levels of pelvic support according to DeLancey). This comprehensive approach would target a specific defect, aiming to treat its cause, not just its clinical presentation. Such a methodology revision could significantly improve surgical outcomes, which are currently associated with a relatively high recurrence rate. Especially after anterior colporrhaphy, where the patient’s native tissue is used to reconstruct the vesical fascia, the recurrence rate was estimated at around 30% at one-year follow-up. This fact suggests that anterior colporrhaphy should not be considered the method of choice for the treatment of any case of a cystocele [4]. However, the high recurrence rate should probably not be solely attributed to the shortcomings of the surgical technique but primarily to the inadequate qualification for operating treatment, without considering the exact location of the defects in the pelvic floor (central or lateral at level II) and the influence of the apical defect. Hence, the urogynecological examination described in this study evaluates the impact of level I defects on pelvic organ prolapse in level II of the anterior compartment. The inclusion of an apical defect in surgery planning has the potential to make a significant impact on the decision-making process. Such an approach could alter the surgical management of pelvic organ prolapse and promote methods that focus on repairing
the anatomical cause of the defect rather than just its clinical presentation.

**MATERIAL AND METHODS**

**Patients**

This epidemiological study was conducted in the Department of Gynecology and Urogynecology, AFM Cracow University and included 302 women aged 27 to 88 years (mean age 56). All the patients underwent surgical treatment for cystocele.

The inclusion criteria were cystocele (bladder prolapse) of at least POP Q II stage, and cystocele-related complaints. Furthermore, the investigated baseline characteristics comprised: age, parity, the number of assisted vaginal deliveries, cesarean section, the weight of the biggest child, body mass index (BMI), family history of POP, concurrent disorders and lifestyle. In turn, patient exclusion criteria included: previous pelvic floor surgery or vaginal surgery and genital cancer. This study was approved by the Andrzej Frycz Modrzewski Cracow University Bioethics Committee, with approval number KBKA/26/O/2017.

**Methodology of the urogynecological examination of the cystocele**

The patients with moderately filled bladders (about 200–250 mL as assessed by ultrasound measurement) were placed in the lithotomy position on a gynecological chair. The examination was performed by one of three clinicians of similar expertise, starting with an assessment of the vulva, perineum, and vagina at rest and maximal Valsalva maneuver.

Then, using two Kristeller specula, the following defects and their severity were evaluated:

- Using anterior and posterior specula — level I defect.
- Using the posterior specula — defects at anterior compartment, level II — cystocele, and level III — urethrocele. Level I defect influence on the cystocele was assessed by observing the changes of cystocele extension during level I repositioning using posterior specula.
- Using the anterior specula — defects at posterior compartment, level II — recto- or enterocele, which were not taken into account in this current study.

Then, after inserting both specula, the patient was asked to perform the Valsalva maneuver, during which the specula were slowly pulled out of the vagina, and the position of
the reference point for level I was assessed. When a level I defect was combined with a cystocele, it was necessary to gently insert the posterior speculum to restore the leading part of the prolapse back to the anatomical position of level I. Moreover, during the relocation of the level I defect, any possible changes in the presentation of the cystocele were evaluated. The cystocele may completely disappear if it was solely caused by the level I defect. In the case of a cystocele caused by a mixed defect at levels I and II, repositioning to level I using posterior specula causes the prolapse to get smaller but not disappear. In this situation, the examiner should assess the extension of the cystocele before level I repositioning, and evaluate it again after repositioning, while simultaneously determining the type of level II defect (lateral or central). For a cystocele caused by a lateral defect, the vesical fascia is unilaterally or bilaterally detached from the arcus tendinous, and vaginal rugae are preserved. In contrast, in the case of a cystocele caused by a central defect, the vaginal mucosa appears smooth (Fig. 1A, B). Finally, a cystocele caused exclusively by a lateral or central defect at level II requires the absence of an apical defect.

Urogynecological examinations to assess the cystocele were also supplemented with transvaginal and if necessary abdominal sonography, with the additional use of pelvic floor sonography [5]. In our department, ultrasonography is an integral part of urogynaecological examination to complement the assessment of level II defects, exclude paraurethral changes, and evaluate inner genital organs. However, the results of the ultrasound examination were not analyzed in this study.

To assess a pelvic organ prolapse, the basic POP-Q scale was used to evaluate the extent of the prolapse. In turn, DeLancey’s three levels of pelvic support allowed examining the impact of level I defects (apical defect) on level II prolapse in the anterior compartment.

Statistical analysis

Data analysis was performed using the Statistica v.12 software. The Shapiro-Wilk test was used to assess the normal distribution of the obtained data. Two of the compared groups showed normal distribution and were analyzed using the Student’s t-test. In turn, the Kruskal-Wallis test was performed to evaluate differences between the remaining five groups. The results were expressed as means ± SD or median, with a p-value of ≤ 0.05 considered statistically significant.
Defects causing cystocele

The described method of urogynecological examination allowed us to distinguish cystoceles caused by an apical defect (level I) from those resulting from isolated lateral or central (level II) or concomitant level I and II defects. Thus, this approach allowed to differentiate five groups of cystoceles causing defects in the pelvic floor:

1. Cystoceles caused by an isolated central defect at level II.
2. Cystoceles caused by an isolated lateral defect at level II.
3. Cystoceles caused by an isolated apical defect at level I.
4. Cystoceles caused by an apical defect combined with a central defect at level II.
5. Cystoceles caused by an apical defect combined with a lateral defect at level II.

This study did not analyze level II and III defects in the posterior compartment and level III defects in the anterior compartment, which usually show little anatomical manifestation but result in urethral closure dysfunction.

Patient characteristics

Among the 302 female patients aged 27–88 years, 188 (62%) were postmenopausal, and 114 (38%) premenopausal. Regarding BMI, 51% of the patients exhibited normal weight, 3% were underweight, 32% were overweight, and 14% were obese. Finally, when it came to familiar POP, approximately one-third of the patients (28%) had a positive family history. Patient demographic and clinical characteristics, as well as lifestyle habits, are presented in Table 1.

Frequency of the five analyzed defect types

Apical defect was present in 218 patients (72.2% of the study population), while mixed cystoceles caused by concomitant defects at level I (apical) and II (central or lateral) were recognized in 125 women. In this group, 96 patients were diagnosed with a mixed apical/lateral defect, and 29 patients had a mixed apical/central defect. Thus, a lateral cystocele was 3.3-times more frequent than a central cystocele combined with a level I defect (Tab. 2). Cystoceles caused exclusively by a defect of the vesicovaginal fascia were found in 84 patients (27.8% of the study population). In 13 patients, a cystocele caused by a central defect was found, while 71 patients were diagnosed with a cystocele caused by a lateral defect (Tab. 2). Therefore, in the studied population, isolated lateral defects were 5.5-times more
often recognized than their central counterparts.

**Age of patients, BMI distribution, and frequency of family history**

The proportions of pre- and postmenopausal patients, BMI distribution, and frequency of family history in all five types of POP are presented in Table 1. Analysis of differences between parameters and types of defects has shown that the number of pregnancies, parity, the weight of the biggest newborn and age at first delivery did not show statistically significant correlations with the analyzed data. However, significant differences were found in two of the parameters (age and BMI). The mean age in mixed apical/central cystocele was significantly higher compared to lateral (p < 0.001), apical (p = 0.012) and mixed apical/lateral (p = 0.031) defects. Similarly, mean values of BMI were significantly higher in mixed apical/central cystocele than in lateral (p = 0.002), apical (p = 0.003) and mixed apical/lateral (p = 0.005) defects. In turn, cystoceles caused by isolated central or mixed apical/central defects were observed more often in women overweight or obese over 50 years of age.

Furthermore, the mean age of women with a family history of POP was significantly lower (p = 0.035) than those without such history. Interestingly, the proportions of women with family history in the eleven established age groups were higher in younger women (under 45 years of age).

**DISCUSSION**

The examination technique described above used the POP-Q scale in its basic form to describe the severity of the defect. In turn, DeLancey’s three levels of pelvic support expanded by the impact of level I on the cystocele formation were used to outline the type of defect or its absence at levels I to III. The methodology based on those two scales is a simple clinical tool for standardizing the evaluation of both the severity and the type of defects leading to pelvic organ prolapse.

As it was mentioned before, patients whose primary cause for complaint is a level I defect will likely not benefit from treatment using surgical techniques aimed to repair level II prolapse. They usually present level I defects causing a cystocele, which may look similar to those at level II in a superficial gynecological examination. Unfortunately, in such cases, anterior colporrhaphy is often performed. However, this technique is dedicated to repairing central defects of the vesicovaginal fascia, the least common type at level II of the anterior compartment. Hence, it is not a causal treatment for this group of patients, rarely resulting in
long-term improvement. This assumption seems to be supported by high recurrence rates of vaginal approaches such as anterior colporrhaphy, characterized by an initial success rate of 30–70% [5]. The cause of these statistics may lie in a lack of recognition of an apical defect’s influence, as well as a lack of lateral and central defect differentiation within level II of the anterior compartment while planning surgery. The presumed reasons for the low long-term success rate of anterior colporrhaphy were confirmed in this study, as only 4.3% of patients in the study group were diagnosed with an isolated central defect, while 9.6 % exhibited a mixed apical/central cystocele. Although many authors note a high correlation between the presence of apical defect and cystocele, or a reduction of a cystocele after apical defect correction, these observations are rarely considered in the process of surgical planning. In this study, after cystocele was treated at level I, it often did not require further correction at level II. Moreover, it seems that the number of cystocele recurrences is significantly higher in the absence of proper level I support.

Interestingly, Rooney et al. [6] showed that most anterior vaginal wall prolapse cases are correlated closely with a prolapse of the vaginal apex (apical defect). Hence, the patients affected with such conditions will not benefit from surgical treatment aimed solely at level II defects. Moreover, other researchers investigating pelvic floor repair procedures have concluded that the occurrence of the apical defect is strongly correlated with anterior vaginal wall prolapse, and moderately correlated with posterior vaginal wall prolapse. Hence, they suggested that most anterior vaginal wall prolapse cases require correction in the area of the apical defect [7]. This approach seems to be consistent with the observations of this study.

The data collected indicates the crucial role of the apical defect in the pathogenesis of a cystocele, with such dependency shown in 72.2 % of patients. In this group, it seems imperative to repair level I defects, which is likely to reduce the number of future recurrences. Previous studies have shown that 53–77% of cases of a cystocele can be attributed to an apical defect. Therefore, this condition should be considered during the planning of corrective procedures for pelvic organ prolapse [6, 8]. Moreover, Kantartzis et al. [7] emphasized the consideration of apical defects in the planning of surgical procedures, based on the evaluation of 1,358 surgeries of apical defect correction in a group of 2,465 hysterectomy patients with cases of total uterine prolapse. It was found that cases without primary correction of the apical defect correlated more frequently with subsequent cystocele surgery (23.8% vs 9.4%, p < 0.001), and less frequently rectocele (3.4% vs 12.2%, p < 0.001) or combined recto- and cystocele correction (16.4% vs 25.6%, p < 0.001). Furthermore, Wu et al. [9] proved that
patients with POP who underwent surgery without a correction of apical defects had higher anterior compartment follow-up surgery rates. This data supports the notion that that apical defects could be the etiological factor for anterior compartment prolapse.

In our study, cystoceles caused exclusively by an apical defect were found in 30.8% of the examined women. In these patients, only treatment of the apical defect will lead to a full correction of the cystocele. The optimal treatment for patients with a cystocele caused by a level I defect should be chosen based on uterine fixation (cervix or vaginal cuff in patients after a hysterectomy) to the edge of the anterior longitudinal ligament on the sacral bone. Surgical methods such as hysterosacropexy, cervicosacropexy, and colposacropexy should be performed nowadays laparoscopically. Furthermore, in transvaginal surgery, sacrospinous fixation can also be used for apical defect treatment. Unfortunately, in Europe, hysterectomy is frequently performed as the procedure of choice for incomplete and complete uterine prolapse. This procedure is not optimal, as it does not allow for the elimination of apical defect [10]. Moreover, during a hysterectomy, the uterosacral ligaments are ligated, which may be an iatrogenic factor for the future development of vaginal vault prolapse.

In cases of level II defects in the absence of a level I defect, differentiation between central and lateral defects is crucial in choosing a correct surgical approach. An anterior colporrhaphy is only recommended for treatment of central defects. Moreover, in the case of a lateral defect, reconstructive surgery using alloplastic materials should only be performed in elderly and polymorbid patients, while the remaining majority should be treated using laparoscopic lateral repair. In turn, combined techniques should be used in the case of mixed defects at levels I and II, depending on their severity. Finally, patient reproductive plans should also be taken into consideration when deciding on the course of treatment.

Lateral or mixed defects (apical/lateral) are the most common among premenopausal women. This tendency is often caused by injuries suffered during delivery. It has been shown that about 27–45% of women undergoing native tissue repair (anterior colporrhaphy) need follow-up surgery due to relapse [11]. However, after applying mesh implants, the follow-up surgery rate was reduced to around 13%. Unfortunately, the scope of the study did not include an analysis of which kind of cystocele appears among the studied women. However, as central and lateral defects can be corrected using mesh implants, such an approach could improve the successful end-effect of the surgery and decrease the rate of relapse. Furthermore, the fixation of mesh arms on the sacrospinal ligaments provides additional level I support.

Further results revealed that premenopausal women were most diagnosed with lateral
defects (56%). Positive family history was more frequent in this group, while BMI values remained in the normal weight range. Hence, it can be speculated that genetic predisposition may increase the risk of lateral defects at level II in the anterior compartment. This condition could be considered a risk prediction factor during birth planning to avoid recurrence of pelvic floor defects. A recent study shows that the relative risk of POP was higher in patients with family history, increasing with the numbers of affected first-degree relatives. Additionally, it was estimated that positive paternal family history of POP results in a lower risk than maternal history [12]. Twin studies seem to confirm the significant contribution of genetic factors (about 40%) in the etiology of prolapse [13]. In contrast, in the postmenopausal patients of the study group, the impact of family history was significantly lower but over 50% of patients were obese or overweight. Central or mixed defects (apical/central) were the most common in this group. In those patients, lifestyle and aging seem to be predominant risk factors in the cystocele development.

It is worth mentioning that Vasin et al. [14] carried out histological and immunohistochemical studies of vaginal wall tissue in peri- and postmenopausal women with POP. These studies have revealed a low ratio of type I:III collagen, especially in patients with severe POP (stage III or more). Moreover, changes in the levels of other mediators involved in connective tissue remodeling were observed. However, whether these changes resulted from a genetic predisposition is unknown, as no genetic analyses were performed.

Summarizing, the urogynecological examination methodology taking the influence of level I defects on the defects at level II of the anterior compartment into account during cystocele assessment could become a valuable tool for causal operative treatment planning in pelvic organ prolapse. However, further analyses of recurrence rates following corrective surgery are needed. The preliminary retrospective analysis of data from our department regarding surgical cystocele treatment showed a 4–8% recurrence rate in 300 patients during the follow-up period of six months to five years (data not published). In the study group, the frequency of recurrences seems to depend mainly on the type of defect and the surgery method.

Additionally, more extensive epidemiological studies should be carried out to determine the incidence of the defects specified in the DeLancey’s three levels of pelvic support, and to develop imaging methods for an apical defect, particularly in ultrasonography and magnetic resonance imaging (MRI). Sonography has limited significance in assessing the
apical defect [15], as it does not allow the diagnosis of over 70% of POP cases. While MRI seems more promising, it is not a standard urogynaecological examination procedure in surgical planning.

**CONCLUSIONS**

In conclusion, this study suggests a significant role of the apical defect in the development of pelvic floor disorders in women, especially in the anterior compartment. Hence, the authors propose a simple and effective assessment method of level I defect influence on cystocele using Kristeller specula. The surgery qualification process is crucial for successful POP correction, with misdiagnosis possibly resulting in ineffective treatment of a significant patient group. The methodology used in this study could potentially allow minimize recurrence rates after POP surgery. Taking into account the influence of level I defects on cystocele formation while planning surgery can improve the therapeutic results and significantly reduce the recurrence rate. However, further wide-scale clinical studies are required to confirm this notion fully.

**What’s new?**

The study showed that apical defect plays a significant role in the development of cystocele. Surprisingly, the apical defect was present in over 72% of women who reported complaints related to the presence of a cystocele. Currently, the impact of the apical defect on cystocele formation is often not considered when planning surgical procedure, which exposes a large group of patients to ineffective treatment. In fact, cystocele repair is associated with a relatively high recurrence rate. Due to the above, authors suggest that the influence of an apical defect should be considered during the planning of cystocele surgery. Further studies and evaluation of this approach could potentially result in an improvement of surgical management of pelvic organ prolapse. Furthermore, if the role of apical defect in cystocele formation were confirmed on a wider scale, it could lead to introduction of surgical methodology focused on repairing the anatomical cause of the defect rather than just its clinical presentation.

**Author contributions**

PS project development conducted the clinical examination, manuscript writing. WKS
conducted the clinical examination, manuscript writing, data collection. HS conducted the clinical examination, manuscript writing, and data collection. JL manuscript editing. ASC data analysis and manuscript writing. All authors edited and approved the final version of the manuscript.

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**Conflict of interest**

None declared.
REFERENCES


Table 1. Patient baseline characteristics

<table>
<thead>
<tr>
<th>Patient characteristics/variable</th>
<th>Type of cystocele</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>Central (C)</td>
</tr>
<tr>
<td>13 (4.3%)</td>
<td>71 (23.5%)</td>
</tr>
<tr>
<td>Age (mean ± SD)</td>
<td>58.8 ± 12.74</td>
</tr>
<tr>
<td>Number of pregnancies</td>
<td>2.2 (1–4)</td>
</tr>
<tr>
<td>Parity, mean (range)</td>
<td>1.9 (1–3)</td>
</tr>
<tr>
<td>Instrumental delivery (%)</td>
<td>4</td>
</tr>
<tr>
<td>Caesarean section (%)</td>
<td>4</td>
</tr>
<tr>
<td>Weight of the biggest child [g], mean (range)</td>
<td>3.571.0 (2.700–4.690)</td>
</tr>
<tr>
<td>Age at first delivery, mean ± SD/median (range)</td>
<td>25.0±3.6 (25.0 (18–32)</td>
</tr>
<tr>
<td>BMI, mean (range)</td>
<td>26.8 (19–37)</td>
</tr>
<tr>
<td>Menopause (n)</td>
<td>11</td>
</tr>
<tr>
<td>Family history of POP (n)</td>
<td>2</td>
</tr>
<tr>
<td>Hernia/varices/asthma (n)</td>
<td>1/4/3</td>
</tr>
<tr>
<td>-------------------------</td>
<td>-------</td>
</tr>
<tr>
<td>Smoking (n)</td>
<td>1</td>
</tr>
</tbody>
</table>

Ap/C — mixed apical and central defect; Ap/L — mixed apical and lateral defect
Table 2. Distribution of defects in level I and II in the anterior compartment

<table>
<thead>
<tr>
<th>Levels of defects</th>
<th>Number of patients in the study group</th>
<th>Types of defects</th>
<th>Number of patients in the group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Defects at level I or level I and II</td>
<td>218</td>
<td>Isolated apical defect</td>
<td>n = 93 (42.7%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mixed apical/lateral defect</td>
<td>n = 96 (44.0%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mixed apical/central defect</td>
<td>n = 29 (13.3%)</td>
</tr>
<tr>
<td>Defects at level II</td>
<td>84</td>
<td>Central defect</td>
<td>n = 13 (15.5%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lateral defect</td>
<td>n = 71 (84.5%)</td>
</tr>
</tbody>
</table>
Figure 1. Types of cystocele; (A) lateral defect on level II, anterior compartment; (B) central defect on level II, anterior compartment