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RESEARCH

ASSOCIATION BETWEEN STAGE 2 OR HIGHER PELVIC ORGAN PROLAPSE AND BONE MINERAL DENSITY IN POSTMENOPAUSAL WOMEN

ABSTRACT

Introduction: Because of the similarities in the pathophysiology of pelvic organ prolapse and osteopenia, we aimed to investigate the existence of a relationship between stage 2 or higher pelvic organ prolapse and bone mineral density.

Materials and Method: The hospital database between July 2011 and July 2012 was searched for women who underwent surgery for stage 2 or higher pelvic organ prolapse (study group). An additional search was conducted for women who underwent surgery for other benign gynaecological indications with stage 0 or stage 1 pelvic organ prolapse (control group).In total, 1652 women aged 40–68 years with adequate medical data were identified. Two hundred and sixteen patients with stage 0 or stage 1 pelvic organ prolapse and stage 2 or higher pelvic organ prolapse were compared in terms of bone mineral density.

Results: The difference between the two groups was not statistically significant for osteoporosis (p=0.347) but osteopenia was significantly more prevalent in the study group compared with the control group (p=0.012). In addition, women with stage 2 or higher pelvic organ prolapse had significantly lower femoral trochanteric and lumbar spine T and Z scores than those with absent prolapse.

Conclusion: This study found that the prevalence of osteopenia was higher among women with stage 2 or higher pelvic organ prolapse compared with those with stage 0 or stage 1 pelvic organ prolapse. In particular, the presence of stage 2 or higher rectocele or cystorectocele was associated with an increased risk of osteopenia.

Key Words: Pelvic Organ Prolapse; Osteoporosis; Bone Density; Osteopenia.

ARAŞTIRMA

POSTMENAPOZAL DÖNEMDEKİ KADINLARDA 2. DERECE VE ÜSTÜ PELVİK ORGAN PROLAPSUSU İLE KEMİK MİNERAL YOĞUNLUĞU ARASINDAKİ İLİŞKİ

Öz

Giriş: Bu çalışmanın amacı pelvik organ prolapsusu ve osteopeni patofizyolojisindeki benzerlikler nedeniyle 2. derece ve üstü pelvik organ prolapsusu ile kemik mineral yoğunluğu arasındaki ilişkiyi araştırmaktır.

Gereç ve Yöntem: İkinci derece ve üstü pelvik organ prolapsusu nedeniyle Temmuz 2011-Temmuz 2012 tarihleri arasında opere olan hastaların kayıtları incelenmiştir (çalışma grubu). Sıfır ve 1. derece pelvik organ prolapsusu olan ve diğer benign nedenlerle opere olan hastaların kayıtları da incelenmiştir (kontrol grubu). Düzenli kayıtları olan 40-68 yaş arasında 1652 hasta saptanmıştır. Sıfır ve 1. derece pelvik organ prolapsusu ve 2. derece ve üstü pelvik organ prolapsusu olan 216 hasta kemik mineral yoğunluğu açısından karşılaştırılmıştır.

Bulgular: Osteoporoz açısından iki grup arasında istatistiksel bir fark saptanmaz iken (p=0,347), osteopeni çalışma grubunda istatistiksel olarak anlamlı olacak şekilde fazla saptanmıştır (p=0,012). Ek olarak, 2. derece ve üstü pelvik organ prolapsusu olan hastalarda femur boynu ve lomber vertebra T ve Z skoru kontrol grubuna göre daha düşük saptanmıştır.

Sonuç: Bu çalışmada osteopeni prevelansı 2.derece ve üstü pelvik organ prolapsusu olan grupta kontrol grubuna göre daha yüksek bulunmuştur. İkinci derece ve üstü rektosel veya sistorektosel varlığı özellikle osteopeni riskinde artışla ilişkilidir.

Anahtar Sözcükler: Pelvik Organ Prolapsusu; Osteoporoz; Kemik Yoğunluğu; Osteopeni.

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INTRODUCTION

Pelvic organ disorders are an important health concern for women, affecting their quality of life. These disorders occur as any combination of compartmental defects of vaginal support and multiple defects are common (1,2). The prevalence varies widely across studies because of underreporting and a lack of consistent definitions. The etiology of pelvic organ prolapse (POP) remains poorly understood.Reduced stability of the pelvic floor due to trauma or chronically raised intraabdominal pressure is the key underlying mechanism. Pathology specimens show insufficient collagen and changes in the extracellular matrix of the pelvic floor in patients with POP (3). Furthermore, recent studies suggest that these changes in the pelvic floor may be a focal manifestation of a systemic collagen deficiency and may extend beyond the pelvic compartment. Alterations in pulmonary compliance, joint hypermobility and skin changes are also described in patients with POP (4-6).

Similar pathophysiology is involved in the development of osteopenia and osteoporosis, which reflects deficits in bone connective tissue quality, including loss of bone mass and extracellular matrix (7,8). Osteopenia and osteoporosis are also prevalent conditions and share similar risk factors such as advancing age, smoking, glucocorticoid use and menopausal status. The National Osteoporosis Foundation predicts that by the year 2020, 14 million adults older than 50 years will be affected by osteoporosis, and this increased incidence will lead to an increase in the number of bone fractures (9).

Because of the similarities in the pathophysiology of POP and osteopenia, we hypothesized that women with stage 2 or higher POP would have a lower bone mineral density (BMD) compared with women with stage 0 or stage 1 POP, controlling for known potential confounders. In this study, we aimed to investigate the existence of a relationship between stage 2 or higher POP and BMD.

MATERIALS AND METHOD

This retrospective observational study was performed in the Obstetrics and Gynecology Department at Tepecik Training and Research Hospital. The institutional review board approved the study and all participants gave informed consent.

The study design and study population have been described in detail in our previously published study that investigated the existence of a relationship between POP and striae

(6). Briefly, the hospital database between July 2011 and July 2012 was searched for women who underwent surgery for stage 2 or higher POP (study group). An additional search was conducted for women who underwent surgery for other benign gynecological indications with stage 0 or stage 1 POP (control group). The POP-Q system was used to quantify the severity of pelvic organ prolapse, which describes the prolapse of the 3 vaginal compartments in relation to the vaginal hymen. Overall,prolapse was classified according to the most dependent position of the leading edge of the prolapse. Four main types of pelvic organs prolapse were studied(cystocele, rectocele, cystorectocele uterovaginal prolapse) (10)In total, 1652 women aged 40–68 years with adequate medical data were identified. Patients were invited via phone to participate the study. A flow chart of the study design is presented in Figure 1.

Exclusion criteria used were as follows: adrenocortical hyperplasia, Cushing's disease, use of corticosteroids for autoimmune diseases, connective tissue diseases (e.g. Ehlers–Danlos syndrome), dermatological diseases (e.g. lichen sclerosus), use of hormone replacement therapy or BMD medications, long-term use of progesterone and use of drugs that negatively affect bone metabolism (e.g. anticonvulsants or antacids containing aluminium). Premenopausal patients were also excluded to avoid unnecessary BMD testing. The control group was created using 1:1 matching for age,parity and body mass index (BMI) using SAS version 9.1 (SAS Institute Inc., Cary, NC, USA). Demographic characteristics including age, parity, mode of delivery and presence/absence of hypertension and diabetes were recorded. Both groups were compared in terms of BMD.

All BMD assessments were completed on a Hologic Explorer S/N 90310 scanner (Bedford, MA, USA) using Version 12.3.1:7 software. Bone density test results were reported as T and Z scores from the femoral neck and the lumbar spine, respectively.A diagnosis of osteoporosis was defined based on the World Health Organization (WHO) criteria of a T score ≤−2.5 at any one site, osteopenia was defined as a T score >−2.5 to <−1, and normal bone density was defined as a T score ≥ −1 (11).

A pilot study found that 72% and 48% of the subjects had low BMD in stage 2 or higher POP and stage 0 or stage 1 POP groups, respectively.Based on these findings, a minimum sample size of 64 for each group would achieve 80% statistical power for detection of a difference in BMD, using p<0.05 to indicate significance.
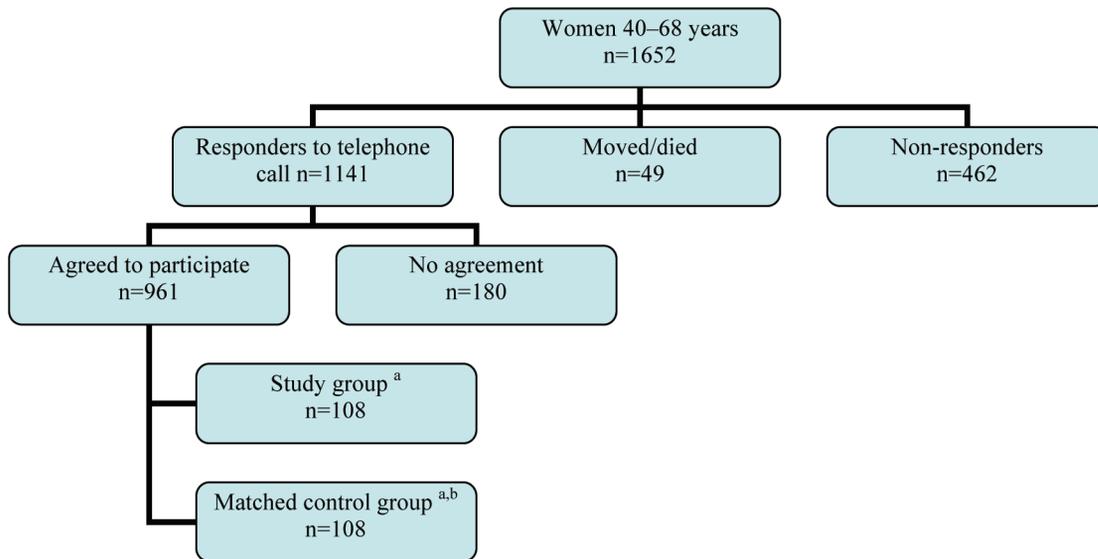
Figure 1— Flowchart of the study.
aBone mineral density (BMD) evaluation was performed, and age and body mass index (BMI) were recorded for each subject.
bThe control group was created using 1:1 matching for age,parity and BMI.

Statistical Analysis

Values for BMD were compared between women with stage 2 or higher POP and those with stage 0 or stage 1 POP. Chi-squared tests were used to analyse qualitative variances and two independent samples t-tests were used to analyse quantitative variances. Multivariate linear regression analyses were conducted to evaluate the association between BMD and POP after adjusting for covariates (age, BMI, hypertension, diabetes and smoking). Descriptive statistics were used to constitute demographic characteristics regarding variances. Logistic regression analysis was performed to calculate risk ratios. A value of $p < 0.05$ was considered to indicate statistical significance. Data were analysed using Statistical Package for the Social Sciences version 18.0 (SPSS Inc., Chicago IL, USA).

RESULTS

The mean age of 216 participants was 55.91 ± 5.55 years. Clinical and demographic characteristics of the two groups are summarised in Table 1. Age, BMI, parity, mode of delivery, smoking status and presence/absence of hypertension and diabetes did not differ significantly between the two groups.

The mean time from surgery to BMD assessment was 10.5 months. The difference between the two groups was not statistically significant for osteoporosis ($p=0.347$) but osteopenia was significantly more prevalent in the study group compared with the control group ($p=0.012$). In addition, women with stage 2 or higher POP had significantly lower femoral trochanteric and lumbar spine T and Z scores than those with stage 0 or stage 1 prolapse (Table 2).

Multivariate analyses controlling for age, BMI, smoking status and co-morbidities revealed that women with stage 2 or higher POP were at an increased risk of osteopenia [odds ratio (OR)=1.42, 95% confidence interval (CI)=1.13–1.92] compared with those in the control group.

After the initial analysis, prolapse was classified according to the most dependent position of the leading edge into four distinct anatomical subtypes for further analysis: cystocele, rectocele, cystorectocele and uterovaginal prolapse. All these subtypes of POP were stage 2 or higher. On multivariate regression analysis, stage 2 or higher rectocele alone or with stage 2 or higher cystocele was shown to be independently associated with low BMD (OR=1.25, 95% CI=1.12–1.37, OR=1.29, 95% CI=1.14–1.35, respectively; Table 3).

Table 1— Clinical and Demographic Characteristics of the Study and Control Groups.

Characteristics	Study Group (n = 108)	Control Group (n = 108)	p
Age (years)	56.37 ± 5.43 (49–68)	55.44 ± 5.66 (48–72)	0.222
Body mass index (kg/m²)	29.06 ± 3.21 (21–38)	28.75 ± 3.12 (23–36)	0.479
Parity	3.42 ± 1.36 (2–6)	3.53 ± 1.23 (2–7)	0.142
Vaginal birth	98 (90%)	100 (%92)	0.183
Caesarean section	10 (10%)	8 (%8)	0.203
Smoking status	3 (3%)	6 (5%)	0.070
Hypertension	26 (24%)	23 (21%)	0.061
Diabetes mellitus	7 (6%)	8 (8%)	0.059
Osteoporosis	19 (17%)	14 (13%)	0.347
Osteopenia	73 (68%)	52 (48%)	0.012
Normal BMD	16 (15%)	42 (39%)	0.001

Data are shown as mean ± standard deviation (range) or n (%).

Table 2— Mean Bone Mineral Density Scores and Standard Deviations.

	Study Group	Control Group	p Value
Lumber T scores	–1,29 ± 1,30	–0,76 ± 1,32	0,003
Lumber Z scores	–0,75 ± 1,06	0,17 ± 1,42	0,001
Femur T scores	–0,70 ± 1,13	–0,21 ± 1,20	0,002
Femur Z scores	–0,43 ± 1,20	0,98 ± 1,41	0,001

Table 3— Associations Between Stage 2 or Higher POP and Osteopenia Reported as Odds Ratios and 95% Confidence Intervals (CI).

POP	n	Odds Ratio (95 % CI)	p-value
Cystocele	33	1.19 (1.14–1.25)	0.64
Rectocele	23	1.25 (1.12–1.37)	0.04
Cystorectocele	27	1.29 (1.14–1.35)	0.03
Uterovaginal prolapse	25	1.12 (0.96–1.27)	0.88
Total pelvic organ prolapse	108	1.42 (1.13–1.92)	0.03

DISCUSSION

This study found that the prevalence of osteopenia was higher among women with stage 2 or higher POP compared with those with stage 0 or stage 1 POP. In particular, the presence of stage 2 or higher rectocele or cystorectocele was associated with an increased risk of osteopenia.

The prevalence of osteopenia in the present study group was higher than reported rates of about 50% in previous studies, similar to the prevalence in the present control group (12-14). Therefore, the high prevalence of low BMD levels in the present study group might be attributed to a common pathophysiology between pelvic floor disorders and osteoporosis.

The relationship between POP and BMD has been studied previously. In the Women's Health Initiative Estrogen Plus Progestin trial, an association was found between clinically significant POP and low BMD in postmenopausal women (15). The authors suggested that the suboptimal collagen status associated with POP might also involve bone collagen and lead to skeletal compromise. Richter HE et al. (16) investigated the association between pelvic floor symptoms and

BMD. They found that women with osteopenia were at an increased risk of faecal incontinence and women with osteoporosis were at an increased risk of large volume urinary incontinence. Pal L. et al. reported that postmenopausal women with moderate to severe prolapse had significantly lower BMD (17).

The mechanisms underlying the association between POP and decreased BMD remain unclear. However, connective tissue deficits, microarchitectural abnormalities and collagen changes have been identified in patients with low BMD and in patients with POP. A reduction in BMD results in an increased risk of osteoporosis and fractures in women (18). Osteopenia and osteoporosis are common chronic disorders which affect a substantial portion of postmenopausal women. Despite the availability of effective preventive treatments, these disorders are frequently underdiagnosed and undertreated. The most serious consequence of these disorders is fractures, which can have a serious negative effect on quality of life. Moreover, low BMD in postmenopausal women is correlated with increased mortality, especially from cardiovascular disease (19).

The early diagnosis of low BMD is vital to help maintain good bone strength during ageing and to avoid debilitating fractures. Multiple expert groups recommend screening women for osteoporosis with a bone densitometry beginning at 65 years of age. However, as reported in the present study, there is an association between stage 2 or higher POP and low BMD and therefore, screening should begin at an earlier age. Women with stage 2 or higher POP should be informed about the future risk of developing osteoporosis and should be informed about avoidable risk factors (such as smoking, sedentary lifestyle and excessive alcohol consumption) and preventive strategies to improve bone health (adequate nutrition, weight-bearing exercise, calcium and vitamin D supplements).

The strength of this study was the investigation of women who had undergone surgery for stage 2 or higher POP with adequate gynaecological examination. Previous studies that have aimed to assess the association between POP and BMD were based on self-reported symptoms (16,20). The present study also investigated possible confounding variables such as age, BMI, parity, mode of delivery, smoking status and the presence/absence of hypertension and diabetes. Women diagnosed with stage 2 or higher POP should be counselled about low BMD. Lifestyle changes and preventive strategies may be effective to decrease the prevalence of low BMD in these women, thus reducing the future risk of osteoporosis and fracture and associated costs.

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