Obesity and pelvic organ prolapse: a systematic review and meta-analysis of observational studies

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BACKGROUND: Studies evaluating the association between obesity and pelvic organ prolapse report estimates that range from negative to positive associations. Heterogeneous definitions for pelvic organ prolapse and variable choices for categorizing obesity measures have made it challenging to conduct meta-analysis.

OBJECTIVE: We systematically evaluated evidence to provide quantitative summaries of association between degrees of obesity and pelvic organ prolapse, and identify sources of heterogeneity.

STUDY DESIGN: We searched for all indexed publications relevant to pelvic organ prolapse up until June 18, 2015, in PubMed/MEDLINE to identify analytical observational studies published in English that reported risk ratios (relative risk, odds ratio, or hazard ratio) for body mass index categories in relation to pelvic organ prolapse. Random effects meta-analyses were conducted to report associations with pelvic organ prolapse for overweight and obese body mass index categories compared with women in the normal-weight category (referent: body mass index <25 kg/m^2).

RESULTS: Of the 70 studies that reported evidence on obesity and pelvic organ prolapse, 22 eligible studies provided effect estimates for meta-analysis of the overweight and obese body mass index categories. Compared with the referent category, women in the overweight and obese categories had meta-analysis risk ratios of at least 1.36 (95% confidence interval, 1.20—1.53) and at least 1.47 (95% confidence interval, 1.35—1.59), respectively. Subgroup analyses showed effect estimates for objectively measured clinically significant pelvic organ prolapse were higher than for self-reported pelvic organ prolapse. Other potential sources of heterogeneity included proportion of postmenopausal women in study and reported study design.

CONCLUSION: Overweight and obese women are more likely to have pelvic organ prolapse compared with women with body mass index in the normal range. The finding that the associations for obesity measures were strongest for objectively measured, clinically significant pelvic organ prolapse further strengthens this evidence. However, prospective investigations evaluating obesity and pelvic organ prolapse are few.

Key words: body mass index, meta-analysis, modifiable risk factor, obesity, pelvic organ prolapse

Introduction

In pelvic organ prolapse (POP), ≥1 of the intrapelvic organs including the uterus, bladder, rectum, and the urethra descend into the vaginal space, presumably due to deficiencies in the pelvic support system that normally provides sustained support.[1,2] POP is a highly prevalent condition in women with prevalence rates ranging from 10% in younger women up to 50% in postmenopausal women.[3-6] Nearly 1 in 10 women will undergo surgical correction for POP in their lifetime.[7]

Aging and parity have been most consistently associated with POP[8-17]; however, these factors are not modifiable. Obesity is a modifiable risk factor that may be influenced on a population level to reduce the public health and economic burden of POP. However, studies evaluating the relationship between obesity and POP have reported inconsistent conclusions. Effect estimates for POP in obese women (body mass index [BMI] ≥30 kg/m^2) range from negative to a 2.5-fold increase in risk, when compared with women of normal weight.[3,4,6,8-12,14,15,17-29] A meta-analysis of measures of obesity and its relationship to POP may not only bring the scientific community closer to a consensus on this association, but may also help identify reasons for heterogeneous findings in the literature.

Therefore, the goals of this review are 2-fold. First, we aim to provide overall effect estimates for POP with regard to degree of obesity, as measured by categories of BMI. We also aimed to evaluate study-level characteristics that may in part help to explain heterogeneous effect estimates reported by studies examining obesity and POP.

Materials and Methods

Search strategy and article review

To conduct this review, the PubMed/MEDLINE database was systematically queried using appropriate search terms relating to POP (Appendix) to identify titles and abstracts of studies indexed since inception of MEDLINE (1971) until the date of search (June 18, 2015). A search start date was not specified to allow inclusion of reliably indexed articles as early as 1946 by MEDLINE by default. The earliest published article qualifying from the specified

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search term (Appendix) dated back to Jan. 24, 1975. Title listings were scrutinized by 2 reviewers to eliminate studies clearly not related to the topic of interest. Abstracts of remaining articles were then reviewed by 2 reviewers to identify original research published in English that evaluated the association between risk factors for POP. Articles describing or comparing surgical procedures for POP were excluded. At the abstract level, if it was unclear whether a given study evaluated risk factors for POP, then the study was retained for full text review in addition to abstracts that clearly indicated evaluating risk factors for POP. A full text review of these articles was then conducted to retain articles that evaluated the relationship between BMI and POP for a qualitative summary of the literature and for further eligibility for meta-analysis.

Eligibility criteria for meta-analysis

Population. Studies that reported effect estimates on the relationship between BMI and POP in women of any age were eligible to be included in the meta-analysis. Studies involving women with or without hysterectomy were included. Women with previous hysterectomy are still at risk of developing other forms of prolapse including vaginal vault prolapse, and anterior and posterior vaginal wall prolapse. Studies specifically evaluating prolapse recurrence following surgery for urinary incontinence or POP were not eligible for analysis. The eligibility criteria for this meta-analysis were kept permissive to extend generalizability of findings to a broad population of women.

Study design. Analytic observational studies of all types including cross-sectional, case-control, and cohort designs with at least 40 cases of POP were eligible to be included into the meta-analysis. A minimum of 40 cases was chosen as criteria to only include estimates from studies that provide relatively reliable estimates of the association between categorical BMI and POP. Additionally, studies needed to report a risk ratio (odds ratio [OR], relative risk [RR], or hazard ratio) or must have provided sufficient information to allow calculation of a relevant effect estimate. For the primary analysis, all of these 3 risk ratios were aggregated together to present a meta-analysis risk ratio, regardless of study design. Case-control studies that specifically matched on BMI status were not considered eligible for analysis.

Outcomes. The primary outcome for this meta-analysis is POP as a dichotomous variable (yes, no). All forms of prolapse reported as POP, uterine prolapse, genital prolapse, enterocele, cystocele/anterior wall prolapse, or rectocele/posterior wall prolapse are counted as an outcome. For our primary aim, we include self-reported symptomatic prolapse, prolapse indicated by *International Classification of Diseases* codes, surgical procedure codes, as well as prolapse measured through pelvic exams by trained professionals for all severities of prolapse. For ease of data aggregation, reports of Baden-Walker halfway grading system of grade $\geq$2 or POP-Quantification (POP-Q) system stage $\geq$II were considered comparable.

Assessment of BMI. Studies that presented risk ratios by categories of BMI were considered eligible for meta-analysis. Ideally, studies must have reported risk ratios for the BMI categorized similar to the World Health Organization (WHO) guidelines: BMI $<$25 kg/m^2 (reference group), BMI 25-30 kg/m^2 (overweight), and BMI $\geq$30 kg/m^2 (obese). In the event studies reported risk ratios for categories of BMI that were not conventional, effect estimates were grouped with the nearest conventional BMI category. For example, if studies presented a risk ratio for BMI $<$25 kg/m^2 (reference) vs BMI $\geq$25 kg/m^2, then these studies were put into the overweight category. In another example, the Progetto Menopausa Italia Study Group[26] used the following BMI categories to report OR: $<$23.8 (reference), 23.8-27.2, and $>$27.2 kg/m^2, which the meta-analyst grouped as normal weight, overweight, and obese, respectively, with $<$23.8 kg/m^2 still serving as the referent category. Despite these inconsistent, yet, overlapping categories, analysis categories are referred to as normal weight, overweight, and obese for exposition. Studies that combined overweight and/or obese individuals into their lowest category (reference category) were not considered comparable and are therefore only described qualitatively. Studies that only provided mean or median BMI measures by case-control status or only calculated risk ratios using BMI as a continuous measure were not considered eligible for meta-analysis with categorical representation of BMI.

Data duplication. In the event $\geq$2 studies used the same or overlapping study populations, the larger of the studies was chosen for the meta-analysis.

Data abstraction. For eligible studies, the following fields were abstracted from each article: study title, first author, year of publication, study design (cross-sectional, case-control, cohort), mean age (SD)/range or median (interquartile range) if provided, percent of postmenopausal women represented in the study if provided (or could be estimated if the study provided adequate information for estimation), racial/ethnic composition of study if provided (or could be estimated based on country of study), method of POP assessment (symptomatic prolapse through self-report, or objectively measured prolapse), categories of BMI utilized by authors, risk ratios provided (OR, RR, or hazard ratio) by each category of BMI, raw numbers for risk ratio calculation by categories of BMI and POP status if adjusted risk ratios or unadjusted risk ratios were not provided, information on whether study adjusted for key covariates (yes, no), and the list of covariates adjusted for in regression models. When a given study provided $\geq$2 risk ratios for varying definitions of POP for the same population (symptomatic POP, objective POP with any grade of POP, or objective POP with clinically significant POP), then both reported risk ratios were abstracted as separate entries and marked as duplicate to avoid aggregating