Original Research

Timing of Office-Based Pessary Care

A Randomized Controlled Trial

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OBJECTIVE: To evaluate the influence of pessary visit intervals on development of vaginal epithelial abnormalities.

METHODS: We conducted a randomized, noninferiority trial of office-based pessary care. Eligible participants were adult women wearing a ring, Gellhorn, or incontinence dish pessary to treat pelvic organ prolapse or incontinence or both. Patients were randomized 1:1 to routine pessary care (office visits every 12 weeks, "routine" arm) or to extended pessary care (office visits every 24 weeks, "extended" arm). The primary study outcome was rate of vaginal epithelial abnormalities (epithelial break or erosion) at the final study visit (48 weeks). The predetermined noninferiority margin was 7.5%.

RESULTS: From January 2015 through June 2017, inclusive, 448 patients were screened and 130 were randomized, 64 to the routine arm and 66 to the extended arm. Baseline characteristics of the study arms were similar with the exception of pessary type, with ring pessary more common in the routine arm and Gellhorn pessary more common in the extended arm (P=.02). The rate of epithelial abnormalities at the final study visit (48 weeks) was 7.4% in the routine arm and 1.7% in the extended arm (difference, −5.7 percentage points; 95% CI −7.4 to −4), which met the criterion for noninferiority. Rates of all types of epithelial abnormalities did not differ between arms at any time point. Increasing duration of pessary use (P=.003) and history of prior epithelial abnormalities were associated with development of epithelial abnormalities (P=.01). Other than epithelial abnormalities, no adverse events related to pessary use occurred in either arm.

CONCLUSION: In women who receive office-based pessary care and are using a ring, Gellhorn, or incontinence dish pessary, routine follow-up every 24 weeks is noninferior to every 12 weeks based on incidence of vaginal epithelial abnormalities.

CLINICAL TRIAL REGISTRATION: ClinicalTrials.gov, NCT02371083.

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Vaginal pessaries often are used as first-line treatment of pelvic organ prolapse and stress urinary incontinence. Pessaries are recommended for patients who do not desire surgery or who are poor surgical candidates.[1] Studies show that pessaries improve prolapse symptoms, quality of life, bowel symptoms, and body image perception.[2–6] Although the benefits of pessary use are widely studied, guidelines on caring for patients using pessaries are lacking and practices vary widely. In a recent survey of members of the International Urogynecology Association, the interval of pessary cleaning ranged from weekly to yearly.[7] A survey of members of the Royal College of Obstetricians and Gynaecologists found that most U.K.-based clinicians change pessaries every 6 months and there was a trend toward fewer complications at increasing follow-up intervals.[8] A survey of gynecologists in the United States revealed that the most common follow-up visit schedule is every 3 months.[9]

The goal of monitoring patients is to assess fit of the pessary, adverse effects or complications, and patient satisfaction with pessary as a treatment method. The most common adverse effect of pessary use is vaginal epithelial abnormalities such as granulation tissue or erosions.[10] There are no existing data to determine at what interval patients need be evaluated to prevent

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pessary-related adverse events or complications. For patients to whom we provide complete pessary care, we typically remove the pessary every three months. We conducted a randomized trial of women undergoing office-based pessary care to evaluate whether extending the visit interval from 12 to 24 weeks was noninferior with respect to development of vaginal epithelial abnormalities.

METHODS

This is a randomized, noninferiority trial of office-based pessary care. This study was approved by the Hartford Healthcare Institutional Review Board and was registered at ClinicalTrials.gov (NCT02371083) before enrollment of any study participants. Consecutive patients were recruited at the Hartford Hospital Division of Female Pelvic Medicine and Reconstructive Surgery from January 2015 through and including June 2017. This study was designed and reported using CONSORT (Consolidated Standards of Reporting Trials) guidelines.[11]

Women wearing a ring, Gellhorn, or incontinence dish pessary to treat pelvic organ prolapse or incontinence or both were eligible to participate. Only those who were receiving office-based care were included. Patients were excluded from study participation if they were using a pessary other than a ring, Gellhorn, or an incontinence dish, or if they had presence of vaginal granulation tissue or ulceration or erosion of the vaginal epithelium as this typically prompts shorter interval follow-up or short-term pessary removal. Patients also were excluded if they removed the pessary between scheduled office visits. Participation was not offered at the time of a new pessary fitting. A nurse practitioner (C.M.) offered study participation to candidates at routine pessary follow-up visits. All participants gave written informed consent. The allocation sequence was generated by simple randomization using a computer and was concealed by use of sequentially numbered, sealed, opaque envelopes. Once informed consent was obtained, patients were randomized (K.P.) 1:1 to one of two study arms: 1) routine arm or 2) extended arm. Patients in the routine arm were scheduled for pessary care with pessary removal and cleaning every 12 ± 2 weeks; those in the extended arm were scheduled for pessary care with pessary removal and cleaning every 24 ± 2 weeks. Patients were followed for 48 weeks. Therefore, all patients in the routine arm underwent a total of five study visits: a baseline visit at study enrollment, three interim visits, and one final visit. All patients in the extended arm underwent a total of three study visits: a baseline visit at study enrollment, one interim visit, and one final visit. If a patient presented between scheduled study visits, reason was noted and she was allowed to continue in the study.

At the baseline visit, vaginal examination was performed to document a pelvic organ prolapse quantification score[12] to determine prolapse stage and to exclude the presence of vaginal epithelial abnormalities. The following data also were collected: patient age (years), body mass index (BMI, calculated as weight in kilograms divided by height in meters squared), smoking status, history of diabetes mellitus, history of surgery for incontinence or pelvic organ prolapse, history of hysterectomy, indication for pessary use, pessary size and type, duration of pessary use of the current pessary (and in total if the patient had used other pessaries in the past), whether the patient had an intimate partner, use of aspirin, use of anticoagulation therapy, parity, bother from vaginal discharge (Likert scale with 1=not bothersome to 5=very bothersome), presence of vaginal bleeding, and history of vaginal epithelial abnormalities. We also documented whether the patient was using hormone therapy and the route of administration.

At interim visits and at the final study visit, patient data were assessed for updates: new medications (aspirin, anticoagulation, hormone therapy), degree of bother related to vaginal discharge, and presence of vaginal bleeding. At interim visits, when the pessary was removed, a vaginal examination was performed to evaluate for the presence of epithelial abnormalities and adhesions. When abnormalities were noted, they were described in appearance, location, number, and size. If present, the epithelial abnormality was classified based on a system created by the first author (Table 1). If there was a change in pessary type or size, this was documented. If the pessary was changed to a type other than ring, Gellhorn or incontinence dish, the patient continued in the study as scheduled. If the pessary was removed temporarily to allow healing of an epithelial abnormality, the patient continued in the study. If the pessary was removed and there was no plan to replace the pessary, the patient was withdrawn from the study. Any concerning vaginal bleeding was evaluated as clinically indicated based on patient history and exam findings.

At the final visit, all participants underwent a vaginal examination, including a pelvic organ prolapse quantification score. At the final visit, patients in the extended arm were asked whether they preferred less frequent pessary care. If a patient presented for a visit in addition to the scheduled study visits, data were collected on the interim visit and the participant's symptoms or reason for visit reason were recorded. All study visits and examinations were performed by the same individual (C.M.) who was not masked to study

Table 1. Vaginal Epithelial Abnormality Classification System

Type	Description
0	No abnormalities
1	Epithelial erythema
2	Granulation tissue
3	Epithelial break or erosion 1 cm or less
4	Epithelial break or erosion greater than 1 cm

arm assignment. Throughout the trial, patients were encouraged to call the office with any concerns that could represent a potential adverse event: vaginal pain, discharge, bleeding, or if the pessary became dislodged. At each visit, all patients were routinely assessed for adverse events through screening questions and physical examination. Study methods were not changed after the start of the trial.

The primary outcome of this study was incidence of types 3 and 4 vaginal epithelial abnormalities (Table 1) at the final study visit. Secondary outcomes included rate of all types of vaginal epithelial abnormalities at 24 and 48 weeks (final study visit), patient satisfaction, degree of bother due to vaginal discharge, and number of unscheduled visits. Additionally, patient characteristics were evaluated for association with development of vaginal epithelial abnormalities. Outcomes were not modified after the start of the trial.

Based on an abstract presented at the Society of Gynecologic Surgeons' Annual Scientific Meeting, 2015 (unpublished), Letham et al showed a 7.5% rate of epithelial abnormalities from year 0 to year 4 of pessary use. This value was taken as a baseline rate, and a clinically significant difference was chosen to be double that, as an absolute percentage (ie, 15%). Given a noninferiority margin of −7.5 percentage points, a sample size of 118 from a population of approximately 7,500 would afford 83% power to detect a proportion of 0.15 using a one-sided binomial test for noninferiority. The target significance level was 0.05, with an assumption that the actual proportion was 0.075. To allow for an anticipated 5% dropout rate, power analysis indicated that 126 participants were required (63 per arm).

All analyses were conducted using an intent-to-treat principle by two of the authors (K.P., D.M.O.). Descriptive statistics were presented for each arm at baseline. Continuous variables are presented as mean±SD and were compared using Student's *t*-test. Comparison of frequencies and other categorical variables between the two arms was performed with a Pearson χ^2 test or Fisher's exact test, as appropriate. Numbers of vaginal epithelial abnormalities were reported for each arm as number and percent per study visit time point and were compared using a χ^2 test. Patient characteristics were assessed for association with development of epithelial abnormalities using Pearson χ^2 or Mann-Whitney U tests, as appropriate. SPSS 21 and MedCalc 14 were used for all analyses. An a priori alpha level of 0.05 was used such that all results yielding $P<.05$ were deemed statistically significant.

RESULTS

From January 16, 2015, through June 30, 2017, inclusive, 448 patients were screened for eligibility and 130 consented to participate (Fig. 1). Participant demographic and baseline characteristics are listed in Table 2. There were no differences between the study arms at baseline except for pessary type; those in the routine arm were more likely to use a ring pessary, and those in the extended arm were more likely to use a Gellhorn pessary ($P=.02$).

The rate of types 3 and 4 vaginal epithelial abnormalities was 7.4% in the routine arm and was 1.7% in the extended arm. The between-group difference of −5.7 percentage points (95% CI −7.4 to −4.0) met our criterion for noninferiority of extended-interval pessary care (Fig. 2).

Rate of vaginal epithelial abnormalities did not differ between study arms at any time point for any type of abnormality. The majority of patients (91.2%) in the extended arm preferred the schedule of less frequent pessary examinations.

Degree of bother due to vaginal discharge was evaluated with a 5-point Likert scale where higher numbers indicated a greater level or degree of bother. Patients in both arms reported similar degree of bother related to vaginal discharge with mean (±SD) 1.39 (±0.75) in the routine arm and 1.34 (±0.86) in the extended arm ($P=.73$).

Fourteen patients in the routine arm and 12 patients in the extended arm had at least one unscheduled visit; there was no statistical difference between the arms in percentage of patients who presented for unscheduled visits (32.7% [routine] vs 19.7% [extended], $P=.59$). Total number of unscheduled visits also did not differ ($P=.62$) between arms: 34 in the routine arm (a mean of 2.4 unscheduled visits per patient with at least one unscheduled visit) and 24 in the extended arm (a mean of 2 unscheduled visits per patient with at least one unscheduled visit). The most common indication for unscheduled visits was to follow up vaginal epithelial abnormalities diagnosed at a prior visit (29.3%). No patients presented for an unscheduled visit for vaginal bleeding or vaginal discharge.

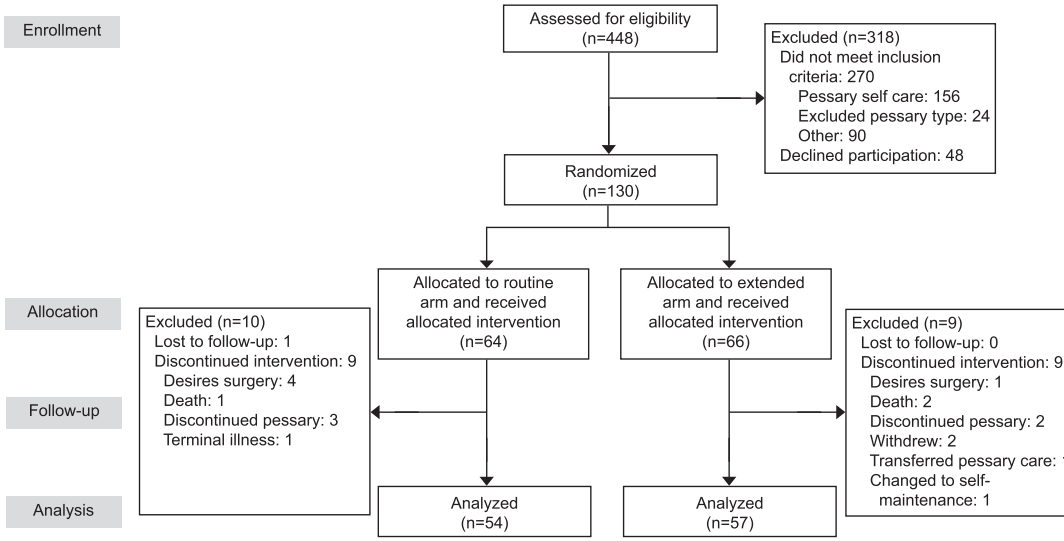

Fig. 1. Participant enrollment.

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Patient characteristics were evaluated for association with development of epithelial abnormalities. History of epithelial abnormalities before study participation was associated with epithelial abnormalities of types 1–4 (P=.01) and with epithelial abnormalities of types 3–4 (P=.02). Total duration of pessary use was associated with types 1–4 epithelial abnormalities (P=.003) but not with types 3–4 abnormalities (P=.73).

Epithelial abnormalities were not associated with patient age, BMI, prior hysterectomy, smoking status, prior prolapse surgery, use of aspirin, use of anticoagulants, pessary type, pessary size, vaginal estrogen use, pessary discomfort, vaginal bleeding, or vaginal discharge.

There were no vaginal adhesions around the pessary at any study visit in either of the study arms. Other than vaginal epithelial abnormalities, there were no other complications related to pessary use in this study.

The rate of patient withdrawal from the study was similar between arms: nine (14.3%) in the routine arm and nine (13.6%) in the extended arm (P=.91). Reason for withdrawal from the study also did not differ between the arms (P=.39).

DISCUSSION

In this randomized trial of office-based pessary care, we demonstrated that extended interval (every 24 weeks) pessary care was noninferior to routine care (every 12 weeks) for patients wearing ring, Gellhorn, or incontinence dish pessary based on incidence of types 3 and 4 vaginal epithelial abnormalities. There were no differences between the groups regarding rate of any type of vaginal epithelial abnormalities per study visit, number of unscheduled study visits, or degree of bother due to vaginal discharge. The majority of participants in the extended group preferred less frequent pessary care. Only longer lifetime duration of pessary use and history of epithelial abnormalities prior to study participation were associated with the development of vaginal epithelial abnormalities.

The known or anticipated complications associated with ongoing pessary use include vaginal discharge, spontaneous pessary expulsion, vaginal spotting, and vaginal ulcerations or abrasions.[13] A systematic review found that the most common pessary complication is superficial vaginal epithelial erosion.[10] Risk factors for erosion included long-term uninterrupted use or placement of a pessary that is too large.[10] Based on our results, uninterrupted use up to 6 months is not a risk factor for development of epithelial erosion.

Many health care providers consider vaginal erosion to be a concerning complication of pessary use as this may be the earliest sign of risk for fistula formation. Serious pessary complications such as fistula formation and pessary migration are rare and are often due to long-term neglect.[10,14] The frequency of these complications is not well described. In the literature, fistula formation related to pessary use has been noted in pessaries that were neglected for "several years."[10,14] There were no cases of pessary incarceration, migration, or fistula formation in the current sample, which suggests that serious complications take greater than 6 months to develop, and may be related to risk factors not present in the current sample. Although our results indicate that increasing the interval between pessary care visits is

Table 2. Baseline Demographics

Variable	Routine Arm (n=64)	Extended Arm (n=66)
Age (y)	79.8±7.2	78.1±7.5
BMI (kg/m^2)	27.6±6.2	27.1±6.2
Parity	3.0 (2–4)	3.0 (2–4)
Race		
Asian	1 (1.6)	0
Black	3 (4.7)	3 (4.5)
Caucasian	56 (87.5)	62 (93.9)
Hispanic	4 (6.3)	1 (1.5)
History of DM	7 (10.9)	11 (16.7)
History of hysterectomy	21 (32.8)	20 (30.3)
Current smoker	3 (4.7)	2 (3.0)
History of POP surgery	5 (7.8)	6 (9.1)
History of incontinence surgery	4 (6.3)	7 (10.6)
Aspirin use	30 (46.9)	35 (53.0)
Anticoagulant use	5 (7.8)	4 (6.1)
History of VEA	26 (43.3)	17 (28.3)
Time since most recent VEA (mo)	8.6±7.6	9.9±8.8
Pessary type		
Gellhorn	18 (28.1)	34 (51.5)
Ring	44 (68.8)	30 (45.5)
Incontinence dish	2 (3.2)	2 (3.0)
Pessary size (in)	2.75±0.35	2.86±0.48
Pessary indication		
Prolapse	52 (81.3)	56 (84.8)
Incontinence	1 (1.6)	4 (6.1)
Prolapse and incontinence	11 (17.2)	6 (9.1)
Duration of pessary use (mo)		
Current pessary	9.5 (3.0–28.5)	7.0 (3.4–23.3)
Total	24.0 (9.0–52.0)	12.5 (5.0–48.0)
Sexually active	1 (1.6)	3 (4.5)
Desired visit frequency		
Less often	48 (75.0)	55 (83.3)
No change	16 (25.0)	11 (16.7)
More often	0	0
Vaginal estrogen use	45 (70.3)	51 (77.3)
Degree of bother from vaginal discharge		
1 (no bother)	52 (81.3)	54 (81.8)
2	5 (7.8)	7 (10.6)
3 (neutral)	1 (1.6)	0
4	6 (9.4)	5 (7.6)
5 (maximum bother)	0	0
Epithelial abnormality type		
0	57 (89.1)	56 (84.8)
1	7 (10.9)	8 (12.1)
2	0	2 (3.0)
3	0	0
4	0	0
Prolapse stage		
Anterior		
0	4 (6.3)	2 (3.0)
1	17 (26.6)	10 (15.2)
2	21 (32.8)	25 (37.9)
3	22 (34.4)	26 (39.4)
4	0	3 (4.5)
Apical		
0	16 (25.0)	12 (18.2)
1	36 (56.3)	33 (50.0)
2	4 (6.3)	4 (6.1)
3	8 (12.5)	11 (16.7)
4	0	6 (9.1)
Posterior		
0	12 (18.8)	6 (9.1)
1	20 (31.3)	28 (42.2)
2	20 (31.3)	16 (24.2)
3	12 (18.8)	13 (19.7)
4	0	3 (4.5)

BMI, body mass index; DM, diabetes mellitus; POP, pelvic organ prolapse; VEA, vaginal epithelial abnormality.
Data are mean±SD, median (interquartile range), or n (%).

statistically noninferior and clinically safe, it is important that health care providers emphasize importance of ongoing follow-up to prevent patient loss to follow-up. Many health care providers of pessary care believe that use of vaginal estrogen decreases risk of epithelial abnormalities, but data to support this assumption are limited and conflicting.[15–17] Our data do not suggest an association between epithelial abnormalities and the use of vaginal estrogen; however, the majority of participants were on vaginal estrogen. Therefore, we are unable to make definitive conclusions about the use of estrogen to prevent pessary complications.

Strengths of this project include the randomized study design and the novelty of the subject matter. There are currently no evidence-based guidelines for pessary care and multiple publications have indicated that this information is of importance in clinical practice.[1,7–10,14] These results are generalizable to the majority of women undergoing office-based pessary care because ring and Gellhorn are commonly used pessaries, exclusion criteria were not overly burdensome, and the rate of epithelial abnormalities seen in the routine arm is similar to the baseline rate used in the power calculation.

Weaknesses in this project include the fact that the examiner was not masked to study arm

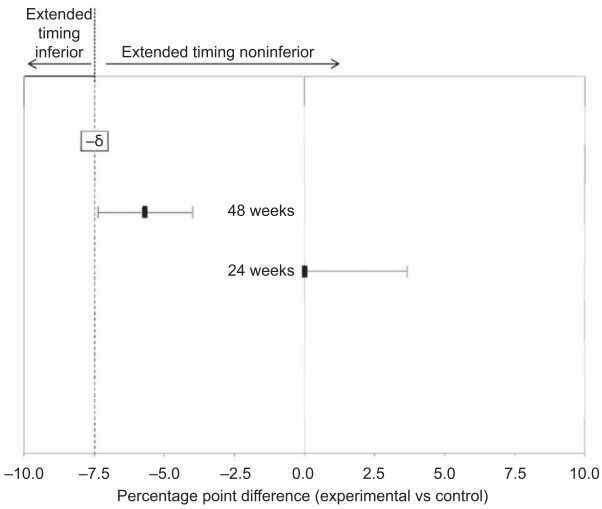

Fig. 2. Primary outcome results. The difference in rates of vaginal epithelial abnormalities at 24 and 48 weeks is shown, with two-sided 95% CIs. Difference in rates –7.5% or less indicates extended timing inferior to routine time; difference in rates greater than –7.5% indicates extended timing noninferior.

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assignment, the vaginal epithelial abnormalities rating system is not validated, and that more participants in the extended arm were using a Gellhorn pessary. These and other unknown factors may have influenced study findings. Future studies stratifying participants by pessary type, history of vaginal epithelial abnormalities, and vaginal estrogen use could help to clarify these issues. We are unable to make conclusions about other types of pessaries or about women who periodically remove their own pessary. Although we did not find differences between groups in rate of vaginal epithelial abnormalities at any study visit, it is important to note that the secondary outcomes were not considered in the power analysis.

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Authors' Data Sharing Statement

Will individual participant data be available (including data dictionaries)? *No.*

What data in particular will be shared? *Not available.*

What other documents will be available? *Not available.*

When will data be available (start and end dates)? *Not applicable.*

By what access criteria will data be shared (including with whom, for what types of analyses, and by what mechanism)? *Not applicable.*

PEER REVIEW HISTORY

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