Contemporary Clinical Trials 30 (2009) 178–189

Contents lists available at ScienceDirect

Contemporary Clinical Trials

journal homepage: www.elsevier.com/locate/conclintrial

Operations and pelvic muscle training in the management of apical support loss (OPTIMAL) trial: Design and methods ☆,☆☆

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ARTICLE INFO

Article history:
Received 11 June 2008
Accepted 10 December 2008

Keywords:
Pelvic organ prolapse
Vaginal prolapse
Uterine prolapse
Stress urinary incontinence
Randomized surgical trial
Factorial design
Pelvic floor muscle training
Behavioral therapy
Sacrospinous ligament fixation
Uterosacral ligament suspension

ABSTRACT

The primary aims of this trial are: 1) to compare surgical outcomes following sacrospinous ligament fixation to uterosacral vaginal vault suspension in women undergoing vaginal surgery for apical or uterine pelvic organ prolapse and stress urinary incontinence and 2) to examine the effects of a structured perioperative program consisting of behavioral techniques and pelvic floor muscle training compared to usual care. This trial is performed through the Pelvic Floor Disorders Network (PFDN), which is funded by National Institute of Child Health and Human Development. Subjects will be enrolled from hospitals associated with seven PFDN clinical centers across the United States. A centralized biostatistical coordinating center will oversee data collection and analysis. Two approaches will be investigated simultaneously using a 2×2 randomized factorial design: a surgical intervention (sacrospinous ligament fixation versus uterosacral vaginal vault suspension) and a perioperative behavioral intervention (behavioral and pelvic floor muscle training versus usual care). Surgeons have standardized essential components of each surgical procedure and have met specific standards of expertise. Providers of the behavioral intervention have undergone standardized training. Anatomic, functional, and health-related quality of life outcomes will be assessed using validated measures by researchers blinded to all randomization assignments. Cost-effectiveness analysis will be performed using prospectively collected data on health care costs and resource utilization. The primary surgical endpoint is a composite outcome defined by anatomic recurrence, recurrence of bothersome vaginal prolapse symptoms and/or retreatment and will be assessed 2 years after the index surgery. Endpoints for the behavioral intervention include both short-term (6-month) improvement in urinary symptoms and long-term (2-year) improvement in anatomic outcomes and prolapse symptoms. This article describes the rationale and design of this randomized trial, focusing on several key design features of potential interest to researchers in the field of female pelvic floor disorders and others conducting randomized surgical trials.

☆ This trial is registered at clinicaltrials.gov under Registration # NCT00597935.

☆☆ Grant support: supported by grants from the National Institute of Child Health and Human Development and the NIH Office of Research on Women's Health (U01 HD41249, U10 HD41250, U10 HD41261, U10 HD41267, U10 HD54136, U10 HD54214, U10 HD54215, and U10 HD54241).

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doi:10.1016/j.cct.2008.12.001

1. Introduction

Pelvic floor disorders, including pelvic organ prolapse (a condition in which the uterus, vagina, bladder and/or rectum bulge into or outside of the vagina) and urinary incontinence (involuntary urinary leakage), are common in women. One in nine American women will undergo at least one surgery for prolapse and/or urinary incontinence by the age of 80 [1]. Within five years of their first surgery, approximately 13% undergo a repeat operation, and over their lifetime, as many as 29% will undergo another surgery for prolapse or a related condition [1,2]. Given these high rates of initial and repeat surgery, there is clearly a need for high quality trials to improve surgical management strategies.

While prolapse surgery can be performed through an abdominal or vaginal route, current data suggest the preferred route for most prolapse surgery in the United States is vaginal, with as many as 80%–90% of surgeries being performed through this approach [1,3,4]. Prolapse often involves a combination of support defects, but loss of apical support is usually present in women with more advanced degrees of prolapse that extends beyond the hymen [5–7].

There is growing recognition that adequate support of the vaginal apex is an essential component of a durable surgical repair for women with advanced prolapse [5,8–10]. Numerous vaginal surgical procedures have been described for treatment of apical prolapse, with two of the most popular being the sacrospinous ligament fixation (SSLF) and the uterosacral vaginal vault suspension (ULS). The use of these procedures varies geographically and by training.

The SSLF procedure attaches the vaginal apex to the sacrospinous ligament either unilaterally or bilaterally, typically using an extraperitoneal approach. Available data suggests that while apical recurrence after SSLF is infrequent (<10%), recurrence of anterior vaginal prolapse affects approximately 30% of patients [11–23]. The ULS procedure attaches the vaginal apex to the uterosacral ligaments using an intraperitoneal approach. Data from uncontrolled case series have been used to suggest that the ULS may have greater anatomic success than SSLF, particularly with regard to the anterior segment [8,24–28]. Unfortunately, no comparative data exist to provide information about which technique is safer, more durable, and/or provides greater symptomatic relief. While both surgical techniques are clinically useful, it is essential to establish whether one is better, to optimize current clinical care, as well as inform the design of future trials, possibly comparing traditional vaginal apical repairs with mesh-augmented repairs or comparing routes of surgery (abdominal vs. vaginal).

Behavioral therapy, including pelvic floor muscle training (PMT) with or without biofeedback is an effective therapy for stress urinary incontinence (SUI), urge urinary incontinence, and fecal incontinence with almost no adverse consequences [29–32]. There is growing interest in evaluating behavioral and physical therapies as an adjunct to prolapse surgery in order to minimize pelvic floor disorders symptoms post-operatively and perhaps even improve anatomic outcomes of the prolapse surgery [32–35]. One published study reported results of perioperative PMT in women undergoing prolapse surgery, finding fewer urinary symptoms and better quality of life after surgery among women receiving perioperative PMT compared to a control group receiving usual care [34].

The principal aims of the Operations and Pelvic Muscle Training in the Management of Apical Support Loss (OPTIMAL) trial are 1) to compare surgical outcomes after SSLF versus ULS and 2) to assess the role of perioperative behavioral and pelvic floor muscle training versus usual care in women undergoing vaginal surgery for apical or uterine prolapse and SUI using a 2×2 randomized factorial design. The purpose of this paper is to describe the rationale, design and challenges of planning the trial, focusing on several key design features of interest to researchers in the field of female pelvic floor disorders and others conducting randomized surgical trials.

2. Methods

2.1. Design overview

The OPTIMAL trial is a collaborative multi-centered surgical trial performed by the Pelvic Floor Disorders Network (PFDN), a cooperative network of investigators from seven clinical sites and a Data Coordinating Center (DCC) supported by the National Institute of Child Health and Human Development (NICHD) of the National Institutes of Health (NIH) (Appendix). This protocol was developed as a collaborative effort of members from all seven PFDN clinical sites and the DCC. All participating sites in the PFDN, received institutional review board approval for this randomized surgical trial.

The OPTIMAL trial compares SSLF to ULS with or without perioperative behavioral and pelvic floor muscle training (BPMT) in women undergoing vaginal surgery for Stage 2–4 pelvic organ prolapse and SUI using a 2×2 factorial study design. The overall design is shown in Fig. 1. A standardized

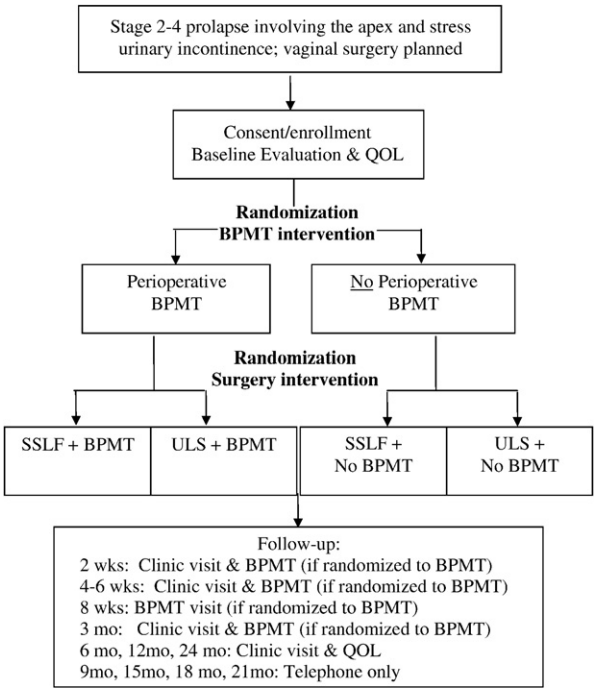

Fig. 1. Study Flow Chart. BPMT = behavioral and pelvic floor muscle training; QOL = quality of life assessment by the data coordinating center's Quality of Life Interviewing Center; SSLF, sacrospinous ligament fixation; ULS, uterosacral ligament suspension.