RESEARCH PROTOCOL

Date	11-04-16
Title	Do cranberry juice capsules reduce the risk of urinary tract infections in patients with indwelling urinary catheters following urogynecologic surgery?
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Hatton #	**16-087**

Purpose of Study

- The incidence of urinary tract infection (UTI) in women undergoing pelvic floor gynecologic surgery is high, ranging from 10-64% (Falagas, Athanasiou, Iavazzo, Tokas, & Antsaklis, 2008). A recent randomized trial showed that cranberry juice capsules significantly reduced the incidence of UTI in patients undergoing elective gynecologic surgery (19% vs 38%; odds ratio 0.38 with confidence interval 0.19-0.79) (Foxman, Cronenwett, Spino, Berger, & Morgan, 2015).
- Cincinnati Urogynecology Associates, TriHealth Inc incorporated this clinical regimen into their standard practice in early 2016. Currently, all patients who undergo pelvic floor gynecologic surgery and are discharged from the hospital with an indwelling urinary catheter postoperatively are prescribed cranberry juice capsules to reduce the risk of UTI.
- The purpose of this study is to determine if the addition of cranberry juice capsules to our discharge medication regimen for patients discharged home with an indwelling urinary catheter following pelvic floor gynecology surgery reduced the incidence of UTI.
    - **Primary Aim:** To determine the incidence of UTI in patients who were discharged home with an indwelling urinary catheter following pelvic floor gynecologic surgery in those who were prescribed cranberry juice capsules compared to those who were not.
    - **Secondary Aim:** To determine potential risk factors for postoperative UTI, other than urinary catheter use, such as certain demographic and perioperative factors including the following:
        - Age, race, BMI, tobacco use, medical comorbidities, type of surgery performed, type of anesthesia, intraoperative intravenous fluid administration, estimated blood loss, and duration of catheter use.

Hypothesis or Research Question

- We hypothesize that the addition of cranberry juice capsules reduced the incidence of UTI in patients discharged home with an indwelling urinary catheter following pelvic floor gynecologic surgery, compared to patients that had similar treatment without cranberry capsules.
- We further hypothesize that the addition of cranberry juice capsules reduced the duration of catheter use for those patients requiring postoperative catheterization following pelvic floor gynecologic surgery.

Background

Urinary tract infections (UTI) continue to be one of the most common healthcare-associated infections encountered today (Magill et al., 2012). The majority of these healthcare-associated UTIs are attributed to the use of urinary catheters (Hooton et al., 2010). Unfortunately, urinary catheter use is often unavoidable—as in the setting of postoperative urinary retention (POUR). Generally speaking, POUR can be characterized by any impairment in bladder emptying following surgery (Geller, 2014). Previous research has illustrated that POUR is a particularly common issue following urogynecologic surgery, with incidence rates of 1.4-43% (Dorflinger & Monga, 2001; Hakvoort, Elberink, Vollebregt, Ploeg, & Emanuel, 2004; Partoll, 2002). This means that a substantial number of patients will be discharged from the hospital with urinary catheters, putting them at substantially increased risk of developing a postoperative UTI. From an internal review of previously completed studies, approximately 54% and 25% of patients are discharged with a catheter following pelvic reconstructive surgery and suburethral sling procedures, respectively (Crisp et al., 2016).

The incidence of UTI has been estimated to be 3-4% per year for women in the general population (Foxman, 2014). However, for women undergoing urogynecologic surgery, the incidence of UTI is significantly greater, ranging from 10-64% (Falagas et al., 2008). As alluded to above, this increased incidence is likely related to postoperative urinary catheter use. Other risk factors for postoperative UTI have been postulated including age, menopausal status, history of recurrent UTIs, duration of catheter use, and increased distance between the urethra and anus (Foxman et al., 2015; Sutkin et al., 2010).

Previously, there has been much focus on the use of antibiotics to reduce the incidence of UTI in patients with indwelling urinary catheters. According to the most recent Cochrane Review, there remains limited evidence to indicate that receiving prophylactic antibiotics reduces the rate of bacteriuria and other signs of infection in surgical patients who undergo bladder drainage for greater than 24 hours postoperatively (Lusardi, Lipp, & Shaw, 2013). More recently, the focus of UTI prevention has turned to cranberry capsules.

Cranberry products are a potential nonantimicrobial method for UTI prevention, as cranberry proanthocyanidins have been shown to inhibit the adherence of P-fimbriated *Escherichia coli* to uroepithelial cells (Howell, Vorsa, Der Marderosian, & Foo, 1998). Because *E coli* is the culprit behind most UTIs, cranberry products remain an appealing UTI prevention strategy. However,

the evidence continues to be conflicting (Jepson, Williams, & Craig, 2012; Juthani-Mehta et al., 2016).

A recent randomized trial published in a high-impact journal showed that cranberry juice capsules significantly reduced the incidence of UTI in patients undergoing elective gynecologic surgery (19% vs 38%; odds ratio 0.38 with confidence interval 0.19-0.79) (Foxman et al., 2015). As a result of this new data, Cincinnati Urogynecology Associates, TriHealth Inc incorporated cranberry capsules into their standard practice as of March 2016. This change was made in an effort to reduce the incidence of UTI in patients requiring urinary catheterization following urogynecologic surgery. Currently, all patients who undergo urogynecologic surgery and are discharged from the hospital with an indwelling urinary catheter postoperatively are prescribed cranberry juice capsules, in addition to the standard discharge medication regimen.

However, the use of cranberry capsules has not been consistently shown to improve these outcomes in other subgroups of patients at risk (Juthani-Mehta et al., 2016). Furthermore, compliance and actual use of the capsules is uncertain, since patients may elect not to fill the prescription or fail to take the medication appropriately.

We aim to determine if the addition of cranberry juice capsules to the discharge medication regimen for patients discharged home with an indwelling urinary catheter following pelvic floor gynecology surgery significantly reduced the incidence of UTI, compared to a separate cohort that did not have cranberry prescribed. Given recent publications, our hypothesis is that the addition of cranberry juice capsules did reduce the risk of UTI. If we determine that cranberry capsules did in fact reduce the incidence of UTI in our study population, we can feel confident in continuing to incorporate this prevention method in our standard practice.

Research Plan

- **Study Design**
  - Retrospective chart review

- **Setting for the study**
  - The retrospective chart review will be performed on TriHealth EPIC platform at one of the various clinical locations.

- **Participants**
  - Study population: All women 18 years of age or older, who underwent pelvic floor gynecologic surgery (for the indication of pelvic organ prolapse or stress urinary incontinence) performed by a physician at Cincinnati Urogynecology Associates, TriHealth Inc between April 2015 and September 2015, and April 2016 and September 2016, who required indwelling urinary catheter use upon discharge from the hospital.
  - A chart review will be performed on all patients who underwent pelvic floor gynecologic surgery performed by a physician at Cincinnati Urogynecology

Associates, TriHealth Inc between April 2015 and September 2015, and April 2016 and September 2016 to determine which patients required discharge with an indwelling urinary catheter.

- The charts of those patients who required catheterization postoperatively will be reviewed further and will make up our study population of interest.
- Inclusion criteria
  - Adults 18 years of age or older
  - Underwent pelvic floor gynecologic surgery (for the indication of pelvic organ prolapse or stress urinary incontinence) performed by a physician at Cincinnati Urogynecology Associates, TriHealth Inc between April 2015 and September 2015, and April 2016 and September 2016
  - Required indwelling urinary catheterization upon discharge from the hospital postoperatively
- Exclusion criteria
  - Intraoperative bladder injury, fistula repair, urethral diverticulectomy, or any other need for prolonged catheterization
  - Complications in the 2 weeks following surgery requiring reoperation and subsequent catheter use
  - Allergy to cranberry or its components
  - Failure to present for both the two-week and six-week postoperative office visit
- Sample size
  - Cranberry juice capsules were incorporated into the standard practice of Cincinnati Urogynecology Associates, TriHealth Inc in mid-March 2016. We plan to review six months of data from similar time frames of 2015 and 2016. This will allow us to capture a similar number of patients in the exposure (cranberry juice capsules, 2016) and no exposure (no cranberry juice capsules, 2015) groups.
  - Given the fact that Cincinnati Urogynecology Associates, TriHealth Inc typically performs 400 surgeries annually, we estimate that reviewing a total of 12 months of data will result in accessing approximately 400 charts.

- **Data Collection**
  - Independent variables: cranberry juice capsules prescribed as part of discharge medication regimen
  - Dependent variables: UTI as defined by documentation of positive urine culture or treatment by an involved provider, with documentation in the Epic chart within 6 weeks postoperative.
  - Each chart will be reviewed and the following data will be collected or extrapolated:
    - General demographic data – Name, date of birth, age, race, weight, height, BMI, parity, tobacco use, medical comorbidities, date of surgery, surgery performed, date of discharge, intraoperative and postoperative

complications, type of anesthesia, intraoperative intravenous fluid administration, estimated blood loss, discharge medications, postoperative urine cultures, prescribed UTI treatment, duration of catheter use, and any postoperative complications or readmissions (fever, ileus, hematoma, transfusion)

- **Intervention or experimental aspect of the study**
  - No intervention will occur as part of this study.
  - There are no potential risks to the study population by any aspect of the study.

- **Statistical Analysis**
  - The primary outcome is the incidence of UTI in patients who were discharged home with an indwelling urinary catheter after pelvic floor gynecologic surgery. To compare the primary outcome between two groups with/without cranberry capsules, the odds ratio and corresponding confidence interval will be utilized. Descriptive statistics will be generated for demographic information such as age, race, BMI, Parity etc. The independent samples t-tests or Mann-Whitney U test will be employed for continuous variables and the Fisher's exact or Pearson Chi-square tests for categorical variables to test any significant difference between two groups. Logistic regression will be implemented to determine potential risk factors for postoperative UTI.

Ethical Considerations

- **Informed consent**
  - Since this is a retrospective study, waivers of Informed consent and Authorization will be requested.
- **Privacy information**
  - Extensive efforts will be made to ensure and maintain participant confidentiality. All identifying information will be maintained in a secure area at all times. All communication between staff members regarding participant data will occur via the Subject ID number only. However, identifying information will be retained in the original/source documents.
  - The Excel spreadsheet will be stored on a password protected, encrypted TriHealth computer for ten years following study closure, and then purged.

Cost/Budget

- This study will incur no cost to the institution, the participants, or the investigators.

Estimated Period of Time to Complete Study

When will study begin?	January 2017
Protocol Development Completed	2 weeks
Admin Review Time	2 weeks
IRB Approval	3 weeks
Data collection	4 weeks
Data analysis	2 weeks
Presentation development (if applicable)	2 weeks
Manuscript Development (if applicable)	4 weeks
Journal submission process (if applicable)	4 weeks
Study closure	2 weeks

- **When and how will results be disseminated?**
  - The results will be disseminated by way of an oral or poster presentation at a national meeting, and with publication in a high-impact journal.

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