Can Cranberries Contribute to Reduce the Incidence of Urinary Tract Infections? A Systematic Review with Meta-Analysis and Trial Sequential Analysis of Clinical Trials

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Abbreviations and Acronyms

PAC = proanthocyanidin
RCT = randomized controlled trial
rUTI = recurrent UTI
TSA = trial sequential analysis
UTI = urinary tract infection
WRR = weighted risk ratio

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Purpose: We sought to clarify the association between cranberry intake and the prevention of urinary tract infections.

Materials and Methods: This systematic review, which complies with the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analysis) statement, was done as a meta-analysis and trial sequential analysis of clinical trials.

Results: The findings clearly showed the potential use of cranberries for the clinical condition of urinary tract infection. Cranberry products significantly reduced the incidence of urinary tract infections as indicated by the weighted risk ratio (0.6750, 95% CI 0.5516–0.7965, p <0.0001). The results of subgroup analysis demonstrated that patients at some risk for urinary tract infections were more susceptible to the effects of cranberry ingestion.

Conclusions: The results of the current study could be used by physicians to recommend cranberry ingestion to decrease the incidence of urinary tract infections, particularly in individuals with recurrent urinary tract infections. This would also reduce the administration of antibiotics, which could be beneficial since antibiotics can lead to the worldwide emergence of antibiotic resistant microorganisms.

Key Words: urinary tract infections, fruit and vegetable juices, disease susceptibility, proanthocyanidins, study publication bias

Urinary tract infections are common and among the most frequent medical conditions requiring outpatient treatment.[1] Approximately 80% of all UTIs occur in women and 20% to 30% of women with a UTI will experience recurrence.[1] rUTIs, defined as at least 3 UTI episodes in the last 12 months or 2 episodes in the last 6 months, can develop in susceptible individuals and they are a significant source of patient morbidity and health care costs.[2] In individuals with rUTIs low dose antibiotic prophylaxis for several months can be recommended.[1] However, antibiotics are the main cause of the development of antibiotic resistance and such prolonged treatments can lead to increased resistance.[1] The increasing prevalence of *Escherichia coli* isolates resistant to antimicrobial agents has stimulated interest in nonantibiotic methods to prevent UTIs.[1]

Prophylaxis with cranberries is a potential prevention strategy with health benefits associated with the high concentrations of polyphenols

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such as PACs in these berries.[3,4] PACs are stable phenolics with antiadhesion activity against *E. coli*.[3] They act as receptor analogues and inhibit *E. coli* adhesion to cells by binding to the fimbrial tips.[3]

The effects of cranberry ingestion in the prevention of UTIs were systematized in 2 previous reviews with meta-analyses.[5,6] The most recent one suggested that there is insufficient evidence that cranberries decrease the number of UTIs since the pooled findings were based on a small number of studies.[5] Considering this together with the results of recent clinical trials evaluating cranberries to prevent UTIs we performed this systematic review, which complies with the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analysis) statement. The review was followed by meta-analysis and TSA (http://www.ctu.dk/tsa/), a newer approach that can assist in decreasing the likelihood of a type I error, to clarify the association between cranberry intake and the prevention of UTIs.

METHODS

Search Strategy

The search was performed in September 2016 in several electronic databases, including PubMed®, Scopus®, SciELO (Scientific Electronic Library Online), Cochrane Library and Web of Science™ using the terms (cranberr* OR Vaccinium) AND (urinary tract infections OR UTI) AND clinical trial AND human. According to the PRISMA statement, titles and abstracts of the records retrieved were screened and the full texts of those considered relevant were analyzed. Two of us independently performed the literature search with disagreements resolved by consensus with another of us. To be included in this work studies had to be clinical trials in humans, present a true control group and report the number of patients who experienced at least 1 UTI at the end of followup period (outcome of interest).

Data Extraction

Two of us independently assessed and extracted the data. Information was collected on the proportion of patients with at least 1 UTI and on study characteristics (supplementary table 1, http://jurology.com/). The RR served as the measure of effect for the outcome of interest.

Bias Assessment Risk

The bias risk of each included RCT was assessed with the Cochrane Library tool. This risk, which was classified according to 7 domains, was independently assigned by 2 of us with discrepancies resolved through discussions (fig. 1). Results were presented as a risk of bias summary and a risk of bias graph, which were sketched with RevMan, version 5.3.5 (http://community.cochrane.org/).

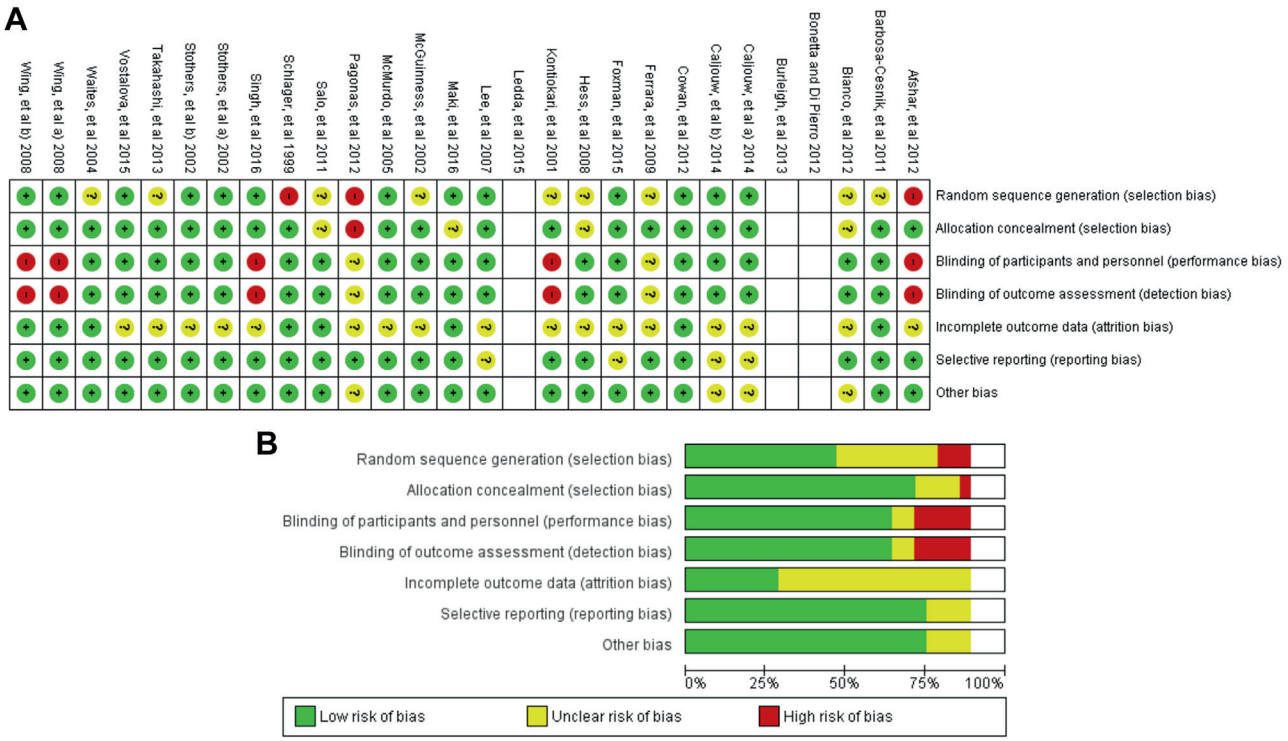

Figure 1. Results of review author judgments of risk of bias assessment regarding methodological quality of included studies. *A*, summary of each risk of bias item for each included study.[2–4,7–10,13–30] *B*, each risk of bias item shown as percent across all included studies.