Statistical Analysis Plan

Post Procedural Infections in Antibiotic Prophylaxis-Free Transperineal Prostate Biopsy : A Double Blinded Randomized Controlled Clinical Trial, A 2 Center Experience in the Philippines

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Introduction

This SAP describes how outcomes will be analyzed for the randomized controlled trial comparing no antibiotic prophylaxis versus antibiotic prophylaxis in men undergoing transperineal prostate biopsy.

Study Design

This is a prospective, randomized, double-blind, parallel-group (1:1), controlled non-inferiority trial. The non-inferiority margin was set at 5%. Men aged 40–75 indicated for prostate biopsy, meeting inclusion/exclusion criteria were included. Sample size was calculated at 120.

Objectives

General Objective

To compare incidence infectious complications in patients given antibiotic prophylaxis versus no prophylaxis among patients at St. Luke's Medical Center Global City and Quezon City from March 2024- January 2024

Specific Objective

1. To compare the incidence of urinary tract infection and sepsis between patients without and with antibiotic prophylaxis undergoing prostate biopsy.

2. To compare Hospital admissions, Emergency room visits, and non-infectious complications between the no prophylaxis versus prophylaxis groups.

Outcomes

Primary outcome is the incidence of Urinary tract infection and Sepsis. Urinary tract infection is based on the European Association of Urology guidelines on infection. Localized UTI is defined as having symptoms of Dysuria, Urgency, Frequency, Incontinence, and

Pressure or cramping in the lower abdomen. Systemic UTI is defined by the presence of localized symptoms plus one of the following: Fever or hypothermia, Rigors, shaking or chills, Delirium, Hypotension, Tachycardia, and Costovertebral angle pain and tenderness. Mild, and Self-limiting lower urinary tract symptoms such as hematuria and dysuria which spontaneously resolves will not be assessed as urinary tract infection, as these are commonly seen after prostate biopsy and rarely require treatment.

Secondary outcome includes the following: 30 day hospital admissions, 30 day emergency room visits, and non-infectious complications such as acute urinary retention will be recorded.

Populations

- Intention-to-Treat (ITT): All randomized participants analyzed as assigned.
- Per-Protocol (PP): Excludes major protocol deviations.
- Safety Population: All participants who received study drug (placebo or Cefoxitin).

Statistical Analyses

Sample Size and Sampling Technique

A minimum sample of 60 patients per group is needed for a non-inferiority study with binary outcomes. Basourakos, et al reported that rates of post-biopsy genitourinary infections were 1.35% in the AP group and 1.22% in the NAP group. The target set was at least 80% power and 90% confidence interval. This was computed using Sealed Envelope Ltd. 2012. Power calculator for binary outcome non-inferiority trial. There are paucity of data regarding post prostate biopsy infections in patients without antibiotic prophylaxis. Similarly, data on post biopsy infections in Filipinos are lacking. A study reported by Yaddao, et al., published in the Philippine Journal of Urology, reported an infection rate of 5% occurring after biopsy, hence, we chose 5% as our non-inferiority limit.

Data Analysis

To assess the primary and secondary outcomes, we analyzed the 90% confidence interval (CI) of the difference in proportions, following Altman's recommendation. Non-inferiority was established if the upper bound of the 90% CI was less than 5%. Descriptive statistics, including median, percentages, 90% CI, or interquartile range (IQR), were reported as appropriate. For comparisons between groups, an independent t-test was used for continuous variables, while the chi-square or Fisher's exact test was applied for categorical variables. All statistical calculations were performed using MedCalc Statistical Software version 23.2.6.

Safety Monitoring

- Early stopping rule: Stop if >2 mild infections or >1 severe infection (sepsis) in the no-prophylaxis arm before full accrual.
- SAEs will be recorded and reviewed by the safety monitor.

Reporting

- Baseline characteristics will be summarized by arm.
- Results will be reported with CONSORT flow diagram, tables of outcomes, and subgroup analyses.

Table Shells

Table 1. Baseline Characteristics (by arm)

		No Antibiotic	**Antibiotic**		**p value**
Age					
BMI					
Charlson					
1					
2					
3					
4					
Prostate Volume					
PSA					
Number of Cores					
	All	**No Antibiotic**	**Antibiotic**		**p value**
Cancer Detected					
Yes					
No					
Gleason					
Gleason 6 (3+3)					
Gleason 7 (3+4)					
Gleason 7 (4+3)					
Gleason 8 (4+4)					
Gleason 9 (4+5)					
Gleason 9 (5+4)					
Gleason 10 (5+5)					

Table 2. Primary Outcome (30-day infection)

	All		No Antibiotic		Antibiotic		Difference		p value
	n, %	90% CI	n, %	90% CI	n, %	90% CI	Value	90% CI	
Primary Outcome									
Urinary Tract Infection [Yes]									
Sepsis [Yes]									
Bacteriuria									
Secondary Outcome									
UTI Requiring Hospitalization [Yes]									
30 Day readmission Rates [Yes]									
30 day Emergency Room Visits [Yes]									
Non Infectous Complications [Yes]									

Figure Shell

Figure 1. CONSORT Flow Diagram