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COMPARISON OF INFECTIVE COMPLICATIONS BETWEEN TRANSRECTAL AND TRANSPERINEAL PROSTATE BIOPSY IN SUSPECTED CARCINOMA PROSTATE PATIENTS .

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ABSTRACT

Prostate cancer (PCa) ranks third as the cause of cancer-related death for men and is responsible for about one-fourth of newly detected malignancies in the western world. It is alarming to note that about 4.04 million years of healthy life are lost annually due to prostate cancer. The study is designed to compare infective complications of transrectal and transperineal systematic biopsy considering both clinically and microbiologically identified infective risks and complications.

KEYWORD

Prostate Cancer, Transperineal Systematic, Transperineal Systematic Biopsy, Periprostatic Block

ARTICLE HISTORY

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INTRODUCTION:

Prostate cancer (PCa) ranks third as the cause of cancer-related death for men and is responsible for about one-fourth of newly detected malignancies in the western world. It is alarming to note that about 4.04 million years of healthy life are lost annually due to prostate cancer.[1]

Herbert et al..[2] found that average incidence rate for prostate cancer in India ranged 5.0-9.1 per 100,000/year, whereas the comparable rate in the United States is 110.4 for whites and 180.9 for blacks.

The study is designed to compare infective complications of transrectal and transperineal systematic biopsy considering both clinically and microbiologically identified infective risks and complications.

METHODOLOGY:

Inclusion criteria included patients who were recommended to undergo prostate biopsy for suspected prostate cancer based on one or more of the following:

1. High PSA value (more than 4ng/ml)
2. Abnormal digital rectal examination (DRE) findings;
3. Hypoechoic areas found during examination of the prostate by transrectal or abdominal ultrasound;
4. Abnormalities identified by MRI of the prostate(such as T2 weighted)

Exclusion criteria included patients who are unable to undergo TRUS due to any condition such as:

1. Previous proctectomy.
2. Anal stenosis or any painful anal conditions.

Consecutive consenting patients meeting the inclusion and exclusion criteria were included in the study.

Patients were randomized into two groups- Patients in Group 1 underwent TRPB, and those in Group 2 underwent TPPB. Simple randomization was done. Allocation concealment was done by sealed envelope technique

Study procedure:

All patients took Ciprofloxacin (500 mg) orally 60 minutes before the procedure. A cleansing enema was not administered in the morning before biopsy as part of the preparation.

After obtaining consent for the procedure, the procedure was performed under local anesthesia with the periprostatic block with 20ml 1% Inj. Lidocaine under transrectal ultrasound guidance using the technique described by Nash[3] and modified by Knobloc[4].

Patients were given oral Fluoroquinolone tablet 500 mg 1 hour before the procedure and were advised a three-day course of antibiotics covering both aerobes and anaerobes.

All biopsies were performed under real-time ultrasound guidance (Famio SSA-530A Model Ultrasound; Toshiba Medical Systems) , Japan), using a transrectal bi-planar transducer for TPBx and a transrectal end-fire transducer for TRPB respectively using an 18-gauge automatic Magnum Biopsy Gun (C R Bard, Inc., Covington, GA, USA) .

For TPPB, patient was placed in a dorsal lithotomy position.

For TRPB, left lateral decubitus with knees and hips flexed, with buttocks at the margin of the table to allow probe manipulation without obstruction.

DRE was done to confirm the initial findings before the procedure by any technique.

Prostatic block was given (10 ml of 2% Lidocaine) under TRUS guidance and 12 samples were taken as per the template

under software guidance for uniform spacing utilizing an 18-gauge automatic Magnum Biopsy tool (C R Bard, Inc., Covington, GA, USA) and preserved separately in 10% formalin bottles.

The patient is observed for any active rectal bleed and if present lignocaine jelly soaked gauze piece is placed in the rectum, and digital compression applied for few minutes.

The biopsy procedure ended when patients got up from the operating table and relevant data were recorded.

Outcome variables

Primary outcome measures :

- Blood culture one hour after the procedure.
- Urine culture 2 to 5 days after the procedure.
- Leucocyturia 2 to 5 days after the procedures.
- Any febrile episode within 48 hours.
- Any hospital admission for sepsis.
- Any dysuria experienced by the patient after 24 hours and its duration.

Secondary outcome measures:

Patient's perception of pain during the procedure as recorded on a visual analogue scale of one (no pain) to ten (extreme pain). Urologists comfort on a analogue scale of one (no difficulty) to ten (extreme difficulty).

Time is taken for the procedure.

Variable wise statistical tests used for data analysis -

Continuous variables are analyzed as a mean and standard deviation for normally distributed data and as median and IQR for other data. Categorical variables are represented as frequency and proportions. The appropriate test of significance are performed (categorical variables Chi-square test or Fishers Test and for quantitative variables t- test are applied). The Univariate and Bivariate analysis is done to find out the statistically significant value. To control the confounding variables, multivariate analysis will be done for variables identified as significant in univariate analysis.

RESULTS:

126 patients were enrolled during the study period , out of which 3 did not met the inclusion criteria, 1 declined to participate and two patients were left out due to other reasons.

The remaining 120 patients were randomized in two groups namely Transperineal (TP) and Transrectal (TR) group.

Three patients in Transperineal and six patients in Transrectal group cannot be included in final results as they did not follow up further.

Following is a CONSORT (Consolidated Standards of Reporting Trials) diagram for the study.

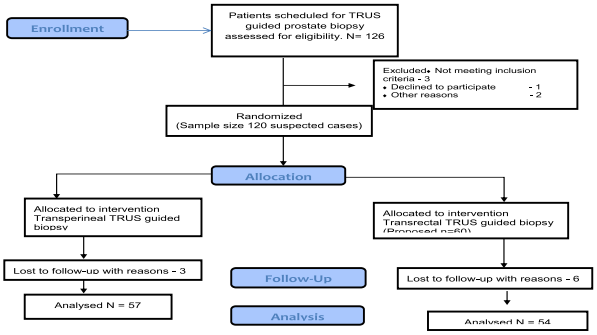

Table 1. Participants in both groups are comparable in base line characteristics.

S. NO.		TRANSPERINEAL GROUP	TRANSRECTAL GROUP
1.	Participants	57	54
2.	Mean Age	66	65
3.	Mean BMI	29.6	29.2
4.	Average Gleason score	8	8
5.	Co morbidities	23	22
6.	Hypo echoic nodule (TRUS)	17	16

Fig 2. Post op urine culture is not influenced by presence of comorbidities.

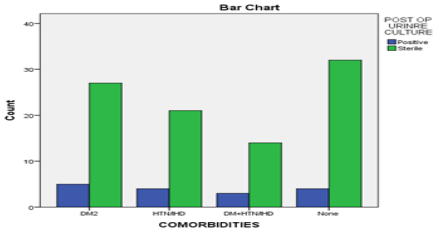

Table 5 TPPB is more painful; Urologist comfort was same for both technique

CHARACTERSTIC FEATURE	BIOPSY TECHNIQUE			
	Transperineal		Transrectal	
	N	Median	N	Median
PTS'.PAIN PERCEPTION(VAS)	57	4.00	54	3.00
UROLOGIST COMFORT	57	2.00	54	2.00

Table7. Comparative tabulation between TPPB and TRPB

Parameter	Category	BIOPSY TECHNIQUE				Result
		Transperineal		Transrectal		
		Count	Column N %	Count	Column N %	
Most painful step	Anaesthesia	38	67.9%	13	24.1%	p<0.05
	Sampling	7	12.5%	9	16.7%	p>0.05
	Probe insertion	9	16.1%	16	29.6%	p<0.05
	None	1	1.8%	14	25.9%	p<0.05
	Others	1	1.8%	2	3.7%	p>0.05
PREOP URINE CULTURE	Present	5	7.1%	3	5.6%	p>0.05
	Sterile	52	92.9%	51	94.4%	p>0.05
PREOP URINE R/M	Bacteria Present	7	10.7%	7	13.0%	p>0.05
	NAD	50	89.3%	47	87.0%	p>0.05
PRESENCE OF ANY HYPOECHOIC NODULE	Present	15	26.8%	20	37.0%	p>0.05
	Absent	42	73.2%	34	63.0%	p>0.05
BLOOD CULTURE (1 HR POST OP)	Sterile	57	100.0%	54	100.0%	p>0.05
	Growth Present	0	0.0%	0	0.0%	p>0.05

POST OP URINRE CULTURE	Positive	3	6.1%	13	24.1%	p<0.05
	Sterile	54	93.9%	41	75.9%	p<0.05
POST OPLEUCOCYTOURIA	Present	8	13.6%	28	51.9%	p<0.05
	Absent	49	86.5%	26	48.1%	p<0.05
FEBRILE EPISODE WITHIN 48 HOURS	Present	1	01.7%	10	18.5%	p>0.05
	Absent	56	98.3%	44	81.5%	p>0.05
HOSPITAL ADMISSION FOR SEPSIS	1	1	01.7%	4	7.4%	p>0.05
	2	56	98.3%	50	92.6%	p>0.05
DYSURIA >24 HOURS	Present	7	13.0%	12	21.2%	p>0.05
	Absent	50	87.7%	42	78.8%	p>0.05
HEMATURIA >24 HOURS	Present	15	27.3%	27	50.0%	p<0.05
	Absent	42	72.2%	27	50.0%	p<0.05
RECTAL BLEED >48 HOURS	Present	1	1.5%	11	20.4%	p<0.05
	Absent	56	98.5%	43	79.6%	p<0.05
BIOPSY REPORT	Adeno carcinoma	23	40.9%	25	46.3%	p>0.05
	Benign pathology	34	59.1%	29	53.7%	p>0.05

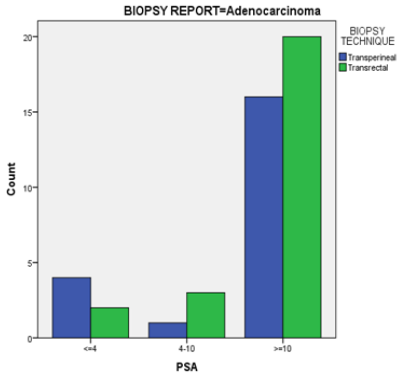

Fig 5. Higher PSA values are associated with increased probability of cancer detection by either technique.

In our study presence of dysuria was seen in 13.0 % in TPPB patients and 21.2% in TRPB patients. Blood culture (taken within one hour of the procedure) was sterile in all the patients in both the arms i.e. TPPB and TRPB.

DISCUSSION:

Our study showed that febrile episodes within 48 hours were seen in 18.5% patients of TRPB arm as compared to 1.7% in TPPB arm. These findings are similar to the findings in other studies.

A study was done by Rosario et al..under the "The ProtecT "[5]study to prospectively look into the short term outcomes of prostate biopsy in about 1200 men detected to have cancer-based on PSA within 35 days of TRPB had shown that post-TRPB 18% had febrile episodes. About 1200 patients underwent TRPB in this study.

The prospective study by Le Hang[6] employing about 340 patients and assessing the overall suitable technique between the two options had shown that about 9% of patients in TRPB arm experience fever whereas it is about 2% in TPPB.

Blood culture (taken within one hour of the procedure) was sterile in all the patients in both the arms i.e. TRPB and TPPB. This indicates that potentially serious bacteraemia is uncommon in either of the biopsy techniques when covered with appropriate periprocedural antibiotics..
Kelly[7] in 2010 studied bacteraemia and bacteriuria after TRPB in about 50 patients in a prospective study and found that bacteraemia was present in 16% of the patients. It has been found overtime that incidence of bacteriuria has been decreasing in different studies.

It was noticed by him that after TPPB, bacteraemia was present in 40% cases and dysuria was present in 27% patients. However, it was found that bacteraemia was not clinically significant and organisms belonged to skin commensals.

Our study showed that post op urine positive urine culture was seen in 24.1% cases in TRPB arm as opposed to 6.1% in TPPB arm. 51.9% patients in TRPB arm had postop leucocyturia as compared to 13.6% in TPPB arm.

We hypothesize that one contributing factor could be the greater chance of urethral penetration in TRPB (as indicated by the lower incidence of dysuria and hematuria as discussed below) may result in a greater risk of febrile complication when associated with bacteriuria.

Given the above finding we feel that if urine microscopic examination is negative for Leucocyturia in a patient with post prostate biopsy dysuria, bacteriuria(UTI) is unlikely.

In our study , hospital admission for sepsis (defined as body temperature >38^0 C or less than 36^0 C, heart rate more than 90/minute, respiratory rate >20/min , WBC <4x109/L (<4000/mm^3), >12x109/L (>12,000/mm^3), or 10% bands) was seen in 1.7% of patients in TPPB as opposed to 7.4% patients in TRPB arm..

ProtecT [5] study had shown that post biopsy sepsis as a major concern given the rise in quinolone - resistant strains of E.coli and hospital admission rate was nearly 1.3%.

Miller et al.[8] in his retrospective study analysed 197 records of patients who underwent either TRPB or TPPB during 1996-2000 in Australia and concluded that TPPB is associated with complications like sepsis and hospital admission ,which may be required in about 1.2% cases and is statistically insignificant when compared with TRPB.

A retrospective study of 634 cases published by Lona Vyas et.al.[9] attributed negligible incidences (<1%) of urosepsis in TPPB biopsies. This study was aimed to study the indications, results and safety profile of patients undergoing TPPB. Post biopsy rectal bleed was lasting more than 48 hours, was present in 20.4% in TRPB arm and 1.5% in TPPB arm. This result was clinically significant.

The rectal bleed in TPPB is perhaps due to inadvertent penetration of the biopsy needle into the rectum in some cases. The frequency of this complication is similar to other published studies.
El Udeh[10] prospectively studied 100 patients about overall complication and cancer detection rates in an African country and found that about 27.9% presented with rectal bleed after TRPB. However, this figure was 10.2 % for TPPB.

Rosario et al.[5] had shown in his study that post-biopsy rectal bleed was seen in about 36.8% patients.

In our study hematuria was seen in 50% patients of TRPB arm and 27.3% patients of TPPB arm and difference was found to be significant. Post biopsy hematuria was not found to cause any hemodynamic instability; however, patients and relatives need to be counselled regarding this aspect.

The reason for a greater proportion of TRPB patients having hematuria is not readily apparent.We hypothesise that urethral penetration may be more likely as the direction of the biopsy needle is perpendicular to the urethra in TRPB whereas in TPPB the direction of biopsy needle penetrating the prostate is roughly parallel to the urethral axis.

Efesoy O[11] who prospectively studied complications in 12 core prostate biopsy in 2049 patients concluded that post TRPB, hematuria is seen in 66.7% of participants.

Miller et al.[8] had shown post-biopsy hematuria might be seen in up to 84% of patients in TRPB.

In our study cancer detection rate was similar in both techniques 46.3 % with TRPB patients and 40.9% of TPPB arm patients. Thereby indicating that the two techniques are equivalent in cancer detection.

Hara R et al..[12], in his prospective study employing 246 patients between 2003-05 had found no difference with regards to cancer detection rates and complications between the two techniques.

A meta-analysis by Shen [13] in 2012employing various databases and analysing seven RCT covering about 980 patients, also did not found any difference in complications and cancer detection rates between the two techniques and stressed TPPB as a safe option.

Our study showed that TPPB is associated with greater discomfort to the patient. (Median VAS – 4) as compared to TRPB technique (Median VAS -3), but this difference was not significant.

The most painful step in TRPB technique is the step of TRUS probe insertion whereas in TPPB it is the step of the prostatic block.

A study by Le-Hang Guo [14] had similar findings, and median VAS in their study in TPPB arm was 4 and that for TRPB arm it was 2.

EI Udeh, 2014[10] showed mean VAS >5 for transrectal biopsy in his study.

Similarly, Damiano et al.[15] in their Questionnaire based evaluation of prostate biopsy complication comparing different biopsy schemes evaluated 177 patients and had shown mean VAS of > 5 for TRPB patients.

Urologist's comfort was same for the two biopsy techniques.

Although TRBP group had a lower mean level of procedure-related discomfort as compared to TPPB in our study, the lack of statistical significance of this finding in our study as compared to the abovementioned studies could be because of a smaller sample size is taken for detecting infective complications rather than discomfort.
In our study, no patient reported post-biopsy hematospermia in either arms. Our cohort of patients was mostly belonged to the elderly group and was less sexually active and may be the contributory reason for the above finding. A study by El Udeh[10] also had nil incidence of post-biopsy hematospermia.

In our study patients with higher PSA values had higher cancer detection proportion irrespective of the technique used and higher values (>10) were associated with higher Gleason scores.

Zivkovic S[16] studied the relationship between PSA values and histopathologic differentiation of prostate carcinoma in about 40 patients and concluded that higher the PSA value more is the probability of cancer detection.

Mean operative time for that of TRPB technique is 21 minutes and TPPB TRUS biopsy procedure was 27 min. This greater time required for TPPB is also observed in the study by Le Hang [14].

In Le Hang study time for TRPB procedure it was 14 minutes, and for TPPB procedure it was 17 min.

Our prospective randomised study is one of the very few studies investigating the infective complications of two prevalent techniques of prostatic biopsy in suspected patients with prostate carcinoma. One of the strengths of this study is that procedures were performed by different surgeons which simulates the real life urology practice.

Despite this, the differences observed in infective complications are significantly higher in TRPB.

One of the limitations of the study was that it was not blinded.

While blinding of the urologist would not have been possible an attempt to blind the patient could have been done.

The other limitation was that there were some dropouts in both arms but more in the TRPB arm.

However, we feel that the overall dropout rate was small and it is unlikely that this would have biased our results.

In summary this study strongly indicates that transrectal TRUS-guided prostate biopsy is associated with greater risk of infective complications, sepsis and hospital admissions without compromising cancer detection.

While multi-centric studies and meta-analyses of RCTs may be required to obtain stronger evidence, until the issue is settled transperineal TRUS-guided prostate biopsy for the diagnosis of prostate cancer must be recommended in the interest of patient safety. The patient must, however, be counselled about the greater discomfort during the procedure.

We can conclude that TPPB TRUS-guided biopsy for suspected patients of carcinoma prostate is associated with better patient safety profile about infective complications and morbidity.

There is no difference about cancer detection rates, and the presence of comorbidities does not increase the risk of complications.

Our prospective randomised study is one of the very few studies investigating the infective complications of two practised techniques of prostatic biopsy in suspected patients with prostate carcinoma.

One of the strengths of this study is that procedures were performed by different surgeons which simulate the real life urology practice. Despite this, the differences observed in infective complications are significantly higher in TRPB.

One of the limitations of the study was that it was not blinded. While blinding of the urologist would not have been possible an attempt to blind the patient could have been done to make the study more powerful statistically.

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