

Digital Rectal Examination as a Test for Screening for Prostate Cancer: A Systematic Review

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Received: October 12, 2020; **Published:** December 30, 2020

DOI: 10.31080/ecmi.2021.16.01008

Abstract

Objectives: Prostatic carcinoma is considered the second most common cancer in males after lung carcinoma. Early screening and detection become essential for a better prognosis. Many screening tests are used for prostatic carcinoma; however, digital rectal examination is considered the easiest and the least expensive test. That's why we assess the usefulness of digital rectal examination in primary care settings.

Methods: Four databases were searched using specific search terms. We included assess the risk of failure of root canal therapy in diabetic patients and the prevalence of root canal therapy failure, and different outcomes reported in diabetic patients. The studies were assessed for the quality of evidence using the NIH quality assessment tool before being included for the review.

Results: Fifteen studies fulfilled our inclusion criteria and had passed the quality assessment to be included for the qualitative evidence synthesis. Based on these studies, digital rectal examination had good predictive value in older black males, and when it is combined with prostatic specific antigen. However, there is still a debate about the level of prostatic specific antigen that should be combined with digital rectal examination.

Conclusion: Digital rectal examination is still considered one of the most important screening tests for prostatic carcinoma. However, its results should be interpreted cautiously and should be combined with other screening tests.

Keywords: Digital Rectal Examination; Prostatic Carcinoma; Prostatic Specific Antigen; Screening; Primary Care

Introduction

Screening for cancer has become a necessity in recent days particularly those tumors that have a high incidence in population [1]. Prostate cancer is one of these tumors that have a high prevalence in the world ranking as the second most common tumor in men after

lung cancer [2]. It is estimated to affect over one million and a half patients worldwide, every year. The mortality rate in prostate cancer is estimated to be 3.8% among all cancer mortality in men indicating the necessity of early detection and treatment [2].

During the early stages of prostate cancer, the patients are either asymptomatic or present with minimal symptoms like difficulty during micturition, increased frequency, and nocturia. Usually, these symptoms may be incorrectly diagnosed [3]. That is why screening of prostatic cancer is mandatory for early diagnosis and treatment. The screening tests are usually performed in the absence of any symptoms or indications for the disease [4]. The most common screening tests for prostatic carcinoma are either digital rectal examination, prostatic specific antigen, and trans-rectal ultrasound-guided biopsy [4]. These tests were assessed in many studies to identify the most convenient test and whether it would decrease mortality from prostatic cancer. Moreover, it will decrease metastatic symptomatic cases. On the other hand, studies found that screening for prostate cancer would only benefit about five percent of the diagnosed cases. Also, false-positive rates are high for these tests exposing many patients to the danger of chemotherapy or radiation [4-6].

For digital rectal examination, it is used routinely with prostatic specific antigens to early detect cancer. However, many studies did not find any significant improvement in the survival rate of the patients. On the contrary, it had resulted in many false positive resulting in the use of invasive maneuvers that will increase risks of erectile dysfunction, urinary incontinence, and pain apart from exposure to non-necessary treatment options [2,5-7].

This ignited confusion to the treating physicians; some recommended using both digital rectal examination and prostatic specific antigens for males over 50 years old, others recommended not using them for males aging 55 or less without a history of prostatic cancer [4,7].

This was supported by the low sensitivity and positive predictive value of the digital rectal examination estimated to be 53.2% and 17.8% in asymptomatic men aged 39 to 92 years old. Nevertheless, it had 83.6% specificity for the diagnosis of prostate carcinoma [6].

This study was set out with the aim to understand the pros and cons of the digital rectal examination in primary care settings for prostatic cancer screening.

Methods

Database search

A comprehensive search approach was applied to four databases PubMed, Google Scholar, SCOPUS, and ISI web of science. The keywords used were ("Prostate") AND ("adenoma" OR "adenocarcinoma" OR "tumor" OR "tumour" OR "neoplasm" OR "cancer" OR "carcinoma" OR nodule) AND ("digital rectal examination" OR "digital rectal examination" OR "rectal" OR "rectum") AND ("biopsy" OR "needle" OR "image-guided biopsy"). We restricted our search to human studies.

Inclusion and exclusion criteria for screening

Specific inclusion criteria were used to identify high quality and studies that fulfill the goals of this study. Inclusion criteria are studies that assessed the use of digital rectal examination in primary health care and assessed the accuracy of the techniques. The abnormal digital rectal examination was not defined in this review. We depended on the definition in each study. Books, review articles, letters to the editor, editorial reports, case reports, and conference abstracts and duplicates were excluded.

Screening for studies

The retrieved studies from each database were screened based on inclusion and exclusion criteria. First, Title/abstract screening was conducted by three independent reviewers. The included studies were then screened thoroughly to make sure it fulfills the target of this

review. Each study was reviewed thoroughly to extract and build a qualitative review.

Quality assessment of the included papers

The quality of the included studies was evaluated by three reviewers using the QUADAS-2 tool. The tool is used to assess the accuracy of diagnostic tests by assessing two main aspects: risk of bias and applicability concerns using four domains in the first and three domains in the second aspect [8].

Results and Discussion

Search results

The four databases yield 821 studies that fulfilled the inclusion criteria. The flow of the search and screening process is illustrated in figure 1.

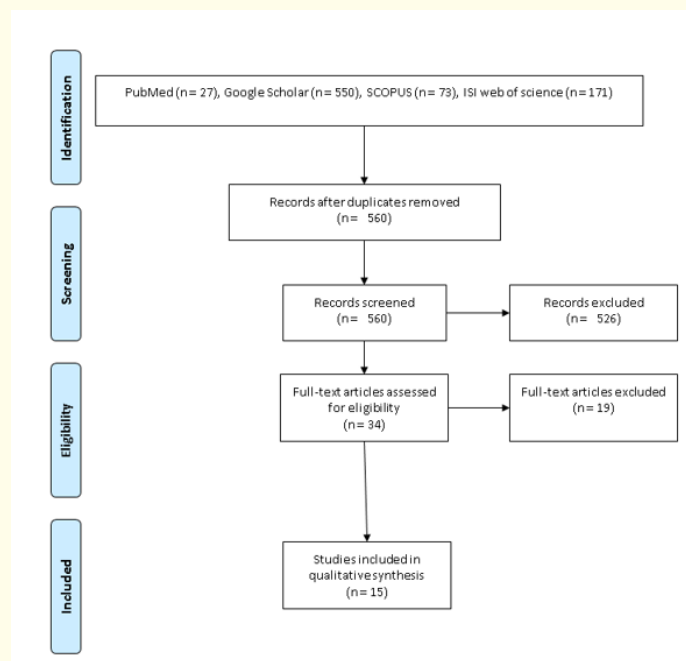


Figure 1: PRISMA flowchart summarizing the search process in this study.

Quality assessment

Most studies had good quality except for three studies in table 1. Most studies used biopsy as the reference test. Flow and timing domains were not fulfilled by most studies in figure 2.

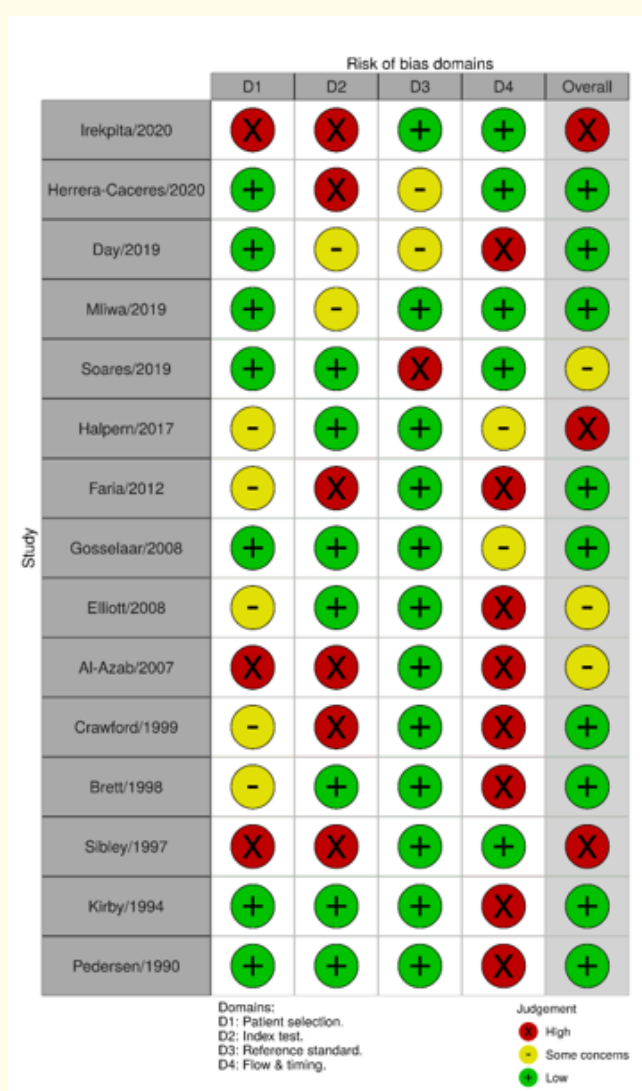


Figure 2: QUADAS-2 results for each included study.

Study	Country	Design	Age (mean)	Patients screened (N)	Patients undergone biopsy (N)	Specificity	Sensitivity	Positive predictive value
Irekpita/2020 [14]	Nigeria	Prospective, cross-sectional, hospital-based, two-center study	Range (41 to over 80)	131	131	NA	NA	Adenocarcinoma (73.3%) Nodule (23.1%) Nodular hyperplasia (66.5%)
Herrera-Caceres/2020 [21]	Canada	Prospective study	65	3481	3481	90% (physician) 82% (before the biopsy)	19% (physician) 34% (before the biopsy)	44% (physician) 45% (before the biopsy)
Day/2019 [15]	United Kingdom	Retrospective study	NA	307	307	NA	NA	NA
Mliwa/2019 [19]	Tanzania	Cross-sectional study	70.72	373	NA	82.3%	76.8%	82%
Soares/2019 [18]	Brazil	Cross-sectional study	Range (40-80)	13,625	NA	NA	NA	NA

Halpern/2017 [20]	United States	Retrospective cohort	Median age 62	35,350	1713	NA	NA	NA
Faria/2012 (Faria et al.)	Brazil	Prospective cohort	61.2	17 571	1647	NA	NA	Normal PSA (23.5%) Abnormal PSA (70.9%)
Gosellaar/2008 [17]	Netherlands	RCT	55-75	28349	5040	NA	NA	48.6 in the first screening round 21.1% in the second and third screening round.
Elliott/2008 [12]	United States	Cross-sectional	60 -75	1564	1564	NA	NA	NA
Al-Azab/2007 (Al-Azab., et al.)	Canada	Cross-sectional study	63.2	1796	1796	NA	NA	NA
Crawford/1999 [22]	United States	Cross-sectional	40 - 79	116,073	4160	Abnormal PSA and normal DRE (63.1%) Normal PSA and abnormal DRE (49%) Abnormal PSA and abnormal DRE (87.9%)	Abnormal PSA and normal DRE (34.9%) Normal PSA and abnormal DRE (27.1%) Abnormal PSA and abnormal DRE (38%)	Abnormal PSA and normal DRE (277%) Normal PSA and abnormal DRE (17.7%) Abnormal PSA and abnormal DRE (56%)
Brett/1998 [9]	Australia	Prospective population-based study	50-79	211	11	NA	NA	NA
Sibley/1997 [16]	United States	Cross-sectional	73	50	50	NA	NA	60%
Kirby/1994 [13]	United Kingdom	Prospective cohort study	55 to 70	568	29	NA	NA	NA
Pedersen/1990 [11]	Sweden	Prospective study	50 - 69	1494	44	NA	NA	27% for general practitioners 30% for urologists

Table 1: Patient characteristics of the included studies.

Patient characteristics

Fifteen studies assessed the accuracy of the digital rectal examination either retrospectively or prospectively. The age of patients ranged from 41 to 80 years old. Other characteristics including sensitivity, specificity, and positive predictive value are reported in table 2.

Study	Risk of Bias				Applicability concerns		
	Patient selection	Index test	Reference standard	Flow and timings	Patient selection	Index test	Reference standard
Irekpita/2020 [14]	High	High	Low	Low	High	High	Low
Herrera-Caceres/2020 [21]	Low	High	Unclear	Low	Low	High	Unclear
Day/2019 [15]	Low	Unclear	Unclear	High	Low	Unclear	Unclear
Mliwa/2019 [19]	Low	Unclear	Low	Low	Low	Unclear	Low
Soares/2019 [18]	Low	Low	High	Low	Unclear	Unclear	Low
Halpern/2017 [10]	Unclear	Low	Low	Unclear	High	Low	Low
Faria/2012 [20]	Unclear	High	Low	High	Low	Unclear	Low
Gosselaar/2008 [17]	Low	Low	Low	Unclear	Low	Low	Low
Elliott/2008 [12]	Unclear	Low	Low	High	Unclear	Unclear	Low
Al-Azab/2007 (Al-Azab, <i>et al.</i>)	High	High	Low	High	Unclear	Unclear	Low
Crawford/1999 [22]	Unclear	High	Low	High	Low	Unclear	Low
Brett/1998 [9]	Unclear	Low	Low	High	Low	Low	Low
Sibley/1997 [16]	High	High	Low	Low	High	High	Low
Kirby/1994 [13]	Low	Low	Low	High	Low	Low	Low
Pedersen/1990 [11]	Low	Low	Low	High	Low	Low	Low

Table 2: Quality assessment results of the included studies.

Digital rectal examination as a screening for prostatic carcinoma

All studies used digital rectal examination as an initial screening test for the detection of any abnormal prostatic lesions. Some studies combined it with other tests like prostatic specific antigen, transrectal ultrasound, and biopsy. Based on these studies, the digital rectal examination had more accurate results when it was combined with other screening tests.

The definition of the abnormal digital rectal examination was not the same all over the included study. For instance, two studies determined abnormal digital rectal examination as the presence of nodularity, induration, asymmetry, and absence of median sulcus. They considered enlarged prostate with normal consistency as normal digital rectal examination [9,10]. Pederson, *et al.* defined abnormal digital rectal examination as nodular firm consistency [11]. Other studies considered induration or a palpable nodule is abnormal finding [12,13]. Irekpita, *et al.* found the most commonly reported finding was hard nodular prostate, while the least found feeling was lobar asymmetry [14].

The digital rectal examination had different predictive values based on the country of studied patients in table 1. Halpern, *et al.* found that the abnormal Digital rectal examination had successfully predicted the 10-years incidence. incidence of prostatic carcinoma. Also, it was more accurate when it is combined with prostatic specific antigen [10].

Day, *et al.* reported that digital rectal examination enhanced the discovery of prostatic carcinoma. It avoided delays in the discovery of asymptomatic cases. However, they suggested that in the normal digital rectal examination, an MRI scan of the prostate enhanced the discovery of occult carcinoma compensating for the false results. They recommended adding an MRI scan to digital rectal examination to increase the accuracy and avoid unnecessary biopsy [15].

Besides, Pederson, *et al.* suggested that digital rectal examination is the least expensive method for cancer screening patients. They found that it relieved the costs of screening in old men. They also found that other screening methods would take valuable working or leisure time from the patients [11].

In addition to the previous results, Herrera-Caceres suggested that Digital rectal examination can be used for active surveillance of prostatic carcinoma and follow-up. It showed high accuracy in patients with prostatic carcinoma.

Digital rectal examination had benefits in cases with negative transrectal ultrasound, Sibley, *et al.* revealed that in 14% of cases, Transrectal ultrasound could not detect evidence of prostatic carcinoma while digital rectal examination was positive. That means that digital rectal examination could detect cases that a Transrectal ultrasound would not detect [16].

Factors affecting digital rectal examination results

Not all studies assessed factors associated with the accuracy of digital rectal examination. Age, race, type of the mass, the examining physicians were among many factors that affected the accuracy and predictive power of the digital rectal examination. Elliot, *et al.* found that race affected the results of digital rectal examination as the black had significantly more abnormal findings than other races and it had better sensitivity and specificity than other races [12].

Two studies have found that the accuracy of the digital rectal examination increased with more aggressive and higher stages of prostatic carcinoma. It had higher positive predictive values in the latter stage [13,17]. Gosselaar, *et al.* suggested that abnormal Digital rectal examination had the ability to detect prostatic carcinoma with Gleason score > 7 when it is combined with prostatic specific antigen > 3 ng/ml [17]. Confirming the results of the previous studies, Irekpita, *et al.* found that the positive predictive value of abnormal digital rectal examination increased from 33.5% in nodular hyperplasia to 57.7% in adenocarcinoma [14]. The results of digital rectal examination influenced positive predictive value. For instance, if the physician sensed suspicious nodule and obliterated median groove, PPV will be 23.1%. However, if the physicians sensed lobar asymmetry, the positive predicted value will be 0%. Also, the results correlated with the prostate size. Also, they suggested that the suspicious Digital rectal examination was more common and more accurate in older age specifically in the eighties.

Soares, *et al.* assessed the factors associated with digital rectal examination incidence in primary health care in Brazil. They found that the private health sector cared more and screened for prostatic carcinoma than the public health sector. Men aged 60 - 69, living with a spouse, never smokers, and living in urban areas had more screening visits in the private health sector. In contrast, public health sector, men aged 70 - 79, living with a spouse, abstainers, ex-smokers, with four or more comorbidities, and from urban areas had the highest screening visits [18].

Pederson, *et al.* found that digital rectal examination done by the urologists had more accurate and high predictive power than digital rectal examination done by general practitioners [11].

Relationship to the prostatic specific antigen

All studies found that there was a significant increase in the accuracy of the screening when it is combined with prostatic specific antigen. However, it hardly reached above 50% in most studies. Notwithstanding, a study in Tanzania found that combining the digital

rectal examination with prostatic specific antigen would increase the accuracy up to 85% [19]. The specificity, sensitivity, and positive predictive value increased when prostatic specific antigen was combined with Digital rectal examination [19]. Irekpita., *et al.* found that the results of digital rectal examination significantly correlated with the prostatic specific antigen level. They also proved that the digital rectal examination alone is not able to predict the carcinoma alone and it should be combined with prostatic specific antigen [14]. Elliot., *et al.* found that Digital rectal examination in Asian/pacific islander had more accuracy when combined with prostatic specific antigen than other races [12].

Another study found that a combination of abnormal Digital rectal examination with prostatic specific antigen more than 4.0 ng/ml achieved the best accuracy [20]. Furthermore, prostatic specific antigen was combined with normal digital rectal examination to detect false-negative results and achieving the best detection rate. They estimated the prostatic specific antigen level to be 2.5 - 4.0 ng/mL has the best accuracy [20]. Halpern., *et al.* found that there was a significant increase in the relative risk of prostatic carcinoma in a patient with abnormal Digital rectal examination and high prostatic specific antigen compared to those with abnormal Digital rectal examination and low prostatic specific antigen. The 10-year incidence rate of prostatic carcinoma was highest when abnormal Digital rectal examination was combined with a prostatic specific antigen level above 3 ng/ml. They also found that abnormal Digital rectal examination had limited benefit when it is combined with prostatic specific antigen less than 2 ng/ml [10]. Moreover, the active surveillance showed the most accurate results were obtained when Digital rectal examination was combined with prostatic specific antigen < 2ng/ml [21]. Kirby., *et al.* found that elevating the cut-off of prostatic specific antigen to 6-10ng/ml decreased the false-positive results of the abnormal digital rectal examination protecting the patients from unnecessary invasive maneuvers like biopsy [13].

Crawford., *et al.* found that the combined accuracy of the abnormal digital rectal examination and abnormal prostatic specific antigen differed based on age. The positive predictive value was the highest in patients aged 50 - 59 years. The sensitivity was the highest in males aged 70 - 79 years. The specificity was highest in men aged 40 - 49 years old [22].

The reaction of patients to digital rectal examination

Only three studies assessed the reaction of patients towards maneuver [9,11,13]. Pederson., *et al.* reported that older men were significantly more comfortable than younger patients who showed anxiety. Besides, the anxiety increased when the digital rectal examination was associated with abnormal results irrespective of the age of the patients [11].

On the other hand, Bret., *et al.* also reported that the patients did not find the test disturbing [9]. Kirby., *et al.* supported the findings of Bret., *et al.* as 95% of participants expressed comfort and readiness to do the test again [13].

Conclusion

Based on these studies, the digital rectal examination had a good predictive value for screening for prostatic carcinoma when combined with the prostatic specific antigen. The digital rectal examination had the best results in older age and black males. To be used in primary care, it should be combined with other screening tests as general practitioners lack the experience to identify abnormal digital rectal examination.

Recommendation for Future Work

The technique of digital rectal examination should be standardized across the world. More studies are needed to assess factors affecting the accuracy of the digital rectal examination.

Conflict of Interest

None.

Funding

None.

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Volume 17 Issue 1 January 2021

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