The diagnostic value of digital rectal examination in primary care screening for prostate cancer: a meta-analysis

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Objective. This systematic review examines the diagnostic value of the digital rectal examination (DRE) for the diagnosis of prostate cancer.

Method. Only studies relating to unselected populations and using either biopsy or surgery as the reference standard were included. The methodological quality of the studies was used in an attempt to explain differences between studies.

Results. Fourteen studies were eligible for selection, of which five complied with the predetermined list of 'good-quality' requirements. Between study heterogeneity was high, even within the group of high-quality studies, and could not be explained by the registered indicators of methodological quality.

Conclusions. In this setting, the DRE appears to be a test with a high specificity and negative predictive value, but a low sensitivity and positive predictive value. Neither a positive nor a negative test result is sufficient to enable conclusions without further confirmation.

Keywords. Predictive value of tests, primary health care, prostate neoplasms, sensitivity and specificity.

Introduction

The usefulness of screening for prostate cancer is still under discussion. Crucial to early detection is the availability of valid screening tests. The oldest and least invasive test is digital rectal examination (DRE). Studies aimed specifically at determining the value of DRE for the detection of prostate cancer are rare. However, the development of new diagnostic tests has enabled the conduction of numerous studies in which DRE is compared with other tests.

We performed a systematic review of the literature in order to summarize the data on the value of DRE for screening purposes in primary care. Recently, methods for evaluating diagnostic tests by meta-analysis have been developed. Meta-analysis can be used not only to summarize overall diagnostic accuracy of different tests, but also to determine whether diagnostic accuracy differs among patient subgroups or with varying study designs.[1]

Using such techniques, we assessed the accuracy of DRE in primary care and its relation with various methodological characteristics of the studies.

Methods

Searching the literature

To identify studies that provide data on the value of DRE, we performed a MEDLINE search from 1983 to 1995, using MESH terms as well as free text searching. Older studies were not searched because of the technological improvements that have changed the diagnostic capacities in recent years. Additionally, Famli, a specialized database for studies in family practice was searched and some GP journals were searched manually for diagnostic studies. Thereafter, the references of all retrieved studies were checked for relevant citations. No language restrictions were used.

Inclusion criteria
Studies were included if DRE was compared with biopsy or surgery as a reference standard. The study population had to be unselected with respect to prostate-related signs and symptoms. In addition, true positive and true negative rates as well as false negative and false positive rates had to be presented or it had to be possible to calculate them from the published data. For this reason, in some studies only part of the total study population could be used, yielding results different from those reported in the original papers.

Assessment of methodological quality
Methodological aspects of all studies were assessed using a list of criteria proposed by the Cochrane Methods Working Group on Meta-analysis of Diagnostic and Screening Tests. This list is based on the recent literature[2–4] and regarded as the most recent consensus on criteria for systematic reviews on diagnostic studies. It includes criteria with respect to internal validity, applicability of the results and description of test procedures, as well as indirect measures to estimate study quality. The complete list is presented in the appendix.

Analysis

Sensitivity (sens), specificity (spec), positive predictive value (ppv) and negative predictive value (npv) with their 95% confidence interval (95% CI) were extracted from the papers or calculated on the basis of the published data.

We tested for the possibility of different implicit cut-off points between studies by correlating sensitivity and (1–specificity)[5] and for heterogeneity by using the chi-square test for homogeneity. Statistical pooling was based on a random effects model,[6–8] using FASTPRO version 1.7.[9] Meta-analyses were performed including all studies, and for special subgroups separately. The influence on the diagnostic indicators of setting and methodological characteristics of each individual study was studied using multiple linear regression. Each indicator was used as a dependent variable, while setting (each patient received a personal invitation versus general publicity only), quality of the test procedure description (good if the presence of either induration, asymmetry or nodularity or a combination of these was described), prevalence of prostate cancer in the study population and duration of follow-up were used as independent variables.

Results of high-quality studies were analysed separately. For this group, the following inclusion criteria applied.

- DRE was performed on a complete population (no pre-test selection).

- All patients underwent testing with either prostate-specific antigen (PSA) or transrectal ultrasonography (TRUS) or both.
- All patients with a positive DRE, and in cases with a negative DRE result at least those who scored positive on one other test (PSA or TRUS), were eligible for the reference test.
- The reference test was performed on more than 90% of the people eligible for that test.

Results

Study selection
Forty-nine studies could be identified in which the diagnostic value of DRE was studied. Twenty-one[10–30] of them concerned primary care based screening studies. Two papers reported the results of one study.[22,30] The last one was the most recent;[30] therefore the other[22] was not included. In three studies,[20,24,28] DRE was only performed in cases of an increased PSA. In three additional studies,[15,17,27] only follow-up by a GP was stated as the reference standard, with no presentation of further data about what was done. These six studies were excluded from the analysis. Ultimately, 14 studies fulfilled the inclusion criteria of this meta-analysis, totalling some 22 000 patients.

Characteristics and quality of the studies
Characteristics of the 14 selected studies are presented in Table 1. All were published after 1980. Most patients were over age 50 years. Prevalence rates of detected cancer ranged from 1.2 to 7.3%. The number of patients lost to follow-up was more than 20% in six studies,[16,21,23,26] but very low in the remainder. The percentage of patients eligible for a reference test in which no such test was performed, however, was less than 10% in six studies. The number was not reported in three studies and raised to maximally 39%.[21] Only five studies[10,13,18,19,25] complied with the criteria for a good-quality study, as mentioned previously. In some studies, patients were invited personally by the physician, in others they were attracted by advertisements on television or in local newspapers. None of these studies presented data on the presence of complaints in the screening population.

In most of the studies, it was difficult to determine whether benign prostate hypertrophy was considered a normal or abnormal result.[11,13,14,16,18,19,21,25,26,29,30] To be as consequent as possible we considered every non-enlarged, smooth, symmetrical prostate with a normal consistency as normal. If enough data were presented, we recalculated test results according to this principle. However, some studies reported DRE positive or negative, without defining the criteria that were used.[11,13,14,21,25,26,30]

TABLE 1 *Studies on the diagnostic value of DRE for the diagnosis of prostate cancer: basic characteristics*

Ref	First author (Year of publication)	Setting	Referral filter	Sample size	Preva-lence (%)	% missing reference standard	Age Range	Reference standard used to		Description of test results		Remarks
								Confirm disease	Exclude disease	Considered positive if: (definition)	Considered negative if: (definition)	
10	Kirby, RS (1994)	Primary care screening population	None	568	1.9	2	55–70	Biopsy ⊕ (biopsy performed if DRE ⊕ or PSA ⊕ or TRUS ⊕)	Biopsy ⊖ or (DRE ⊖ and RSA ⊖ and negative results on follow-up)	Benign/enlarged or suspect (nodularity, asymmetry)	Normal	Population invited from several general practice offices, no history of prostatic cancer was required. There are no data on patients which were followed-up
11	Vihko, P (1985)	Primary care screening population	None	771	1.2	?	54–76	Biopsy ⊕ (biopsy performed if DRE ⊕ or TRUS ⊕ or acid phosphatase ⊕ or bonescan ⊕)	Biopsy ⊖ or DRE ⊖ and TRUS ⊖ and acid phosphatase ⊖ and bonescan ⊖) and negative results on yearly follow-up during 3 years	DRE ⊕	DRE ⊕	Population of volunteer veterans of WO II. Probably part of population lost to follow-up not described
12	Chodak, GW (1989)	Primary care screening population	None	2131	1.5	1	45–80	Biopsy ⊕ (biopsy performed if DRE ⊕)	Biopsy ⊖ or DRE ⊖ and negative results on yearly follow up during 5 years	Enlarged/suspect	Benign	Complaints of population not described. Many people lost to follow-up. Many failed to return for follow-up
13	Ciatto, S (1994)	Primary care screening population	None	1425	1.8	0	60–75	Biopsy ⊕ (biopsy performed if DRE ⊕ or TRUS ⊕, when in doubt about biopsy then a return biopsy after 3 months)	Biopsy ⊖ or (TRUS ⊕ and DRE ⊖) and negative results on yearly follow up during 2 years	DRE ⊕	DRE ⊕	
14	Lee, F (1989)	Secondary care screening population	All patients self-referred	784	2.8	?	60–86	Biopsy ⊕ (biopsy performed if DRE ⊕ or TRUS ⊕)	Biopsy ⊖ or (TRUS ⊕ and DRE ⊖)	DRE ⊕	DRE ⊕	50% of population no urological complaints in year prior to study
16	Pode, D (1995)	Primary care screening population	None	1000	3.1	38	50–75	Biopsy ⊕ (biopsy performed if DRE ⊕ or PSA ⊕)	Biopsy ⊖ or (TRUS ⊖ and PSA ⊖)	Suspicious	Normal	Of the 115 patients eligible for biopsy, only 88 agreed to biopsy
18	Dalkin, BL (1993)	Primary care screening population	None	755	3.2	1	50–79	Biopsy ⊕ (biopsy performed if DRE ⊕ or PSA ⊕)	Biopsy ⊖ or (DRE ⊖ and PSA ⊖)	Highly suggestive of malignancy	Normal or subtle abnormalities or asymmetry	Population had no urological complaints
19	Palken, M (1991)	Primary care screening population	None	315	7.3	2	50–86	Biopsy ⊕ (biopsy performed if DRE ⊕ or TRUS ⊕)	Biopsy ⊖ or (DRE ⊖ or TRUS ⊖)	Low suspicion or high suspicion	Benign	Complaints of population not described
21	Teillac, P (1990)	Primary care screening population	None	600	3.0	39	>50	Biopsy ⊕ (biopsy performed if DRE ⊕ or TRUS ⊕ or PSA ⊕)	(DRE ⊖ and PSA ⊖ and TRUS ⊖) if biopsy ⊖ then a yearly follow-up	Suspect	Not suspect	Of the 152 patients eligible for biopsy only 93 agreed to biopsy. Patients in follow-up are not reported
23	Catalona, WJ (1994)	Primary care screening population	None	6630	4.0	30	50–96	Biopsy ⊕ (biopsy performed if DRE ⊕ or PSA ⊕)	Biopsy ⊖ or (DRE ⊖ and PSA ⊖)	Asymmetry or induration or irregularity	Normal	Of the 1965 patients eligible for biopsy only 1369 agreed to biopsy
25	Menor, FA (1990)	Secondary care polyclinical population	?	1512	5.0	0	55–90	Biopsy ⊕ (biopsy performed if DRE ⊕ or TRUS ⊕)	Biopsy ⊖ or (TRUS ⊖ and DRE ⊖)	DRE ⊕	DRE ⊕	
26	Richie, JP (1994)	Primary care screening population	No history of prostatic cancer, acute prostatitis or urinary tract infections	644	3.7	26	50–91	Biopsy ⊕ (biopsy performed if PSA ⊕ or DRE ⊕)	Biopsy ⊖ or (DRE ⊖ and PSA ⊖)	DRE ⊕	DRE ⊕	Of the 221 patients only 163 agreed to biopsy. Patients recruited by advertisement on radio, TV and in newspapers.
29	Gustafsson, O (1992)	Secondary care screening population	None	1782	3.6	?	55–70	Biopsy ⊕ (biopsy performed if DRE ⊕ or TRUS ⊕ or PSA>7 and additional requirements)	Biopsy ⊖ or (DRE ⊖ and PSA ⊖ and TRUS ⊖)	Palpable nodules, induration or asymmetry	Normal	
30	Litrup, PJ (1994)	Primary care population screening	None	2922	5.9	12	55–70	Biopsy ⊕ (biopsy performed if DRE ⊕ or PSA ⊕ or TRUS ⊕)	Biopsy ⊖ or (DRE ⊖ and TRUS ⊖) and yearly follow-up negative	DRE ⊕	DRE ⊕	Of the 943 patients eligible for biopsy only 827 agreed to biopsy

TABLE 2 *The diagnostic value of DRE for the diagnosis of prostate cancer: pooled results*

	All 14 studies[a]	Five good-quality studies[b]
Sens.	0.59 (0.51–0.67)	0.64 (0.47–0.80)
Spec.	0.94 (0.91–0.96)	0.97 (0.95–0.99)
ppv	0.28 (0.20–0.36)	0.47 (0.29–0.64)
npv	0.99 (0.98–0.99)	0.99 (0.98–0.99)

[a]Pooled studies: ref. Nos 10–14, 16, 18, 19, 21, 23, 25, 26, 29, 30.
[b]Pooled studies: ref. Nos 10, 13, 18, 19, 25.

Moreover, no study mentioned the influence of the experience of the examiner or the reproducibility of DRE on the results of the studies.

Many studies failed to report other quality parameters that are on the Cochrane scoring list for diagnostic studies (see Appendix).

The spearman correlation coefficient of sens and 1–spec was 0.12 (and statistically non-significant), indicating absence of a substantial cut-off-point effect.[5] Between-study heterogeneity, however, was highly significant for almost all indicators, even if only high-quality studies were considered.

Linear regression resulted in none of the independent variables showing any significant relation with any of the diagnostic indicators that were studied.

Pooling of the results of the 14 studies, as well as of the results of good-quality studies only, revealed high specificity (0.94) and npv (0.99), low sensitivity (0.59) and very low ppv (0.28) (Table 2).

Five studies satisfied our criteria for a good quality study. When only good-quality studies were included in the meta-analysis, ppv (0.47), sensitivity (0.64) and specificity (0.97) were somewhat higher. However, substantial heterogeneity remained.

Discussion

Diagnostic studies are rather rare, especially in a general practice setting. We therefore were impressed that for this subject 14 studies could be included, most of them published in the 1990s.

Most of them were not designed to investigate the diagnostic value of the DRE, but examined a whole range of methods to diagnose prostate cancer, and only mentioned the results of the DRE to compare its effectiveness with newer techniques. Many studies failed to report a number of quality parameters that were on the Cochrane scoring list. This hampers the judgement of the validity of the results. It seems advisable to standardize the reports of future studies according to these criteria, in the same way as was done for RCTs after the start of the RCT-meta-analysis boom.[31]

Setting
The description of the setting and the procedure of patient recruitment is often poor. Therefore, the judgement of the presence of selection bias and referral filter is difficult. In many screening populations people are not invited personally, but attracted by advertisements on television or in local newspapers. In these cases the population may be biased through self-selection, and may be underrepresenting, but more probably overrepresenting, people with prostate-related complaints. If this were the case, we would not be dealing any more with screening of a symptom-free population and the relative large range of prevalence rates per study would not be very reassuring at this point. As described by Knottnerus,[32] this could influence all diagnostic parameters.

Test description
There are several ways to perform a DRE and to present its results, e.g. the position of the patient is relevant to the accessibility of the prostate gland. Therefore, the characteristics which are scored and the definition of a DRE positive result should be mentioned explicitly.

In most of the studies this was not the case, at least with respect to the classification of benign prostate hypertrophy. Some studies reported DRE positive or negative only, without mentioning the criteria that were used. This was especially so in studies which were directed primarily at the diagnostic value of other tests for detecting prostate cancer.

Reference standard
In some studies,[16,21,23] up to 30% of patients eligible for biopsy were not biopsied, probably due to the invasiveness of the test. Three studies reported that patients with positive DRE results in a screening were sent to their own GP for follow-up.[15,17,27] As no further data on the reference standard were presented, these studies were not included in this meta-analysis.

Applicability of DRE in screening
The DRE appears to be a test with a high specificity and a high negative predictive value. False negative test results are rare; this largely results from the small prevalence of cancer in an unselected population.

The large heterogeneity of the results was a surprising fact. This may be due to the different ways in which the studies were conducted, to differences in the interpretation of DRE or to different methods of inviting a population for screening. Even the five studies considered to be of 'good-quality' showed substantial heterogeneity.

From this study the following two conclusions can be formed.

(i) The evidence from general-practice-based studies for the diagnostic value of DRE for the diagnosis of prostate cancer is based on a large number of low-quality studies and five good-quality studies.

TABLE 3 *The diagnostic value of DRE for the diagnosis of prostate cancer: results of the individual studies*

Ref.	T+Z+	T+Z–	T–Z+	T–Z–	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Likelihood ratio + (95% CI)	Likelihood ratio – (95% CI)	Odds ratio
10	8	6	6	541	57 (53–61)	99 (98–100)	57 (53–61)	99 (98–100)	52 (21–130)	0.43 (0.24–0.79)	120
11	6	21	3	741	67 (63–70)	97 (96–98)	22 (19–25)	100 (99–100)	24 (13–45)	0.34 (0.14–0.86)	70.6
12	32	112	13	1974	71 (69–73)	95 (94–96)	22 (20–24)	99 (99–100)	13 (10–17)	0.31 (0.19–0.48)	43.4
13	17	8	9	1391	65 (63–68)	99 (99–100)	68 (66–70)	99 (99–100)	114 (54–240)	0.35 (0.21–0.59)	328
14	10	19	12	743	45 (42–49)	98 (96–99)	34 (31–38)	98 (98–99)	18 (9.6–34)	0.56 (0.38–0.82)	32.6
16	22	93	9	876	71 (68–74)	90 (89–92)	19 (17–22)	99 (98–100)	7.4 (5.5–9.9)	0.32 (0.19–0.56)	23.0
18	9	33	15	695	38 (34–41)	95 (94–97)	21 (18–24)	98 (97–99)	8.3 (4.5–15)	0.65 (0.48–0.89)	12.6
19	17	28	6	264	74 (69–79)	90 (87–94)	38 (32–43)	98 (96–99)	7.7 (5.0–11)	0.29 (0.14–0.57)	26.7
21	8	18	10	546	44 (40–48)	97 (95–98)	31 (27–35)	98 (97–99)	14 (7.0–28)	0.57 (0.38–0.87)	24.3
23	146	836	118	5530	55 (54–56)	87 (86–88)	15 (14–16)	98 (98–98)	4.2 (3.7–4.7)	0.51 (0.45–0.59)	8.2
25	59	48	16	1389	79 (77–81)	97 (96–98)	55 (53–58)	99 (98–99)	24 (17–32)	0.22 (0.41–0.34)	107
26	16	194	8	426	67 (63–70)	69 (65–72)	8 (6–10)	98 (97–99)	2.1 (1.6–2.9)	0.49 (0.27–0.86)	4.4
29	42	153	23	1564	65 (52–76)	91 (90–92)	22 (16–28)	99 (98–99)	7.3 (5.7–9.2)	0.39 (0.28–0.54)	18.7
30	77	287	95	2471	45 (43–47)	90 (88–91)	21 (20–23)	96 (96–97)	4.3 (3.5–5.3)	0.62 (0.54–0.71)	7.0

T = DRE result.
Z = Gold standard result.

Reporting can be improved, e.g. by systematically refering to the Cochrane criteria list.

(ii) The DRE may have a place as an initial test when screening for prostate cancer. A negative test result of DRE has a high predictive value. The sensitivity being only moderate, however, should prevent the GP from drawing conclusions on the sole basis of such a result. Owing to its very low predictive value, a positive test result cannot be advocated as the basis for any important diagnosis without further confirmation. It therefore is very welcome that in recent studies, the DRE's diagnostic value has been studied in combination with other tests, e.g. ultra-sonography or blood tests.

Appendix: criteria for evaluating the quality of diagnostic studies

Criteria for study validity
1.1 Was the test compared with a valid reference standard?
1.2 Were the test and reference standard measured independently (blind) of each other.
1.3 Was the choice of patients who were assessed by the reference standard independent of the test results?
1.4 Was the test measured independently of all other clinical information?

Criteria relevant to the applicability of the results
2.1 Spectrum of disease (e.g. cancer stage distribution if reference standard positive).

2.2 Spectrum of non-disease.
2.3 Setting.
2.4 Duration of illness before testing.
2.5 Previous tests/referral filter.
2.6 Co-morbid conditions.
2.7 Demographic information.

Test procedures
3.1 Description of how the test was done.
3.2 The explicit threshold used.
3.3 Percentage excluded because test was unfeasible or result was indeterminate.
3.4 Test reproducibility.

Indirect measurements of quality and applicability
4.1 Year of publication.
4.2 Disease prevalence.
4.3 Sample size.
4.4 Prospective or retrospective design.
4.5 Published as a paper or as an abstract.

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