A Study on Correlation of Serum Prostate Specific Antigen with Clinical and Pathological variables in patients of Prostatomegaly
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Abstract
Background: In clinical practice, biopsies are generally performed only when the results of prostate specific antigen (PSA) test or digital rectal examination (DRE) are abnormal. This leads to misdiagnosis of most small prostatic cancers present in many older men. Patients with lower urinary tract infection (LUTS) who have serum PSA levels higher than 4ng/ml are primarily advised to undergo prostate biopsy to rule out cancer. However, PSA is organ specific not disease specific, so the presence of other prostate diseases such as benign prostatic hyperplasia (BPH) and prostatitis may influence its effectiveness for cancer detection. Hence, the PSA based prostate cancer detection is fraught with high false positive rate.

Aim: To evaluate the utility of PSA assay as a method of investigation in diagnosis of prostatic lesion.

Objectives: The use of Serum PSA levels for the early detection of prostate cancer and evaluate its role with other modalities for diagnosis of prostate cancer and to diagnose different diseases of prostate, i.e. prostatitis, BPH in prostatomegaly, and its correlation with Serum PSA levels.

Materials and Methods: This prospective descriptive study was conducted in Index Medical College, Hospital & Research Centre, Indore, M.P, India in the period of August 2019 to July 2021. The patients were selected from the outdoor Department of General Surgery.

Results: A total of 80 male patients presenting with LUTS were included. Their mean age was 68.66 years. The majority i.e. 41 of the study group were in the age group of 61-70 years. 42 of patients had Serum PSA < 4ng/ml. Biopsy proven adenocarcinoma cases 34% of the cases are in the age group of 61-70 years. Out of the biopsy proven adenocarcinoma cases, DRE was suspicious of malignancy in 89%.

Conclusion: Serum PSA levels have a significant correlation with the age group, with the increase in age there is rise in Serum PSA levels. Transabdominal ultrasound, DRE and Serum PSA has high sensitivity in diagnosis of prostatomegaly but it was found that none of the screening tool has got much efficacy in differentiating carcinoma prostate from benign hypertrophy, but the combination of DRE and Serum total PSA or DRE, Serum total PSA and ultrasound abdomen showed higher efficacy in diagnosis of carcinoma prostate. Increase in Serum PSA is directly related to carcinoma, but there is no absolute cut-off for Serum PSA for diagnosis of carcinoma.

Key-Words: Prostate specific antigen, Prostatomegaly, Benign Prostatic Hypertrophy, Digital Rectal Examination, International Prostate Severity Score, Carcinoma Prostate.

Introduction
Prostate enlargement encompasses both benign hyperplasia of prostate (BPH) and carcinoma of prostate. Men with lower urinary tract symptoms (LUTS) are screened for prostate cancer with Serum prostate specific antigen (PSA) testing and digital rectal examination (DRE) as a part of routine prostate assessment. There is a general agreement among clinicians that the PSA test has the highest predictive value for prostate cancer as compared to DRE or trans rectal ultrasound. In clinical practice biopsies are generally performed only when results of a PSA test or DRE are abnormal. This leads to misdiagnosis of most small prostatic cancers present in many older men. The patients with LUTS who have Serum PSA levels higher than 4ng/ml are primarily advised to undergo prostate biopsy to rule out cancer. However, PSA is organ specific not cancer specific, so the presence of other prostate diseases like BPH and prostatitis may influence its effectiveness for cancer detection. Hence, the PSA based prostate cancer detection is fraught with high false positive rate.

Among the malignant tumors, the prostate cancer takes a high place worldwide. The incidence and mortality of disease show a big geographical difference. The increase in incidence started from 1980s. This rapid increase is due to extensive spread of determination of PSA. As a cause of death in men who die of malignancy, the prostate cancer is the third one. In general, the prostate cancer is the disease of the old population. The newly diagnosed patients are over 65 years. Thanks to screening programs, the prostate cancer becomes the disease of middle aged as well. On the contrary with decrease in incidence of prostate cancer in the old ages, there is a continuous rise in the 50–59 years population.
As an early detection of the cause of LUTS is necessary to offer selective treatment to the concerned subjects and also selecting patients for radical prostatectomy in organ confined disease, this study is an attempt to have a comparative analysis among the sensitivity, specificity and positive predictive value of DRE, Serum PSA and ultrasound.

This study may enable us to find out an ideal correlation between Serum PSA levels and various clinical parameters as well as biopsy reports so that a specific treatment can be instituted at an early stage.

Aims and Objectives –

a. The use of Serum PSA levels for the early detection of prostate cancer and evaluate its role with other modalities for diagnosis of prostate cancer.

b. To diagnose different diseases of prostate i.e. prostatitis, BPH in prostatomegaly and its correlation with Serum PSA levels.

Materials and Methods –

Study area – This prospective study was conducted in Dept. of General Surgery, Index Medical College, Hospital and Research Centre, Indore.

Study population – All patients of LUTS with prostatomegaly.

Study period – This study was conducted over 2 years from August 2019 to July 2021

Sample size – A total of 80 patients of BPH with DRE suggestive of grade I prostatomegaly and above were included in the study.

Inclusion Criteria –

i. Men aged >50 years with fresh LUTS specifically attributed to prostate problems

ii. Patients with prostatomegaly grade I and above.

Exclusion Criteria –

a) Men aged <40 years,

b) Patients with features of UTI, calcified or fibrotic prostate, with skeletal or distant metastasis or LUTS caused by any Urological malignancy

c) Patients who had previous prostatic surgery or pelvic radiotherapy or complications of urinary obstruction.

Study design –

Cases of LUTS with prostatomegaly were selected from OPD who were detected to be having Grade I and above prostatomegaly. All patients were evaluated with DRE, ultrasound abdomen, Serum PSA levels and Biopsies of prostate (where indicated) and findings compared and inference drawn.

i. All patients worked up with detailed history, examination with GRE and investigations such as PSA, ultrasonography and prostatic biopsy where indicated.

ii. All patients off Grade 2 and above of prostatomegaly with other nodularity on DRE and or elevated Serum PSA levels underwent prostatic biopsy.

iii. Subsequent review of patients was done in the follow-up visits and findings noted in the Performa.

iv. In this study transabdominal USG size of prostate was evaluated and recorded as: Grade I-<30 g, Grade II- 31-50 g, Grade III- 51-80 g and grade IV- > 80 g.

The findings of systemic DRE performed was noted for all patients as subjective examination according to the following true findings: Hard swelling of the prostate, firm swelling, nodular swelling, irregular surface and obligation of middle sulcus attachment to the mucosa of the rectum. As a routine practice, DRE examination was scheduled after collection of blood sample to avoid an increase in Serum PSA that may follow digital manipulation of the gland.

Blood samples were collected in 5 ml sterile container containing ethylene diaminetetraacetic acid. The samples were centrifuged within 20 minutes after collection at 500x for 10 minutes and sera were stored at - 20 degree Celsius until assay. The total prostate specific antigen was assessed using ELISA. PSA levels <4ng/ml were considered as normal, those between 4 and 10 ng/ml as diagnostic gray zone and >10 ng/ml as indicative of cancer.

All the patients were subjected to ultrasound examination and followed by biopsy if required. Ultrasound was performed using a real time Biplanar 4.0 MHz ultrasound probe.

Biopsies were done under antibiotic cover. Biopsies were taken with true cut biopsy gun from the base, mid gland and apex of the right and left side and also from any suspicious area. Each of the samples was submitted for pathological examination. The post intervention patients were kept for observation for 6 hours and discharged accordingly with the advice to continue antibiotic for 48 hours and to attend OPD or Emergency Room in case any problem such as hematuria, fever, dysuria or hemospermia arises.

Patients were followed-up firstly at three months interval and after 6 months interval.

Data were analyzed using the graphs and Chi-square testing.

Results

A total of 80 male patients with fresh LUTS were included in the study. Their mean age was 68.66 years (range 50-97 years). The patients were selected from the general surgery OPD of Index Hospital & Research Centre, Indore.

Table 1 shows age wise distribution of patients and Table 2 shows age group correlation of Serum PSA. The majority, 41(51.25%) of study group was in the age group of 61-70 years. Out of 80 patients, 42(52.5%) patients had Serum PSA
<4 ng/ml compared to 20(25%) in the range of 4-10 ng/ml, and only 18(22.5%) with Serum PSA >10 ng/ml.

Table 1: Age Distribution

| Age group (years) | No. of Patients | Percentage |
|-------------------|-----------------|------------|
| 50-60             | 15              | 18.75      |
| 61-70             | 41              | 51.25      |
| 71-80             | 14              | 17.50      |
| 81-90             | 09              | 11.25      |
| 91-100            | 01              | 1.25       |

Table 2: Age wise distribution of Serum PSA

| Age group (years) | Serum PSA (ng/ml)<4.0 | Serum PSA (ng/ml) 4.0-10.0 | Serum PSA (ng/ml)>10 |
|-------------------|-----------------------|-----------------------------|----------------------|
| 50-60 (%)         | 12 (15%)              | 8 (10%)                     | 0                    |
| 61-70 (%)         | 25 (31.25%)           | 4 (5%)                      | 6 (8.75%)            |
| 71-80 (%)         | 05 (6.25%)            | 4 (5%)                      | 5 (6.25%)            |
| 81-90 (%)         | 0 (0%)                | 4 (5%)                      | 5 (6.25%)            |
| 91-100 (%)        | 0 (0%)                | 1 (1.25%)                   | 0                    |

Table 3: Age group correlation with biopsies

| Age group (years) | No. of biopsy done | No. of biopsy proven BPH (%) | No. of biopsy proven adenocarcinoma (%) |
|-------------------|--------------------|------------------------------|----------------------------------------|
| 50-60             | 11                 | 11 (33.33%)                  | 0                                      |
| 61-70             | 24                 | 18 (54.55%)                  | 6 (33.33%)                             |
| 71-80             | 09                 | 03 (9.1%)                    | 6 (33.33%)                             |
| 81-90             | 06                 | 01 (3.03%)                   | 5 (27.78%)                             |
| 91-100            | 01                 | 0                            | 1 (5.56%)                              |
| Total             | 51                 | 33                           | 18                                     |

A total of 51 patients underwent biopsy on the basis of either DRE suspicion and/or raised Serum PSA levels, out of which 33(64.7%) had benign disease whereas 18(35.3%) had adenocarcinoma. Among the patients who had biopsy-proven benign diseases 11(33.33%) were in age group 50-60 years, 18(54.55%) in 61-70 years, 3(9.1%) in 71-80 years, 1(3.03%) in 81-90 years and none > 90 years. Compared with biopsy-proven adenocarcinoma group, none in 50-60 years, 6(33.33%) in 61-70 years, 6(33.33%) in 71-80 years, 5(27.78%) in 81-90 years and 1(5.56%) in > 90 years age group.

As shown in table 4, 18 patients had histological proven adenocarcinoma with Serum PSA levels among the patients of proven prostatic malignancy graded as <4 ng/ml, 4-10 ng/ml and >10 ng/ml were 0, 4(22.22%) and 14(77.78%), respectively. The number of biopsy proven benign diseases (BPH as well as prostatitis) patients with Serum PSA levels graded as< 4, 4-10 and > 10ng/ml were 16(48.48%), 13(39.39%) and 4(12.13%).

DRE was suspicious of malignancy in 16(88.89%), whereas DRE was suggestive of benign pathology in only 2(11.11%) patients out of the 20 biopsy-proven adenocarcinoma prostate cases. In 33(64.7%) patients with biopsy suggestive of benign pathology, suspicious DRE was noted in 13(39.39%) cases and 20(60.61%) of the patients had benign feel on DRE.

Table 4: Correlation of biopsy report with Serum PSA and DRE

| Parameters                          | Serum PSA<4.0 | Serum PSA 4.0-10.0 | Serum PSA>10.0 |
|-------------------------------------|---------------|--------------------|----------------|
| Biopsy proven adenocarcinoma (%)    | 0(0)          | 4 (22.22%)         | 15(77.78%)     |
| Biopsy proven Benign (%)            | 16(48.48%)    | 13(39.39%)         | 4(12.13%)      |

Table 5: Correlation of biopsy report with DRE findings

| Parameters                          | DRE +ve | DRE -ve |
|-------------------------------------|---------|---------|
| Biopsy proven adenocarcinoma (%)    | 16(88.89%) | 2(11.11%) |
| Biopsy proven benign (%)            | 13 (39.39%) | 20 (60.61%) |

On USG, 18 patients had Grade-I Prostatomegaly (<30 g) out of which 12 patients had Serum PSA < 4 ng/ml while 6 patients had Serum PSA between 4 and 10 ng/ml. 36 patients had Grade-II Prostatomegaly on USG (31-50g) out of which 20 patients had Serum PSA < 4 ng/ml, 9 patients had Serum PSA between 4ng/ml and 10 ng/ml and 7 patients had Serum PSA > 10 ng/ml. 20 patients had Grade-III Prostatomegaly (51-80 g) out of which 8 patients had Serum PSA < 4 ng/ml.
3 patients had Serum PSA between 4 and 10ng/ml and 9 patients had PSA > 10 ng/ml. 6 patients had Grade-IV Prostatomegaly on USG (>80 g) out of which 2 patients had Serum PSA < 4ng/ml, 2 patients had Serum PSA between 4 and 10 ng/ml and 2 patients had PSA >10ng/ml shown in Table 6.

### Table 6: Correlation of Serum PSA with ultrasound size of prostate

| Serum PSA (ng/ml) | USG Grade I of prostate (<30g) % | USG Grade II of prostate (31-50g) % | USG Grade III of prostate (51-180g) % | USG Grade IV of prostate (>80g) % | Mean |
|------------------|---------------------------------|-----------------------------------|--------------------------------------|-----------------------------------|------|
| <4.0             | 12(15%)                         | 20(25%)                           | 8(10%)                               | 2(2.5%)                           | 46.4 |
| 4.0-10.0         | 6(7.5%)                         | 9(11.25%)                         | 3(3.75%)                             | 2(2.5%)                           | 63.8 |
| >10.0            | 0                               | 7(8.75%)                          | 9(11.25)                             | 2(2.5%)                           | 69.1 |
| Total            | 18(22.5%)                       | 36(45%)                           | 20(25%)                              | 6(7.5%)                           |      |
| Mean             | 2.32                            | 7.92                              | 19.16                                | 8.31                              |      |

Among 80 patients, 29 had International Prostate Symptoms Score (IPSS) in the range of 1-7 (mild), 41 had IPSS between 8 and 19 (moderate), whereas only 10 patients had IPSS > 19 (severe). Mean IPSS score was 9.88 (Table 7). As for the mild IPSS, 18 patients had Serum PSA <4 ng/ml, 4 had Serum PSA between 4 and 10 ng/ml and 7 had Serum PSA > 10 ng/ml. Out of 41 patients with moderate IPSS score 22 had Serum PSA of <4 ng/ml, while 10 and 9 had Serum PSA of 4-10ng/ml and >10 ng/ml, respectively. 10 patients had severe IPSS score with 2, 6 and 2 patients in <4, 4-10, and >10 ng/ml Serum PSA groups respectively.

### Table 7: Correlation of Serum PSA and IPSS Score (n=80)

| IPSS Score | Serum PSA <4 ng/ml | Serum PSA 4-10 ng/ml | Serum PSA >10 ng/ml |
|------------|--------------------|----------------------|---------------------|
| Mild (1-7) | 18                 | 4                    | 7                   |
| Moderate   | 22                 | 10                   | 9                   |
| Severe     | 2                  | 6                    | 2                   |
| Total      | 4(52.5%)           | 20(25%)              | 18(22.5%)           |

As shown in Table-8, 33 patients had benign reports on biopsy, which included 25 of BPH and 8 as prostatitis. Most of the patients with diagnosis of BPH had fallen in PSA range of 4-10 ng/ml. Entire group of patients with prostatitis had serum PSA of either <4 or 4-10 ng/ml. Out of the 18 patients having histological proven malignancy in our study, 14 had Serum PSA of >10 ng/ml whereas 4 had Serum PSA between 4 and 10 ng/ml.

### Table 8: Correlation of Serum PSA with BPH and Prostatitis

| Parameters | Serum PSA <4 ng/ml | Serum PSA 4-10 ng/ml | Serum PSA >10 ng/ml | Total |
|------------|--------------------|----------------------|---------------------|-------|
| BPH (%)    | 8                  | 13                   | 4                   | 25    |
| Prostatitis| 5                  | 3                    | 0                   | 8     |
| Total      | 13                 | 16                   | 4                   | 33    |

Table 9 shows correlation of prostate size with IPSS score 31(38.75%) patients had mild score on IPSS and had prostatomegaly grade I, II, III and IV as 12(15%), 14 (17.5%), 5(6.25%) and 0 (0%), respectively. Among the patients having moderate IPSS score prostatomegaly grades were 6(7.5%), 19(23.75%), 12(15%) and 4(5%) respectively. Patients having severe IPSS score had 0(0%), 3(3.75%), 3(3.75%) and 2(2.5%), respectively.

### Table 9: Correlation of IPSS score and size of Prostate

| IPSS Grade | USG Grade I (<30g)(%) | USG Grade II (31-50g)(%) | USG Grade III (51-80g)(%) | USG Grade IV (>80g)(%) | Total (%) |
|------------|-----------------------|--------------------------|---------------------------|------------------------|-----------|
| Mild (1-7) | 12(15%)               | 14(17.5%)                | 5(6.25%)                  | 0                      | 31(38.75%)|
| Moderate   | 6(7.5%)               | 19(23.75%)               | 12(15%)                   | 4(5%)                  | 41(51.25%)|
| Severe     | 0                     | 3(3.75%)                 | 3(3.75%)                  | 2(2.5%)                | 8(10%)    |
| Total      | 18(22.5%)             | 36(45%)                  | 20(25%)                   | 6(7.5%)                | 80        |
Discussion

A total of 80 male patients presenting with LUTS were included in study. Their mean age was 68.66 years (range 50-97 years). The patients were selected from general surgery OPD. Compared to study done by De et al, in, which mean age of study group was 66 years which was similar to our study group.

The majority i.e. 41 of study group was in the age group of 61-70 years. 42 of patients had Serum PSA <4ng/ml in the entire study group compared to 20 in the range of 4-10ng/ml and only 18 with Serum PSA >10 ng/ml. This shows that with the increase in age group the shift is towards increasing Serum PSA levels. The results of our study were comparable with PSA best practice statement 2009 age specific PSA range for Asian population, which also showed increasing Serum PSA levels with the increasing age.

On the other hand a study conducted by Lin et Al, showed that Serum PSA range for the age group of Taiwanese men was 0.8-1.7 ng/ml which was much lower than the mean Serum PSA in our study, this is probably due to the higher average Serum PSA levels in Eastern Indian population.

In our study among the biopsy-proven carcinoma cases, 33% of the cases are in the age group of 71-80 years (table 6). These results are comparable with study conducted by Anushree and Venkatesh in which maximum incidence of adenocarcinoma was seen in the age group of 70-79 years.

Among the biopsy-proven adenocarcinoma patients, 22.22% patients had Serum PSA levels between 4 ng/ml and 10 ng/ml and 77.78 had Serum PSA levels>10ng/ml, whereas the number of biopsy-proven benign diseases (BPH as well as prostatitis) patients had Serum PSA levels graded as<4ng/ml, 4-10 ng/ml and>10 ng/ml were 48.48%, 39.39% and 12.13% respectively, as shown in table 7. This shows that the correlation of Serum PSA levels in detection of adenocarcinoma prostate was very high. Results of our study were comparable to numerous studies done by Murthy et al, Diamandis, Partin and Oesterling, Anushree and Venkatesh and De et al, who showed higher incidence of adenocarcinoma with higher Serum PSA levels.

Out of the biopsy-proven adenocarcinoma cases, DRE was suspicious of malignancy in 89% whereas DRE was suggestive of benign Pathology in only 11% patients. In 33 patients with biopsy-proven benign Pathology suspicious DRE was noted in about 39.39% of cases and 60.61% of the patients had benign feel on DRE. This correlation was found to be highly significant. This indicates higher pick up rates for carcinoma prostate on DRE. On the contrary, the study conducted by Cooner et al and De et al showed that DRE positivity ranges between 21% and 53%.

The mean size of prostate in our study was 54 gram. The mean Serum PSA for grade I prostatomegaly was 2.32 ng/ml, for grade II 7.92 ng/ml, grade III- 19.16 ng/ml, and for grade IV prostatomegaly was 8.31 ng/ml. There was a significant correlation noted between the prostate size and Serum PSA levels in our study. Comparing the results with studies done by Carvalhal et al and Park et al, who showed mean prostate size of 51.7 gram where as the mean Serum PSA was much less when compared to the prostate size. This variation in our study group is attributable to higher incidence of prostatitis and UTI in our country, which causes a rise in mean Serum PSA.

About 31 (38.75%) patients presented with mild IPSS score of 1-7, 41(51.25%) had IPSS between 8 and 19 (moderate) where as these only 8(10%) had IPSS >19 (severe).

There was a significant correlation noted between the IPSS and Serum PSA levels. Compared to study done by Park et al who showed mean Serum PSA levels with mild, moderate and severe IPSS as 0.55, 0.53 and 0.54 ng/ml respectively. Our results were significantly high.

A total of 51 patients in the study underwent biopsy. 33 patients had benign reports on biopsy, which included 25 of BPH and 8 as prostatitis. Mean Serum PSA range in our study is higher than the study done by Murthy et al, who showed mean Serum PSA levels of<4ng/ml. This is attributable to the higher levels of Serum PSA in Eastern Indian population.

The majority of patients with diagnosis of BPH had fallen in PSA range of 4-10 ng/ml. Entire group of patients with prostatitis had Serum PSA of either <4 or 4-10 ng/ml. This is contrary to the results of Lin et al, in which maximum number of patients had fallen into category of <4 ng/ml Serum PSA, attributable to higher Serum PSA levels in cases of prostatitis.

A significant correlation between IPSS and prostate size was noted in our study, which is contrary to the findings of Vesely et al who showed a poor correlation of Serum PSA with IPSS. A similar study with weak or poor correlation of Serum PSA with IPSS was done by Morote et al and Barry.

Conclusion

Serum PSA levels correlates with the age group, with the increase in age that is rise in Serum PSA levels. Transabdominal ultrasound, DRE and Serum PSA has high sensitivity in diagnosis of prostatomegaly but it was found that none of the single screening tool, that is Serum total PSA, DRE, or ultrasound has got much efficacy in differentiating carcinoma prostate from benign hypertrophy, but the combination of the DRE and Serum total PSA or DRE, Serum total PSA and ultrasound abdomen showed higher efficacy in diagnosis of carcinoma prostate. Increase in Serum PSA is directly related to carcinoma prostate, but there is no absolute cutoff for Serum PSA for diagnosis of carcinoma.

References

1. Mistry K, Cable G. Meta-analysis of prostate-specific antigen and digital rectal examination as screening tests for prostate carcinoma. J Am Board Fam Pract. 2003;16(2):95-101.
2. Abdrabo AA, Fadlalla AI, Fadl-Elmula IM. Significance of serum total prostate specific antigen and digital rectal examination in the diagnosis of prostate cancer. Saudi Med J. 2011;32(11):1133-6.

3. Lin KJ, Pang ST, Chang YH, Wu CT, Chuang KL, Chuang HC, et al. Age-related reference levels of serum prostate specific antigen among Taiwanese men without clinical evidence of prostate cancer. Chang Gung Med J. 2010;33(2):182-7.

4. De S, Das RK, Mukherjee S. Role of prostate specific antigen, digital rectal examination and trans rectal ultra sonography in the diagnosis of prostate cancer in patients with lower urinary tract symptoms. Int J Sci Res (IJSR). 2013;2(3):2319-7064.

5. Anushree CN, Venkatesh K. Morphological spectrum of prostatic lesion: A clinic pathological study. Med Innov. 2012;1(2):49-54.

6. Diamandis EP. Prostate-specific antigen: Its usefulness in clinical medicine. Trends EndocrinolMetab. 1998;9(8):310-6.

7. Carvalhal GF, Daudi SN, Kan D, Mondo D, Roehl KA, Loeb S, et al. Correlation between serum prostate-specific antigen and cancer volume in prostate glands of different sizes. Urology. 2010;76(5):1072-6.

8. Vesely S, Knutson T, Damber JE, Dicuio M, Dahlstrand C. Relationship between age, prostate volume, prostate specific antigen, symptom score and uroflowmetry in men with lower urinary tract symptoms. Scand J UrolNephrol. 2003;37(4):322-9.

9. Barry MJ. Clinical practice. Prostate-specific-antigen testing for early diagnosis of prostate cancer. N Engl J Med. 2001; 344(18):1373-7.

10. Partin AW, Oesterling JE. The clinical usefulness of prostate specific antigen: Update 1994. J Urol. 1994; 152:1358-68.