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Significant Changes in Volume of Seminal Vesicles as Determined by Transrectal Sonography in Relation to Age and Benign Prostatic Hyperplasia

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HAYAKAWA, T., NAYA, Y. and KOJIMA, M. *Significant Changes in Volume of Seminal Vesicles as Determined by Transrectal Sonography in Relation to Age and Benign Prostatic Hyperplasia.* Tohoku J. Exp. Med., 1998, **186** (3), 193-204 —— We evaluated the changes in volume of the seminal vesicles as determined by transrectal sonography in terms of the possible relationship with aging, lower urinary tract symptoms and benign prostatic hyperplasia (BPH) in community based populations in Japan. In 641 men (55-86 years, mean 67) on a mass screening program for prostatic diseases, the maximum horizontal area of the seminal vesicles (MHA) was compared with age, American Urological Association (AUA) symptom index scores and transrectal ultrasonic parameters of the prostate including prostatic volume, transition zone (TZ) volume, TZ index and presumed circle area ratio (PCAR). Simple regression analyses demonstrated that MHA correlated significantly with age, prostatic volume, TZ volume, TZ index and PCAR, but not with AUA symptom index scores. Multiple regression analysis revealed age, prostatic volume and PCAR to be independent determinants of MHA. There was a difference in MHA between subjects with BPH (7.1 ± 2.5 cm^2) and those with a normal prostate (5.6 ± 2.1 cm^2) with a statistical significance. In the morphological evaluation of the seminal vesicles, the significant influence of age and BPH has to be taken into account. ———— seminal vesicles; age; AUA symptom index; benign prostatic hyperplasia; transrectal sonography

Recent progress in imaging modality has enabled the accurate delineation of morphological changes of the seminal vesicles. In particular, transrectal sonography (TRS) occupies a central position among imaging modalities and is currently credited as an indispensable tool for morphological studies of the seminal vesicles (Carter et al. 1989; Asch and Toi 1991).

With the use of TRS, there have been many reports published so far, in which changes in shape and volume of the seminal vesicles have been described in

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relation to certain pathological conditions of the organ, such as seminal vesiculitis (Abe et al. 1989), hematospermia (Etherington et al. 1990; Worischeck and Parra 1994) and prostatic cancer invasion (Scardino et al. 1989; Terris et al. 1990). In these conditions, the dilatation of the seminal vesicles is considered to be one of the most representative ultrasonic findings. It is, therefore, of importance that changes in seminal vesicle volume are to be evaluated with reference to the volume distribution of the seminal vesicles in healthy men.

In the present study, the volume of the seminal vesicles as represented by the maximum horizontal area of the seminal vesicles (MHA) (Terasaki et al. 1993b), which was determined by TRS, was correlated with age, lower urinary tract symptoms and transrectal ultrasonic parameters of the prostate in community-based populations in Japan, with the aim of revealing the clinical significance of dilatation changes of the organ in terms of the possible influence of aging and benign prostatic hyperplasia (BPH).

Material and Methods

Since 1975 we have been conducting a mass screening program for prostatic diseases using TRS in community-based populations aged 55 years or more in Japan (Watanabe et al. 1977). In 1994, a total number of 672 men in 6 rural towns in Kyoto, Shiga and Hokkaido Prefectures underwent mass screening examinations under the program, of whom 10 (1.5%), 9 (1.3%) and 6 (0.9%) were diagnosed as having prostatic stone, prostatic cancer and prostatitis, respectively (Taneike et al. 1997). In 641 (99.1%) of the remaining 647 men, transrectal sonograms were available for planimetry of both the seminal vesicles and the prostate, and they were therefore enrolled in this study. Ages ranged from 55 to 86 years (mean age 67) and examinees were diagnosed as having a normal prostate (504 [78.6%]) or BPH (137 [21.4%]).

The primary study of the mass screening program was comprised of the American Urological Association (AUA) symptom index, digital rectal examination, TRS and serum prostate specific antigen determination. Examinees completed the questionnaire of the AUA symptom index which had been translated into Japanese (Kawabe and Watanabe 1994). A total of symptom scores was obtained by adding the scores for the 7 kinds of symptom to give a range from 0 to 35 points, and was categorized as mild (scores 7 or less), moderate (scores 8 to 19) and severe (scores 20 or more) (Barry et al. 1992).

TRS was performed using a chair-type scanner with a 5 MHz transducer (SSD-520, Aloka, Tokyo). Horizontal sonograms of the prostate and the seminal vesicles were photographed at every 5 mm slice. The largest area of horizontal sonograms of the seminal vesicles was measured by planimetry as MHA, which was recorded at close to the identical plane of sections for reproducibility of measurement (Fig. 1) (Terasaki et al. 1993b). Prostatic volume and transition zone (TZ) volume were calculated using step-section volumetry. TZ index was obtained by

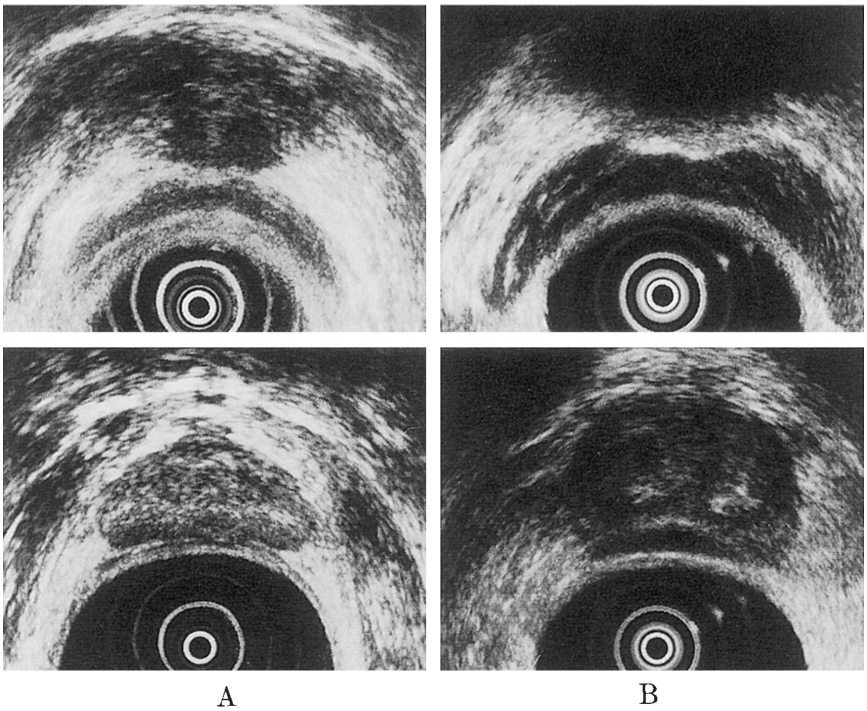


Fig. 1. Representative TRS of the seminal vesicles and the prostate in a 65 year-old man with a normal prostate (A) and in a 70 year-old man with BPH (B). MHA, prostatic volume, TZ volume and PCAR were 3.5 cm^2, 15.5 ml, 1.5 ml and 0.61 in the normal prostate case (A) and 11.2 cm^2, 37.4 ml, 20.8 ml and 0.80 in the BPH case (B), respectively.

dividing TZ volume by prostatic volume (Kaplan et al. 1996). A presumed circle area ratio (PCAR) was also calculated on the horizontal sonograms with the maximum area (Watanabe 1979; Kojima et al. 1997). PCAR is the ratio of the area of maximum prostatic section to the area of a presumed circle having the same circumference as that of the section. When the PCAR was 0.75 or more, the diagnosis of BPH was made. Out of 641 examinees, 137 (21.4%) were diagnosed as having BPH. All ultrasonic parameters were obtained using an image measuring system (Finetec, Tokyo) with a personal computer.

All values in the text were expressed as the mean ± standard deviation (the mean ± S.D.). Student's t-test was used to compare the numerical variables between the groups. The chi-square for trend was adopted to compare percentages between the groups. Simple regression analysis was employed to test the linearity of the relationship between two variables, and multiple regression analysis to test the linear effect of age and ultrasonic prostatic parameters in predicting the MHA. These statistical analyses were performed using commercially available software (Stat View, Abacus Concepts, Inc., Berkeley, CA, USA). For all statistical tests, a p-value less than 0.05 was considered significant.

Results

The distribution of MHA in 641 cases examined is shown in Fig. 2. MHA

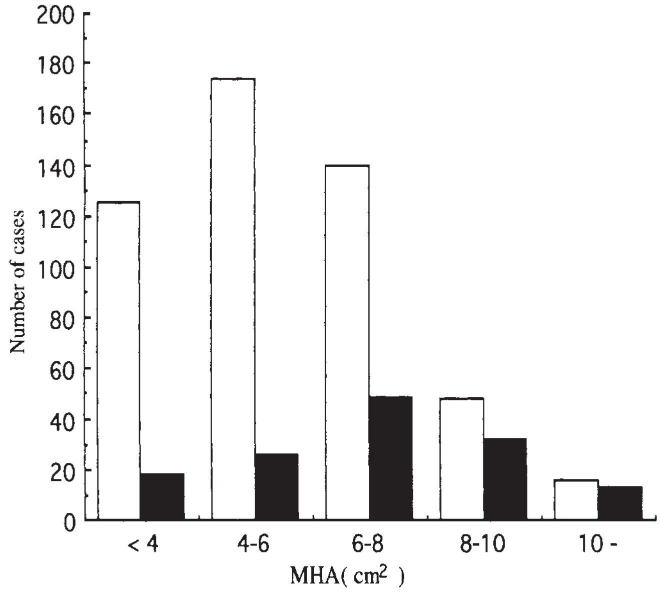


Fig. 2. Distributions of MHA in 504 men with a normal prostate and 137 with BPH. □, Normal prostate; ■, BPH.

TABLE 1. *Regression analyses of maximum horizontal area of the seminal vesicles as a function of age, AUA symptom scores and transrectal ultrasonic parameters of the prostate in 641 men*

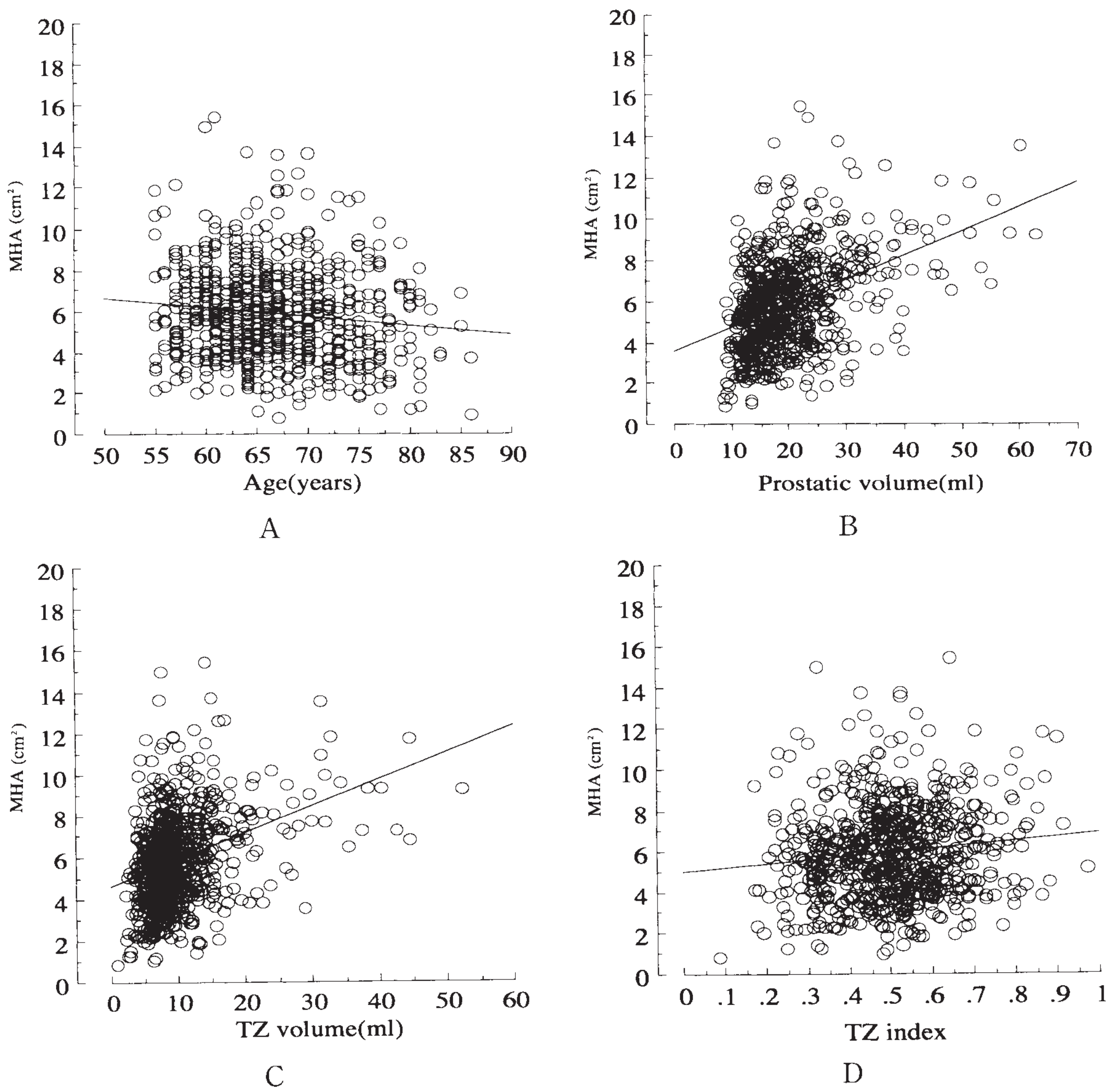
Independent variable	Simple regression		Multiple regression		
	Coefficient (r)	p-value	Coefficient (r)	Adjusted R^2	p-value
Age	−0.125	<0.01			<0.001
Total symptom score	0.018	n.s.			n.s.
Prostatic volume	0.414	<0.001	0.456	0.203	<0.001
TZ volume	0.348	<0.001			n.s.
TZ index	0.110	<0.01			n.s.
PCAR	0.352	<0.001			<0.01

n.s., statistically not significant; PCAR, presumed circle area ratio ; TZ, transition zone.

ranged from 0.84 to 15.5 cm^2 with a mean of 5.9$\pm$2.3 cm^2. Out of the 641 cases, 143 (22.3%), 200 (31.2%), 189 (29.5%), 80 (12.5%) and 29 (4.5%) had MHA of less than 4 cm^2, 4 to 6 cm^2, 6 to 8 cm^2, 8 to 10 cm^2 and 10 cm^2 or more, respectively. The frequency of BPH increased from 12.6% in cases with MHA less than 4 cm^2 to 44.8% in those with MHA of 10 cm^2 or more (p=0.001).

Relationship between MHA and age

MHA decreased as age increased, being 6.0$\pm$2.2 cm^2, 6.1$\pm$2.3 cm^2, 5.7$\pm$2.3 cm^2 and 4.8$\pm$2.1 cm^2 in men aged 55 to 59, 60 to 69, 70 to 79 and 80 years or more, respectively. On simple regression analysis there was a negative correlation



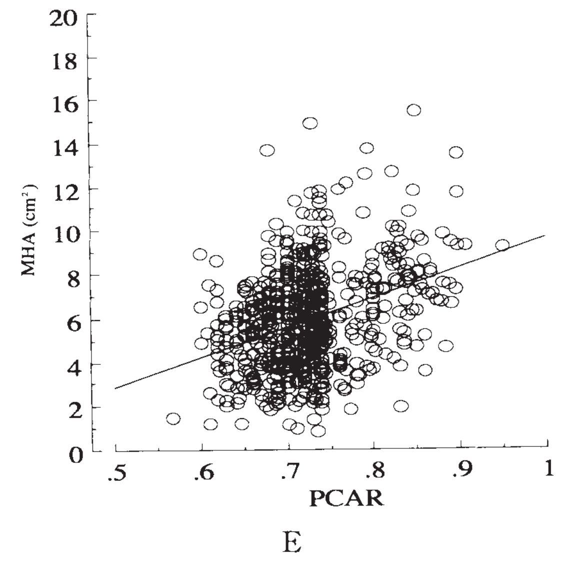


Fig. 3. Relationship of MHA with age ($r = -0.125$, $p < 0.01$, $n = 641$) (A), prostatic volume ($r = 0.414$, $p < 0.001$, $n = 641$) (B), TZ volume ($r = 0.348$, $p < 0.001$, $n = 641$) (C), TZ index ($r = 0.110$, $p < 0.01$, $n = 641$) (D) and PCAR ($r = 0.352$, $p < 0.001$, $n = 641$) (E).

TABLE 2. *Regression analyses of maximum horizontal area of the seminal vesicles as a function of age, AUA symptom scores and transrectal ultrasonic parameters of the prostate in 504 men with a normal prostate*

Independent variable	Simple regression		Multiple regression		
	Coefficient (r)	p-value	Coefficient (r)	Adjusted R^2	p-value
Age	−0.186	<0.001			<0.001
Total symptom score	0.015	n.s.			n.s.
Prostatic volume	0.286	<0.001	0.349	0.115	0.001
TZ volume	0.213	<0.001			n.s.
TZ index	0.017	n.s.			n.s.
PACR	0.192	<0.001			0.01

n.s., statistically not significant; PCAR, presumed circle area ratio; TZ, transition zone.

TABLE 3. *Regression analyses of maximum horizontal area of the seminal vesicles as a function of age, AUA symptom scores and transrectal ultsasonic parameters of the prostate in 137 men with benign prostatic hyperplasia*

Independent variable	Simple regression		Multiple regression		
	Coefficient (r)	p-value	Coefficient (r)	Adjusted R^2	p-value
Age	0.165	n.s.			<0.05
Total symptom score	0.013	n.s.			n.s.
Prostatic volume	0.416	<0.001	0.498	0.226	<0.01
TZ volume	0.313	<0.001			n.s.
TZ index	0.036	n.s.			n.s
PCAR	0.354	<0.001			<0.01

n.s., statistically not significant; PCAR, presumed circle area ratio; TZ, transition zone.

noted between MHA and age with a statistical significance ($r=-0.125$, $p<0.01$, $n=641$) (Table 1, Fig. 3A). This negative correlation was also recognized when analyzed in 504 men with a normal prostate ($r=-0.186$, $p<0.001$), but not in those with BPH (Tables 2 and 3).

Relationship between MHA and AUA symptom score

Neither the total of AUA symptom scores nor the score of each symptom showed any statistically significant correlation with MHA (Table 1). Among subgroups of men with slight ($n=467$), moderate ($n=139$) and severe ($n=35$) symptoms, there was no significant difference in MHA.

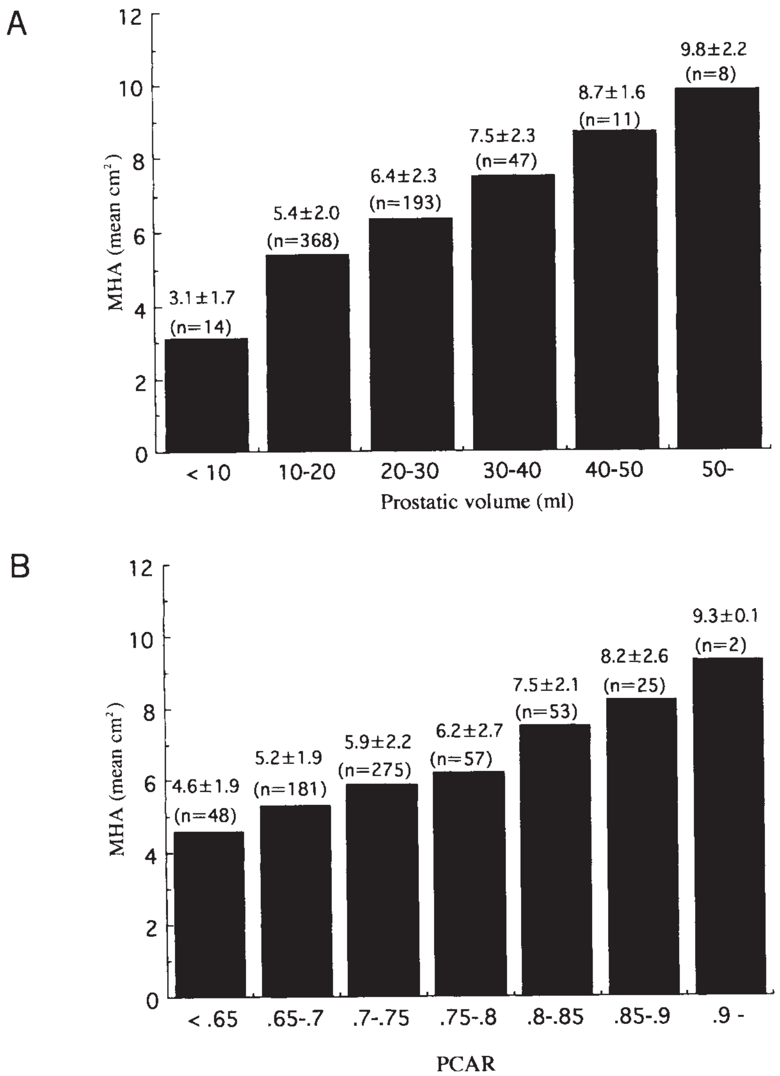


Fig. 4. Distribution of MHA by prostatic volume ($n=641$) (A) and PCAR ($n=641$) (B).

Relationship between MHA and prostatic parameters

MHA correlated significantly with all ultrasonic planimetric parameters of the prostate examined (Table 1). MHA increased from 3.1 ± 1.7 cm^2 in men with a prostate less than 10 ml to 9.8 ± 2.2 cm^2 in those with a prostate of 50 ml or more ($p<0.001$) (Fig. 4A). There was also a significant relationship between MHA and PCAR (Fig. 4B), resulting in a significant increase of MHA in men with BPH (PCAR of 0.75 or more, 7.1 ± 2.5 cm^2, $p<0.001$), compared to those with a normal prostate (PCAR less than 0.75, 5.6 ± 2.1 cm^2). Simple regression analysis yielded the highest correlation coefficient between MHA and prostatic volume ($r=0.414$, $p<0.001$), followed by PCAR, TZ volume and TZ index ($n=641$)(Fig. 3). Similar analyses were also performed in subgroups of men with a normal prostate and those with BPH, demonstrating a significant positive linear relationship between MHA and all ultrasonic parameters but TZ index (Tables 2 and 3).

Multiple regression analysis of MHA as a function of age and prostatic parameters

When analyzed together on the 641 men, multiple regression analysis demonstrated age, prostatic volume and PCAR to be independent significant determinants of MHA (Table 1). This was also the case when analyzed respectively in the subgroups of men with a normal prostate and those with BPH (Tables 2 and 3).

Discussion

Currently, modern imaging modalities such as TRS, computed tomography and magnetic resonance imaging are used clinically for evaluation of the seminal vesicles in terms of the morphological changes in relation to pathological abnormalities. Taking into account the cost, invasiveness and reliability, however, it is certain that TRS is the only diagnostic tool available for the study of the seminal vesicles in routine clinical work. In particular, a statistical study like this one dealing with healthy men in community-based populations could not be performed without the use of TRS.

To date, many authors have described changes in not only the entire shape but also the internal configurations of the seminal vesicles in men with possible pathological abnormalities of the organ. An abnormal dilatation of the seminal vesicles was noted most frequently in patients with congenital anomalies of the seminal vesicles and/or ejaculatory duct (Carter et al. 1989), seminal vesiculitis (Abe et al. 1989) and hematospermia (Etherington et al. 1990; Worischeck and Parra 1994). More frequently, TRS was applied to the seminal vesicles with the aim of detecting prostatic cancer invasion into the organ, and dilatation was considered to be one of the ultrasonic findings suggesting cancer invasion (Scardino et al. 1989; Terris et al. 1990). Thus, volume estimation of the seminal vesicles has an important clinical significance.

Methodologically, transrectal ultrasonic measurement with step section planimetry is likely to be preferable for the volume measurement of the seminal vesicles. As early as 1975, with the use of this technique, Tanahashi et al. (1975) reported a mean volume of the seminal vesicles of 13.7 (range 8.0 to 18.6) ml. It is to be noted, however, that step section volumetry of the seminal vesicles is not always possible, because in practice whole sections of the organ are often difficult to visualize using TRS. With the aim of resolving this disadvantage, Terasaki et al. (1993b) proposed the use of MHA as a substitute to the volume of the seminal vesicles. They reported a strong correlation between MHA and the volume with a correlation coefficient of 0.88 ($p<0.01$) in 76 men in their third to eighth decade. With this in mind, we employed the measurement of MHA in this study. As a result, in 641 (99.1%) out of 647 men, MHA was obtained and used for statistical analysis.

Since it is well known that the seminal vesicles decrease in size directly after ejaculation (Ichijo et al. 1981), seminal vesicle volume as represented by MHA could be affected by recent ejaculation. As to this issue, Carter et al. (1989) found no significant difference in seminal vesicle volume between patients who had recently ejaculated and those who had abstained for 24 hours or longer. Furthermore, a statistical approach dealing with data obtained from as large a number as 641 men seems likely to decrease substantially any bias concerning ejaculation. Taken together, the possible influence of ejaculation on MHA measurement might be disregarded in this study.

In our series of subjects, MHA decreased significantly with age in men with a normal prostate. This negative relationship between seminal vesicle volume and age coincided well with a report by Grayhack (1961), who demonstrated that seminal vesicle weight decreased with age. In addition, using transrectal ultrasonic planimetry Terasaki et al. (1993b) found a significant decrease of seminal vesicle volume with age, ranging from 9.3 ± 2.4 ml in men aged 50–59 years to 5.1 ± 1.1 ml in those aged 80–89 years. A similar age-related change in volume was also found for the prostate. Mori (1982) measured the prostatic volume by TRS in 348 normal subjects and showed that it began to decrease gradually after the age of 40 years. This similar tendency in volume change with aging for the prostate and seminal vesicles might be caused mainly by decreasing serum testosterone levels with aging (Baker et al. 1976). Interestingly, Terasaki et al. (1993a) reported that seminal vesicle volume as evaluated by MHA changed in parallel to the serum testosterone level in patients with prostate cancer treated by LHRH analog and decreased by 11–62%, compared with the baseline.

There has been a controversy concerning the relationship between seminal vesicle volume and BPH. Seminal vesiculography has shown the seminal vesicles rather enlarged compared with those in normal subjects (Vestby 1958). In contrast, Tanahashi et al. (1975), although their subject number was so small, found reduced seminal vesicle volume in BPH (mean 8.3 ml) compared with normal subjects (mean 13.7 ml). The present study confirmed a significant increase in seminal vesicle volume in association with BPH.

Although the pathophysiology of the dilatation of the seminal vesicles in association with BPH remains to be elucidated, obstruction of the ejaculatory duct is likely to be related to this condition. In fertile men, obstruction of the ejaculatory duct is found occasionally with an associated dilatation of the seminal vesicles (Goldwasser et al. 1985). More interestingly, Colpi et al. (1987) have described several infertile patients in whom the seminal vesicles seemed not to empty correctly on ejaculation, and TRS revealed abnormally dilated seminal vesicles. Thus, it is certain that obstruction of the ejaculatory duct is closely involved in the development of seminal vesicle dilatation.

The significant correlation of PCAR with MHA could explain the possible relationship of ejaculatory duct obstruction and seminal vesicle dilatation. PCAR is a prostatic planimetric parameter and represents the roundness of the horizontal sonogram of the prostate. As the horizontal sonogram of the prostate becomes rounder, the PCAR approaches 1.0. In our previous study, PCAR has been shown to correlate significantly with the severity of infravesical obstruction in men with lower urinary tract symptoms (Kojima et al. 1997). Since a hypertrophic prostate can be linked to a closed system in which the internal gland is enclosed by the surgical capsule, the inner gland pushes the capsule out as it grows, resulting in an increase in intraprostatic pressure. Almost the same pressure caused by this expansion may apply to the circumference of the urethra, because it penetrates the center of the internal gland. Accordingly, the degree to which the capsule approximates roundness shows the degree of pressure on the urethra. Similarly, the increased intraprostatic pressure along with the development of BPH would cause an obstruction of the ejaculatory duct.

On the other hand, it is to be noteworthy to analyze the positive relationship between the increased volume of the seminal vesicles and BPH in terms of endocrine factors. As is well known, the prostate is the strong trophic influence of androgens, and the development of BPH has been reported to be associated with elevated levels of serum testosterone, interstitial dihydrotestosterone and nuclear androgen receptors (Walsh 1992). These endocrine changes could affect the physiological property of the semial vesicles. It may be accordingly suggested that the significant increase in volume of the seminal vesicles is caused by the endocrine mechanism which induces BPH.

Although the seminal vesicles were demonstrated to increase in volume in association with BPH, the clinical significance of this fact remains unknown. Since the seminal vesicles are located just beneath the bladder neck and the prostate, this might cause some urological symptoms. However, at least in our series of subjects in community-based populations, the dilatation of the seminal vesicles had no significant correlation with lower urinary tract symptoms as evaluated by AUA symptom scores. Further studies are needed to reveal the possible relationship between seminal vesicle volume and lower urinary tract symptoms in symptomatic patients visiting urology clinics.

Conclusion

The volume of the seminal vesicles changed with aging and the presence of BPH in elderly men in Japan. In the evaluation of the seminal vesicles in relation to pathological changes, the significant influence of age and BPH on the dilatation of the organ has to be taken into account. Both the clinical and pathological significance of seminal vesicle dilatation remains to be elucidated.

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