

A Suggestion of New Integrated Prognostic Factor for Aortic Aneurysm: Tangential Stress Index¹

Jongmin J. Lee, M.D., Yongmin Chang, Ph.D., Hun-Kyu Ryeom, M.D.,
Sang-Kwon Lee, M.D., Yong-Joo Kim, M.D., Ph.D., Duk-Sik Kang, M.D., Ph.D.

Purpose: To construct a useful index for use as a prognostic factor in cases of aortic aneurysm.

Materials and Methods: Using CT or EBT, we studied nine ruptured aortic aneurysms, 40 unruptured aneurysms, and 42 normal aortas, measuring aortic diameter and wall thickness. Systolic, mean or diastolic blood pressure was used as a pressure parameter. Tangential stress (TS) and the tangential stress index (TSI) were calculated by modified Laplace's law.

Results: Average diastolic TS's (TSI's) were 1938 (4.13), 905 (1.84) and 554 (0.94) in ruptured aneurysm, unruptured aneurysm and normal groups, respectively ($p < 0.01$). ROC curves of diastolic TS and TSI were seen in a "useful study" zone. With a threshold of 1230 (2.90) for TS (TSI), the sensitivity and the specificity for differentiation of ruptured and unruptured aneurysms were 100% (100%) and 75% (88%), and the positive and the negative predictive values were 47% (64%) and 100% (100%), respectively ($p < 0.01$). Among systolic, mean and diastolic TS's and TSI's, the diastolic TSI showed the highest specificity at its maximal sensitivity.

Conclusion: Diastolic TSI is a more accurate prognostic factor for aortic aneurysm.

Index words : Aneurysm, aortic
Aorta, CT

Partly because of increased longevity, the incidence of aortic aneurysm is also increasing (1). Recent studies have shown that abdominal aortic aneurysms were detected in 4% of men and women between 65 and 80 years old and 11% of men aged 60 or over (2-5). An aortic aneurysm can be readily detected by measuring aortic diameter; dilatation of 50% or more than expected value, or that of the proximal segment, indicates its presence (6). However, the rupture of an aortic aneurysm is a sudden crisis, and the aneurysm is seldom symptomatic before rupture (1). In previous studies, 42 - 62% of

cases of ruptured aneurysm resulted in the patient's death before reaching the emergency room (7-9). Surgical mortality rates were reported to be between 32% and 70% (8,10,11). The overall mortality of abdominal aortic aneurysm rupture is said to be around 80 - 90% (7,9,12). Furthermore, because of multifactorial circumstances, it is not easy to detect a representative predictive factor for aortic aneurysm rupture.

By integrating blood pressure, aneurysmal luminal diameter, and wall thickness for the prediction of aortic aneurysm rupture and the guidance of proper practice, we have therefore attempted to establish a new basis for prognosis. In this study, we suggest that the tangential stress index of aortic aneurysm can be a useful prognostic factor for true aortic aneurysms.

¹Department of Diagnostic Radiology, School of Medicine, Kyungpook National University

Received November 13, 1998 ; Accepted March 2, 1999

Address reprint requests to : Jongmin J. Lee, M.D., Department of Diagnostic Radiology, School of Medicine, Kyungpook National University of Korea.

Tel. 82-53-420-5472 Fax. 82-53-422-2677 E-mail. jonglee@kyungpook.ac.kr

Materials and Methods

We studied nine cases of ruptured aortic aneurysm (men: women= 5:4) and 40 cases of unruptured aneurysm (men: women= 25:15). A normal control group consisting of 42 subjects (men: women= 22:20) with normal blood pressure and aortic features were also studied. Patients were aged between 24 and 85 (mean, 60) years. In both ruptured and unruptured groups, the most common location of an aneurysm was the infrarenal abdominal aorta (Table 1). All patients and the control group underwent contrast enhanced CT (Hi-speed Advantage, GE, Milwaukee, U.S.A.) or EBT (Ultrafast CT C-150, Imatron, San Francisco, U.S.A.) to measure aneurysmal or normal aortic diameter and wall thickness. Twenty-eight patients and nine normal persons were scanned by spiral CT with 5-10 mm effective slice thickness and 1.0 pitch. The others were examined by EBT with scan parameters of 4-8 mm slice thickness, 0.1-0.2 second scan time and continuous volume mode. The EBT studies were performed prospectively, whereas the spiral CT studies were analyzed retrospectively. Approximately 80-100 ml contrast media (Ultravist 370, Schering, Berlin, Germany) was injected as bolus at a rate of 3-5 ml/sec. Either 5cc of 2% MgSO₄ or test bolus (3-5cc) of contrast media was used to estimate circulation time. In the case of MgSO₄, we measured the elapsed time between bolus injection into a superficial vein and awareness of a burning sensation in the throat.

Contrast-filled luminal diameters and wall thicknesses were measured at the portions of maximal diameter and the thinnest wall within the aneurysm. In the case of an elliptical-shaped lumen, the largest diameter was recorded. Wall thickness was measured at non-thrombosed and non-ruptured portions. In the case of an aneurysm with circumferential thrombosis, the whole thickness including the aneurysmal wall and thrombosis, was measured at the thinnest portion. These measurements were obtained at the maximally magnified images on the consoles or workstation (Insight, Accuimage, San Francisco, U.S.A.). For standardization, images were displayed in a wide window (over 1000 HU) and near the median level gray-scale (Fig. 1). In patients without antihypertensive medication, blood pressures were measured at the time of scanning. The usual blood pressures were obtained from clinical records for either retrospective study, or prospective study with on-

going antihypertensive therapy. Each systolic, diastolic or mean blood pressure was used as a pressure parameter.

To calculate the tangential stress of the aortic wall, modified Laplace's law was adopted.

$$= p \frac{r}{h} \quad (1)$$

$$\left(\begin{array}{ll} = \text{Tangential Stress,} & P = \text{Pressure} \\ = \text{Radius,} & = \text{Thickness of Wall} \end{array} \right)$$

To correct the bias factor due to variability of normal aortic diameter according to aortic level and sex, the tangential stress index was induced by dividing each tangential stress value by the normal value. Normal tangential stress values were calculated on the basis of normal diameters, wall thicknesses, and blood pressures. Normal diameters of four aortic levels (midlevels of ascending aorta, aortic arch, intrathoracic descending aorta and infrarenal abdominal aorta) in both sexes were taken from published data (Table 2). In this study, normal thickness of aortic wall was taken as 1.6 mm at all levels by averaging the thicknesses of normal aorta regardless of sex and aortic level. Aortic diameters were measured as normal for ages in the 4th decade, and nor-

Table 1. Distribution of Aortic Aneurysms

Location	(Number of case)	
	Ruptured	Unruptured
Ascending aorta	1	7
Aortic arch	0	5
Intrathoracic descending aorta	2	2
Infrarenal abdominal aorta	6	29

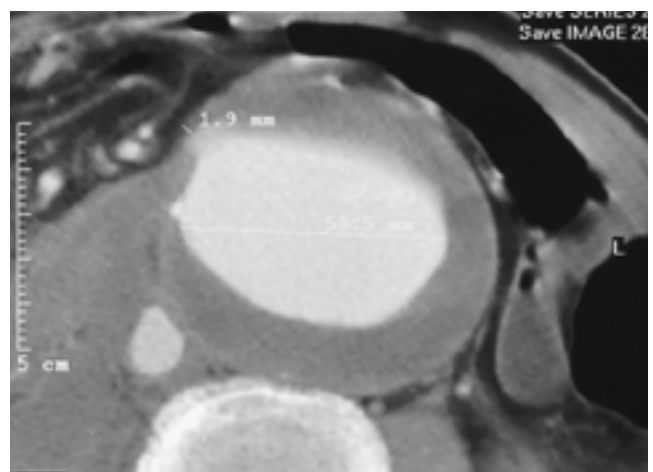


Fig. 1. The Subpixel Measurement of Aneurysmal Diameter and Wall-thickness on Workstation.

mal blood pressure was thus assumed to be 120 / 93 / 80 mmHg.

Statistical analyses (one way ANNOVA range test and Fisher 's exact test) were performed on both tangential stresses and tangential stress indices. To evaluate the effect of wall-thickness parameter on the results of this s-

tudy, Laplace value (unmodified tangential stress)

$$(u) = P \quad (2)$$

was also calculated and analyzed statistically. For comparison, diameter methods, representing the conventional approach, with a threshold of 4 cm and 5 cm, were applied to the same data group.

Results

Maximal luminal diameters of ruptured aneurysms ranged from 40 to 80 (average, 59) mm, while those of unruptured aneurysms ranged from 24 to 83 (average, 43) mm. Average minimal wall-thicknesses of ruptured and unruptured aneurysms were 1.4 mm and 3.2 mm, respectively: average diastolic blood pressures were 95 mmHg (ruptured) and 84 mmHg (unruptured). Fig. 2 shows tangential stresses (TS 's) and tangential stress indices (TSI 's) calculated using systolic, mean and diastolic blood pressures. The average values of each TS and TSI were also calculated (Fig. 3). Average TS and TSI, calculated using diastolic blood pressure, were 1938 (4.13), 905 (1.84) and 554 (0.94) mmHg in ruptured, unruptured, and normal groups, respectively. Differences in diastolic TS and TSI among the three groups were statistically significant ($p < 0.01$). Statistical significance was also noted in other TS 's and TSI 's using systolic or mean blood pressures. ROC curves showed the usefulness of TS 's and TSI 's (Fig. 4). Among TS 's, the systolic TS curve showed the best ROC curve. With respect to TSI curves, mean and diastolic TSI 's appeared to be more useful than systolic TSI. Mean TSI curve showed

Table 2. Calculation of Normal Aortic Diameter at Each Levels and Sexes

a. Normal Aortic Diameters by Aronberg and Horejs (13,14)

		(mm)	
Location		Male	Female
1cm caudad to aortic arch	ascending aorta	32.8	28.0
	descending aorta	22.1	20.6
1cm cephalad to aortic valve	ascending aorta	34.7	33.6
	descending aorta	22.5	19.1
Level or renal artery origin		17.5	15.3
Just proximal to iliac bifurcation		16.0	14.3

On the basis of 4th decades

b. Normal Aortic Diameters at Each Aortic Levels Shown in This Study

		(mm)	
		male	female
Mid-ascending aorta		34	31
	mid-aortic-arch	27	24
Mid-intrathoracic-descending aorta		23	19
Mid-infrarenal abdominal aorta		17	15

Mean values between adjacent ones taken from table a.

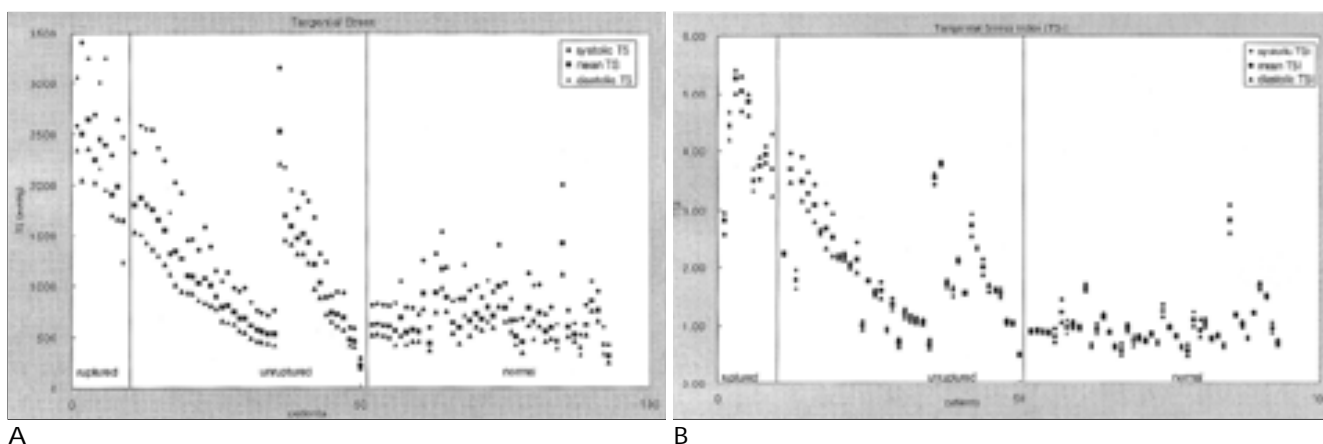


Fig. 2. Tangential Stresses and Tangential Stress Indices of All Subjects.

A. Tangential stress values are plotted in higher region at ruptured aneurysm group than those of unruptured aneurysm and normal groups.

B. Tangential stress index values show more distinct differentiation between three groups. Gaps between systolic, mean and diastolic TSI 's are markedly decreased implying effective bias correction.

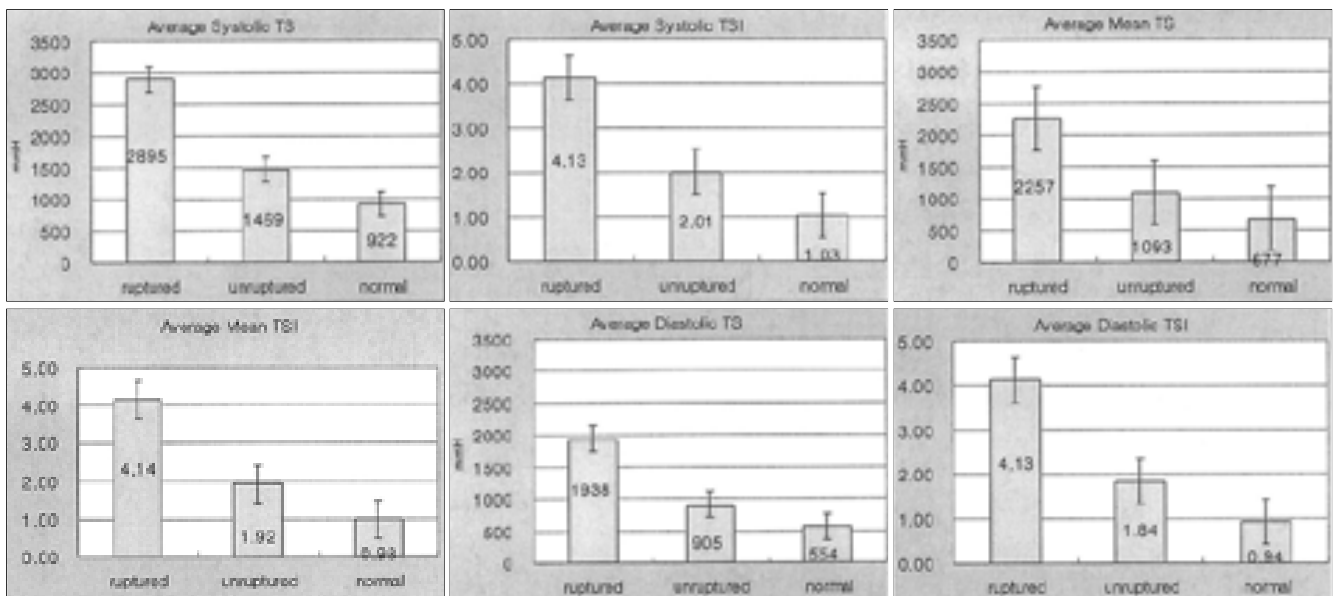
the best result. At a threshold of 1230 and 2.90 for diastolic TS and TSI, ruptured and unruptured aneurysms were readily differentiated. The sensitivity and specificity of TS (TSI) were 100% (100%) and 75% (88%), respectively. Positive and negative predictive values were 47% (64%) and 100% (100%) ($p < 0.01$) (Table 3).

In the case of the diameter method, for fitting to maximum sensitivity (100%), the threshold should be decreased to 40 mm. The other scores were then 43% (specificity), 28% (positive predictive value) and 100% (negative predictive value) (Table 4). ROC curve analysis showed that the diameter method was less useful than TS(I) methods, although the curve was located in the "ordinary study" zone (Fig. 5). By statistical analysis of Laplace values, with each threshold allowing maximal sensitivity (100%), systolic Laplace value was proved to be best, showing 70% specificity, 43% positive predictive value, and 100% negative predictive value (Table 5). All diastolic, mean and systolic TS 's and TSI 's showed better statistical results and ROC curves than when the conventional diameter method and unmodified TS(I) method were used. With regard to sensitivity, diastolic TSI showed higher scores than other TS's and TSI's.

Discussion

Although precise data on the natural course of aortic

aneurysms are not so far available, aneurysmal size and expansion rate have been regarded as good prognostic factors (9-19). Large aneurysms with a diameter of 5 cm or more have been reported to rupture at a rate of 25%-41% within five years (17-19). Aneurysms larger than the body of the 3rd lumbar vertebra have also been described as unstable (18). An expansion rate of more than 1 cm in 6 months has been suggested as another sign of impending rupture (16), and many other predictive factors have been reported. For example, periaortic hemorrhage, contrast extravasation and pain have, as a matter of course, been accepted as signs of impending rupture (20,21). Lorigas and Gaylis suggested that signs of impending rupture include elliptic cross-sectional shape of an aneurysm, focal discontinuity of a calcified rim, and focal transverse outpouching of the aortic wall. Additional signs were obliteration of the anterior or lateral border of the psoas muscle, thin posterior wall on a lumbar osteophyte, eccentric lumen within a thin wall, eccentric lumen with no thrombus between the lumen and outer wall, and aneurysmal diameter over 5cm (16,22). Recent studies have asserted that a high-attenuating crescent within a wall, or a thrombus representing recent hemorrhage, are good prognostic factors (23,24). Although rapid expansion of an aneurysm has been widely accepted as an indicator of instability, no comprehensive study has validated the significance of the



$p < 0.01$ in all TS's and TSI's by one way ANNOVA range test(Tukey)

Fig. 3. Average Tangential Stresses and Tangential Stress Indices.

All average tangential stresses and tangential stress indices differentiate ruptured aneurysm, unruptured aneurysm and normal groups significantly. Especially average diastolic TSI shows the best result in distinction between ruptured and unruptured aneurysm groups.

Table 3. Statistic Analysis of Tangential Stresses & Tangential Stress Indices

a) Systolic TS (threshold= 2000mmHg)			b) Systolic TSI (threshold= 2.50)		
	Positive	Negative		Positive	Negative
Ruptured	9	0	Ruptured	9	0
Unruptured	9	31	Unruptured	10	30
Sensitivity = 100%			Sensitivity = 100%		
Specificity = 78%			Specificity = 75%		
Positive Predictive Value = 50%			Positive Predictive Value = 47%		
Negative Predictive Value = 100%			Negative Predictive Value = 100%		
c) Mean TS (threshold= 1500mmHg)			d) Mean TSI (threshold= 2.50)		
	Positive	Negative		Positive	Negative
Ruptured	9	0	Ruptured	9	0
Unruptured	10	30	Unruptured	6	34
Sensitivity = 100%			Sensitivity = 100%		
Specificity = 75%			Specificity = 85%		
Positive Predictive Value = 47%			Positive Predictive Value = 60%		
Negative Predictive Value = 100%			Negative Predictive Value = 100%		
e) Diastolic TS (threshold= 1230mmHg)			f) Diastolic TSI (threshold= 2.90)		
	Positive	Negative		Positive	Negative
Ruptured	9	0	Ruptured	9	0
Unruptured	10	30	Unruptured	5	35
Sensitivity = 100%			Sensitivity = 100%		
Specificity = 75%			Specificity = 88%		
Positive Predictive Value = 47%			Positive Predictive Value = 64%		
Negative Predictive Value = 100%			Negative Predictive Value = 100%		

($p < 0.01$ in all TS 's and TSI 's by Fisher 's exact test)

other features (16). It is, in addition, impossible to predict the rate of expansion in any one patient; some aneurysms remain stable for years and then expand rapidly. Since all aneurysms are potentially lethal and the rate of expansions and rupture are unpredictable, the criteria for active intervention must be decided on an individual basis (9). Thus accurate prediction is not yet possible.

Total fluid energy within the aorta is the sum of potential and kinetic energy (15), and acts as an expanding force against the aortic wall. Aortic diameter and blood pressure reflect potential and kinetic energy, respectively. The thickness of the aortic wall partly represents wall strength as a defensive factor. To consider these parameters simultaneously we introduced an integrated predicting factor, the tangential stress index.

Luminal diameters and wall thicknesses were measured at each level of maximal diameter and minimal wall-thickness within the aneurysm. In spite of possible overestimation of absolute tangential stress, this method

was used for standardization because the focus of this study was tangential stress index rather than tangential stress itself. The non-thrombosed and non-ruptured area was preferred for measurement of wall-thickness, due to difficulties in depicting the wall in these areas, although minimal wall-thickness including thrombus was used in the case of circumferential thrombosis. However, either because of subtle differences between usually thin aortic and aneurysmal wall, or thick scan slice, measurement of the thickness of aneurysmal wall was not straightforward. For prospective study, we adjusted the slice thickness of the data to that of retrospective study. This adjustment was necessary to reduce possible inter-study experimental error of wall-thickness measurement. For greater accuracy, thickness was measured manually on maximally magnified images, and these were displayed in a wide window setting which covered all densities of contrast enhanced aortic lumen, aortic wall and periaortic tissue. In consoles of EBT or spiral CT, thickness was measured pixel by pixel

el. Furthermore, by using analysis software running on the workstation, subpixel measurements were possible. With this kind of standardization, intraobserver (but not interobserver) error was reduced. We are attempting to overcome this error by, firstly, measuring the thickness of the aortic wall with a modality such as MRI, thus achieving greater conspicuity; secondly, by applying segmentation protocol to the subpixel scale by histogram analysis; and thirdly, by further modifying the modified Laplace's equation, thus reducing the influence of the wall thickness parameter. Although we were able to distinguish between abnormal and normal

Table 4. Verification of Diameter Method

a) Threshold = 50mm

	Positive	Negative
Ruptured	7	2
Unruptured	13	27

Sensitivity = 78%

Specificity = 68%

Positive Predictive Value = 35%

Negative Predictive Value = 93%

b) Threshold = 40mm

	Positive	Negative
Ruptured	9	0
Unruptured	23	17

Sensitivity = 100%

Specificity = 43%

Positive Predictive Value = 28%

Negative Predictive Value = 100%

wall, the parameter for wall strength, in this study, could not be considered because we were unable to measure strength itself. The thrombosis was in addition, regarded as a factor which increased strength; the thickness and diameter of the thrombosed area was thus not measured (2). As for eccentricity of an aneurysm, it was not clear, because of the limited number of eccentric aneurysms, whether or not the TSI method was useful. To clarify the usefulness of this method in an atypical-shaped aneurysm, further study is needed. Although there was still a considerable number of bias factors when measuring wall thickness, TSI provided better results than did Laplace value, implying that wall-thickness was certainly a helpful parameter for more accurately predicting aneurysmal rupture.

With regard to blood pressure parameters, systolic pressure is thought to play a direct role in breaking the aneurysmal wall but diastolic pressure also can increase the kinetic energy of intra-aneurysmal blood flow. Both systolic and diastolic pressure, therefore, might affect aneurysmal rupture by increasing the magnitude of peak and mean forces, respectively, toward the aneurysmal wall. Systolic pressure may fluctuate more than diastolic. For these reasons we analyzed all results by using each systolic, diastolic and mean pressure as a pressure parameter; the parameter was acquired on the basis of the ordinary value to which the patient was usually exposed. In the case of an unrecognized hypertensive patient without a history of antihypertensive medication, blood pressure was measured in the emergency room or scanning room. In the case of a rupture, blood pressure

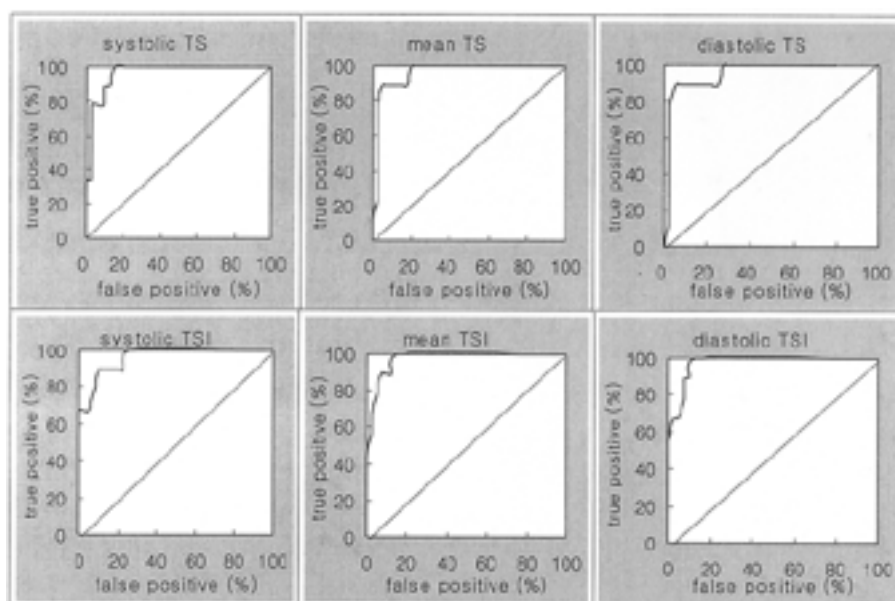


Fig. 4. ROC curves of tangential stresses and tangential stress indices. All curves located at the "useful study" zone. Among tangential stresses the systolic tangential stress showed the best result. However, systolic tangential stress index was located at less useful zone than those of other tangential stress indices. Mean and diastolic tangential stress indices revealed increased accuracy than tangential stresses. The diastolic tangential stress index curve shows the least false positive ratio at the maximal true positive ratio (100%) although the mean tangential stress index curve shows the most perfect curve.

Table 5. Statistical Analysis of Laplace Value (unmodified tangential stress)

a) Systolic Laplace value with threshold of 6600 mmHg.mm (mmHg.min)

	Positive	Negative
Ruptured	9	0
Unruptured	12	28

Sensitivity = 100%

Specificity = 70%

Positive predictive value = 43%

Negative predictive value = 100%

b) Mean Laplace value with threshold of 4930 mmHg.mm (mmHg.min)

	Positive	Negative
Ruptured	9	0
Unruptured	13	27

Sensitivity = 100%

Specificity = 68%

Positive predictive value = 41%

Negative predictive value = 100%

c) Diastolic Laplace value with threshold of 3700 mmHg.mm (mmHg.min)

	Positive	Negative
Ruptured	9	0
Unruptured	16	24

Sensitivity = 100%

Specificity = 60%

Positive predictive value = 36%

Negative predictive value = 100%

could be quite different to normal (presumably lower), and might reduce the tangential stress index, with negative influence on the separation of ruptured and unruptured groups. Our results, however, were significant. In patients receiving antihypertensive medication, the commonly exposed blood pressure was used whether or not blood pressure was within the normal range; this was because any situation which arose was the result of that blood pressure.

Other bias factors of tangential stress itself might be variable normal values of aortic diameter, wall thickness and blood pressure according to sex, aortic level and age. To compensate for these factors we formulated a tangential stress index, which could more exactly predict tangential stress. Among parameters, age was neglected because changes in blood pressure, aortic morphology, and wall strength during the aging process are naturally occurring permissible changes rather than

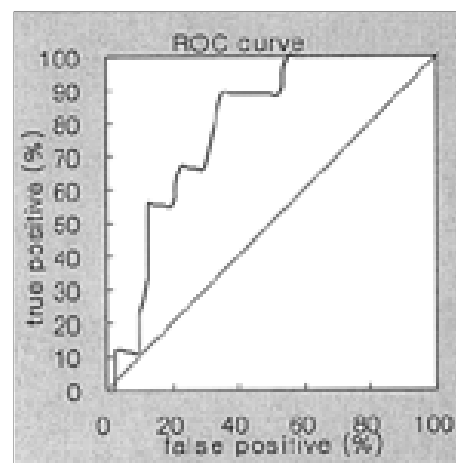


Fig. 5. ROC Curve of Diameter Method.

The curve locates near the "ordinary test" zone.

normal features. These permissible changes were therefore eliminated from standards in order to minimize false negative results. In this study, because the normal group was not large enough to calculate average wall thickness for each condition, normal aortic wall thickness for the normal group was calculated by averaging all values regardless of aortic level, age and sex. As far as we know, the literature contains no reports of measurement of normal thickness of aortic wall at multiple levels. Another limitation of this study was the lack of consideration of the temporal factor; this was because a lot of patients were surveyed retrospectively and few were followed up continuously.

Despite these limitations, the results obtained using the TSI method were better than those provided by the diameter method and other previously reported results. In this study, luminal diameters excluding thrombus thickness were used for standardized measurement, leading to underestimation of real aneurysmal diameter and exaggeration of the sensitivity of the diameter method. However, the sensitivity of the diameter method using 50 mm as a threshold value was lower than that of TS(I) methods. Of equal sensitivity to the TS(I) method, the specificity and positive predictive values of the diameter method were lower than those of the TS(I) method. Although the rate of aneurysmal growth, for instance, can be assumed to express very well the status of interaction between total fluid energy and wall strength, there is no clarification of the result, as mentioned above. The hyperattenuating crescent sign gave a very good result: 77% sensitivity, 93% specificity, 53% positive predictive value and 72% negative predictive value (23,24). However, if the sensitivity of mean TSI was set to a val-

ue similar to that of crescent sign (78%), the specificity, and positive and negative predictive values would be higher (95%, 78% and 95% respectively) than those results. We analyzed our results with emphasis on sensitivity because a false negative result could be crucial in these cases. When sensitivity was emphasized, diastolic TSI was selected as the best method even though the ROC curve of mean TSI revealed the best distribution. The average diastolic TSI value of the normal group in our study was lower than one (0.94), and it was probably due to smaller aortic sizes than those of westerners.

Tangential stress indices can be used to predict the fate of an aortic aneurysm. The method may also be used to conduct surveillance of subtle changes in aortic aneurysm during follow up, and could help establish a treatment regimen when a patient arrives at hospital. After initial TSI checking, the possibility of lowering the TSI into the safe range by antihypertensive therapy could be investigated. If such reduction is impossible, early surgical or interventional treatment is suggested. In recent studies, earlier surgery for rather small aneurysms has already been suggested (25). Fifty percent of patients less than 70 years old with small (< 5cm) aneurysms eventually required surgery, usually because their aneurysms eventually reached 5 cm (26).

In conclusion, tangential stress indices could be used as a more accurate prognostic factor of true aortic aneurysm than conventional methods. In particular, the diastolic tangential stress index could be the best predictor of aortic aneurysmal rupture, with emphasis on sensitivity. However, to eliminate limiting factors and to acquire a more accurate threshold value, further investigation of a large patient population is needed.

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