Ultrasonographic measurement of intima-media thickness of radial artery in pre-dialysis uraemic patients: comparison with histological examination

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Abstract

Background. Increased intima-media thickness (IMT) of the radial artery is associated with early failure of radiocephalic arteriovenous fistula (AVF) in haemodialysis patients. Therefore, non-invasive measurements of radial artery IMT before AVF operations are very important in predicting AVF patency. This study was designed to evaluate the accuracy of high-resolution ultrasonography in measuring radial artery IMT in pre-dialysis uraemic patients.

Methods. This study enrolled 43 pre-dialysis uraemic patients awaiting radiocephalic AVF operations for the first time. In this study, 17 age- and sex-matched uncomplicated hypertensive patients and 15 healthy subjects were included as a control. We measured the internal diameter (ID) and IMT of the radial artery using high-resolution ultrasonography on the wrists of uraemic patients as well as the control group before the AVF operation. We obtained specimens of the radial artery during the AVF operation and directly measured the IMT by histological examination.

Results. The radial artery IMT of the uraemic patients (0.41±0.09 mm) was significantly thicker, compared to both those of the hypertensive (0.33±0.05 mm, P<0.001) and the healthy patients (0.25±0.04 mm, P=0.002). In contrast, the radial artery ID in the uraemic patients (1.85±0.48 mm) was smaller than both that of the hypertensive patients (2.08±0.31 mm, P=0.023) and the healthy persons (2.34±0.37 mm, P=0.001). Radial artery IMT had a negative correlation with radial artery ID in a total of 73 subjects (r = -0.290, P=0.012). The value of the radial arterial IMT measured by sonographic examination correlated significantly with that by histological examination in 43 uraemic patients (r = 0.786, P<0.001) and it correlated significantly with early AVF failure (r = 0.358, P=0.027).

Conclusion. Our data suggest that high-resolution ultrasonography is an effective tool in measuring radial artery IMT in uraemic patients before AVF operation.

Keywords: arteriovenous fistula; haemodialysis; intima-media thickness; ultrasonography

Introduction

It has been recommended that the radiocephalic arteriovenous fistula (AVF) should be the first choice for vascular access for haemodialysis (HD) [1–3]. However, it continues to have a high incidence of early failure, which causes a decrease in the placement of the AVF [4–7]. The cause of most early failures is often unknown although the quality of the radial artery is thought to play an important role [5,8]. As a possible cause, we have reported that pre-existing intimal hyperplasia of the artery, which represents atherosclerosis of the radial artery, is closely associated with early failure of radiocephalic AVF [9]. However, there is no available non-invasive method to examine the presence or absence of the intimal hyperplasia before the AVF operation.

The arterial wall is composed of three layers: intima, media and adventitia. Of the three layers, intima-media thickness (IMT) represents the actual arterial wall and can be easily measured by high-resolution ultrasonography [10]. The increased IMT of the carotid artery is well known to be a non-invasive independent risk factor of cardiovascular mortality, which is easily assessed by high-resolution ultrasonography [11–15]. In recent
studies, we have found that increased IMT of the radial artery by histological examination is associated with early failure of radiocephalic AVF in HD patients [16]. Therefore, if a noninvasive method to detect radial artery IMT is performed before the operation, it would be a great aid to decide on an adequate site for the AVF. We designed this study to: (1) compare the IMT of the radial artery among uraemic patients, uncomplicated hypertensive patients and healthy subjects by using ultrasonographic measurements, and (2) evaluate the accuracy of ultrasonographic measurements of radial artery IMT by comparing them with histological measurements in uraemic patients.

**Patients and methods**

**Patient population**

This study enrolled 43 pre-dialysis uraemic patients awaiting their first radiocephalic AVF operation at Uijongbu St Mary’s Hospital between October 2002 and April 2004. Patients who received all synthetic grafts and native AVF operations on the upper arm were excluded from this study. Out of the 43 uraemic patients, 35 patients (81.4%) had hypertension. The primary renal disease consisted of diabetic nephropathy \( (n = 23) \), chronic glomerulonephritis \( (n = 13) \), hypertensive nephropathy \( (n = 5) \), polycystic kidney disease \( (n = 1) \), and unknown \( (n = 1) \). Subjects for the study included 17 age- and sex-matched uncomplicated essential hypertensive patients (age; 54 ± 7 years, female %; 52.9%) and 15 healthy persons (age; 57 ± 11 years, female %; 53.3%) used as a control group. Uncomplicated essential hypertension was defined as hypertension without any complications such as diabetes mellitus, coronary artery disease, cerebrovascular disease, peripheral vascular disease and renal disease.

**Measurement of IMT and internal diameter (ID) of radial artery by ultrasonographic examination**

High-resolution ultrasonography was used to measure the radial artery on the wrist of uraemic patients before the AVF operation and of control subjects. The examiner was confined to one skilled radiologist to avoid inter-observer variability, using a 12 MHz linear transducer with an HDI 5000 unit (Advanced Technology Laboratory, Bothell, WA). We measured radial artery IMT and ID twice and calculated mean values. The IMT was measured at the posterior wall of the radial artery just above the wrist on a longitudinal ultrasound image. The IMT was defined as the distance between blood-intima and media-advantitia interfaces and the ID was defined as the distance between blood-intima interfaces of anterior and posterior walls (Figure 1).

**Measurements of radial artery IMT by histologic examinations**

The AVF operation was performed using the method of end vein to side artery anastomosis under local anaesthesia. During the operation, a 10 mm long specimen of the radial artery wall was obtained at the incision site and stained with haematoxylin, eosin and trichrome. Slides were examined by a pathologist who was oblivious to the clinical data. IMT was measured as the sum of intima and media layers (Figure 2).

**Follow-up of AVF patency for 1 year after the operation**

AVF patency was prospectively followed-up for 1 year after the operation. First cannulation through the AVF for HD was individualized according to the state of venous maturation 4 weeks after the operation. AVF failure was defined as complete obstruction of the AVF or low blood flow insufficient to support a dialysis flow rate of 200 ml/min.

**Statistics**

All data was expressed with means ± SD. A comparison of mean values of the arterial measurements between uraemic and control groups and between diabetic and non-diabetic uraemic patients was made by using non-parametric Mann-Whitney test. The correlation between the radial artery ID and the IMT values and the correlation of the IMT values between ultrasonographic and histological methods, and
between IMT values and AVF failure were evaluated by Spearman’s correlation test. $P < 0.05$ was considered significant.

## Results

### Clinical characteristics in the uraemic and the control groups

The mean age of the uraemic patients was $57 \pm 13$ years (33–78 years) and the number of females was 23 (53.4%). There was no difference in age, sex, incidence of smoking, and serum cholesterol level among the uraemic patients, hypertensive patients and healthy subjects. Serum albumin levels in the uraemic patients were higher than those in the hypertensive patients ($P < 0.001$) and the healthy subjects ($P < 0.001$) (Table 1).

### Comparison of radial artery IMT and ID values measured by ultrasonography between the uraemic and the control groups

Mean values of radial artery IMT measured by high-resolution ultrasonography in the uraemic patients, hypertensive patients, and healthy persons were $0.41 \pm 0.09$ mm (0.3–0.7 mm), $0.33 \pm 0.05$ mm (0.25–0.39 mm) and $0.25 \pm 0.04$ mm (0.19–0.35 mm), respectively. The radial artery IMT of the uraemic patients was significantly thicker, compared to both those of the hypertensive ($P < 0.001$) and the healthy patients ($P = 0.002$). The radial artery IMT in the hypertensive patients was also thicker than the healthy subjects ($P < 0.001$) (Figure 3). Radial artery ID in the uraemic patients ($1.85 \pm 0.48$ mm) was smaller than that in the hypertensive patients ($2.08 \pm 0.31$ mm, $P = 0.023$) and that in the healthy persons ($2.34 \pm 0.37$ mm, $P = 0.001$). The radial artery ID in the hypertensive patients was also smaller than that in the healthy persons ($P = 0.039$) (Figure 4). The radial artery IMT in the diabetic uraemic patients ($n = 23$) was thicker than that in the non-diabetic uraemic patients ($n = 20$) ($0.44 \pm 0.09$ mm vs $0.38 \pm 0.08$ mm, $P = 0.032$). But there was no difference in the radial artery ID between the two groups ($1.92 \pm 0.41$ mm vs $1.79 \pm 0.53$ mm, $P = 0.212$).

### Correlation between radial artery ID and IMT values in total subjects ($n = 75$)

We evaluated the correlation between radial artery ID and radial artery IMT in total subjects ($n = 75$). There was a significant negative correlation between ID with IMT in all subjects ($r = -0.290$, $P = 0.012$) (Figure 5).

### Correlation of radial artery IMT between ultrasonographic and histologic examinations in 43 uraemic patients

We measured radial artery IMT in the 43 uraemic patients using histological examination of the arterial tissues obtained during the AVF operation. The mean value of radial artery IMT was $0.47 \pm 0.10$ mm (0.25–0.70 mm). The value of radial arterial IMT measured by sonographic examination correlated significantly with that by histological examination ($r = 0.786$, $P < 0.001$) (Figure 6).

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**Table 1.** The comparison of clinical factors among the uraemic patients, hypertensive patients and healthy subjects

<table>
<thead>
<tr>
<th></th>
<th>Normal ($n = 15$)</th>
<th>HBP ($n = 17$)</th>
<th>ESRD ($n = 43$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>$54 \pm 7$</td>
<td>$57 \pm 11$</td>
<td>$57 \pm 13$</td>
</tr>
<tr>
<td>Sex (female %)</td>
<td>$52.9$</td>
<td>$53.3$</td>
<td>$47.8$</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>$23.5$</td>
<td>$20.0$</td>
<td>$23.2$</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>$179 \pm 46$</td>
<td>$190 \pm 25$</td>
<td>$187 \pm 33$</td>
</tr>
<tr>
<td>Albumin (mg/dl)</td>
<td>$4.1 \pm 0.5$</td>
<td>$4.1 \pm 0.5$</td>
<td>$3.5 \pm 0.5^*$</td>
</tr>
</tbody>
</table>

* $P < 0.001$, vs normal and HBP. Normal, healthy subjects; HBP, hypertensive patients; ESRD, uraemic patients.

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**Fig. 3.** The comparison of radial artery IMT measured by ultrasonographic examination among the uraemic patients, hypertensive patients, and healthy persons. See increased IMT of the uraemic patients, compared to the hypertensive patients and healthy person. *$P = 0.002$, vs control, **$P < 0.001$, vs HBP.

**Fig. 4.** The comparison of radial artery ID measured by ultrasonographic examination among the uraemic patients, hypertensive patients, and healthy persons. *$P = 0.001$, vs control, **$P = 0.023$, vs HBP, ***$P = 0.039$, vs control.

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**Fig. 5.** The correlation between radial artery ID and radial artery IMT in total subjects ($n = 75$).
Relationship between radial artery IMT value and early AVF failure

Of the total 43 patients, five patients died with a patent AVF within 1 year after the operation. Of the 38 patients who were alive until the end of the study point, 14 patients experienced AVF failure. We evaluated the relation between radial artery IMT and AVF failure in these 38 patients. The IMT value in the failed group (n = 14) was thicker than that in the patent group (n = 24) (0.46 ± 0.08 mm vs 0.40 ± 0.09 mm, P = 0.032). The IMT value correlated significantly with the AVF failure (r = 0.358, P = 0.027). Radial artery ID in the failed group tended to be smaller than that in the patent group; however, the difference was not significant (1.63 ± 0.40 mm vs 1.96 ± 0.52 mm, P = 0.054).

Discussion

The National Kidney Foundation Dialysis Outcome Quality Initiative (NKF-DOQI) guidelines provide recommendations that native AVF should be first constructed for vascular access to improve quality of life and overall outcomes for HD patients [3]. But native AVF continues to have a high incidence of early failure, thus decreasing the popularity of placement of AVF. Therefore, it is very important to detect before operation poor quality radial arteries that cause early AVF failure [4–7]. Doppler ultrasonography is an objective and noninvasive method to assess the quality of the peripheral vessels [11–15]. Important parameters of the vessels that can predict AVF failure in predialysis uraemic patients before the operation are small diameter of the radial artery and cephalic vein, and low arterial blood flow [5,17,18]. Malovrh [19] have reported that distension capacity of the artery and vein as well as the size of the baseline internal diameter are important to predict AVF patency.

The impact of radial artery IMT on AVF patency in uraemic patients is not well known. We have retrospectively studied the impact of radial artery IMT measured by histologic examination on early AVF failure within 1 year after the operation in 90 uraemic patients. In the 90 patients, the mean value of radial artery IMT in the failed group was thicker than that in the patent group who underwent operation for AVF. The patients whose IMT was more than 500 μm had higher incidence of the AVF failure than the patients whose IMT was less than 500 μm [16]. If we can detect increased radial artery IMT before the operation, it will be helpful for the surgeon to decide on the type of vascular access. Based on these findings, we prospectively performed this study to evaluate the accuracy of ultrasonographic measurements of radial artery IMT by comparing it with histological measurements in uraemic patients. This study clearly demonstrated that radial arterial IMT measured by ultrasonographic examination was similar to findings done by histological examination. Therefore, we suggest that ultrasonographic examination should be used to measure the IMT of the radial artery before the AVF operation in the uraemic patients. This is the first report to compare radial artery IMT between ultrasonographic and histological examinations in uraemic patients.

Clinical risk factors of increased intimal hyperplasia or IMT of the radial artery are known to be old age, diabetes mellitus, hypertension and atherosclerosis [9,16,20]. Due to the high incidence of diabetes mellitus, hypertension and atherosclerosis in uraemic patients, it is suggested that radial arterial IMT in uraemic patients may be thicker than that of age-matched healthy populations. Ejerblad et al. [21] first reported that the radial arterial wall in HD patients measured by
Intima-media thickness of radial artery in uraemic patients

histological examination was significantly thicker than that of control subjects. We selected age-, sex-matched uncomplicated hypertensive patients and healthy subjects as a control and measured radial artery IMT by ultrasonographic examination. This study showed that uraemic patients had thicker radial artery IMT than hypertensive patients and healthy controls.

The IMT can be assessed by B-mode ultrasound and represents a safe, inexpensive, precise and reproducible measure [11–15]. But it has the limitation of inter- and intra-observer variability. In order to minimize these variables in this study, the examiner was confined to one skilled radiologist and the IMT was measured twice for mean values to be calculated. The size of the radial artery diameter is relatively small; the size of radial artery IMT is also small and its normal range is known to be less than 250 μm [20,22]. Therefore, in order to measure it accurately, ultrasonography needs higher resolution than a 7.5 MHz transducer. In this study, a 12.5 MHz transducer was used. The AVF operation was performed uniformly by one vascular surgeon at the same site (on the wrist) using the same surgical technique (end-to-side anastomosis) and the pathologic specimen was evaluated by one pathologist blinded to clinical data.

In this study, the value of radial arterial IMT measured by ultrasonographic examination correlated well with that by histological examination (r = 0.786, P < 0.001). However, some cases showed significant discrepancy between these two methods. This can be explained by two causes: the first is due to the sonographic examiner’s inadequate measurement of the IMT due to small radial artery size, poor ultrasonic window and wavy arterial course; the second is due to different measurement sites between ultrasonographic and histological examinations. The IMT was measured ultrasonographically on the posterior wall of the radial artery. In contrast, the radial artery specimen was obtained on the partial arterial wall at the incision site, which was usually positioned at the anterior wall. If there is irregular arterial wall thickening in the measurement sites of the radial arteries, it could cause a discrepancy in the IMT between these two examinations.

In conclusion, increased radial artery IMT is known to be a risk factor of early AVF failure. Therefore, it is very important to detect poor quality of the radial artery before operation in order to enhance the radiocephalic AVF patency in uraemic patients who are planning to undergo AVF operation. Our data suggest that high-resolution ultrasonography is a simple and effective tool in measuring radial artery IMT. We recommend that the measurement of radial artery IMT by ultrasonography be performed in uraemic patients who have poor vascularity such as old age, diabetes mellitus, and severe atherosclerosis before the radio cephalic AVF operation.

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Conflict of interest statement. None declared.

References


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