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Articles

Performance evaluation of arteriovenous fistula models simulating shunt murmurs in hemodialysis patients

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I. Introduction

Detection of vascular access (VA) dysfunction at an early stage when VA stenosis is slight and avoidance of incorrect timing for performing percutaneous transluminal angioplasty (PTA) are important in VA management. The guideline issued by the Japanese Society for Dialysis Therapy notes the advisability in routine VA management of performing visual observation, palpation, auscultation, and other methods of physical examination in combination with surveillance using ultrasonic (US) diagnostic and other measurement systems according to their availability at the individual facility.

We have previously proposed the use of an acceleration sensor and measurement of shunt murmurs as a new method of VA function assessment that is non-invasive, quantitative, and objective, with acceleration sensing and measurement of the shunt murmur signal and performance of time-frequency analysis by wavelet transformation and representation of the results as a colored map image of the amplitude spectrum of the frequency components. We also reported a method of quantitatively monitoring the decrease over time in VA function by the use of R, the normalized cross-correlation coefficient representing the degree of match between the images, which is calculated with the time-frequency analysis image of the shunt murmur measured during good VA function in a hemodialysis patient taken as reference data and shunt murmur analysis measurement images over time taken as comparative data. However, we were unable to find any reports clearly showing a quantitative relationship between the VA blood vessel stenosis rate and shunt murmur acoustic characteristics. Also remaining unclear is the relationship between the stenosis rate cutoff, which is an indicator of poor blood removal, and the shunt murmur acoustic characteristics. We therefore constructed an arteriovenous fistula (AVF) model to quantitatively assess the change in shunt murmur acoustic characteristics accompanying an increase in the stenosis rate, with a tube simulating vascular elasticity and a Y-shaped tube connecter simulating a AVF. The change in R

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calculated from the simulated shunt murmur measured for each stenosis rate was then investigated. R was also calculated from the shunt murmur of a hemodialysis patient, and the change over time in R from immediately after the first PTA to the next PTA was determined, and its relationship to the values of R calculated from the simulated shunt murmur measured in the AVF model at differing stenosis rates was examined to determine the quantitative relationship between the stenosis rate and the shunt murmur acoustic characteristics.

II. Experimental methods

2-1 Measurement of the simulated shunt murmur in the AVF model and calculation of normalized cross-correlation coefficient R

The outflow-vein side of the Y-shaped tube connecter simulating the AVF anastomosis site was severed 10 mm from its bifurcation. To reproduce the simulated shunt murmur that would serve as a reference for good VA function, a Toughsilon gel tube was connected to the outflow vein side of the Y-shaped tube connector, and the junction was secured with a cable tie. A silicone rubber tube was connected to the inflow artery side and the peripheral artery side of the Y-shaped tube connector, and it thus simulated the standard surgery of AVF side-to-end anastomosis, but clamp closure was performed 20 mm from the connector end of the peripheral artery side to construct an AVF model with a 0% stenosis rate and functionally with no stenosis in the outflow vein downstream of the anastomosis site in end-to-end anastomosis.

To construct the stenosis site, a hole was formed in the center of each of a number of acrylic cylindrical blocks 6 mm in diameter and 10 mm in length. The hole diameters ranged from a maximum of 5.4 mm for 10% stenosis to a minimum of 0.6 mm for 90% stenosis, in stenosis rate increments of 10%. Each block containing the stenosis site was inserted into the outflow-vein side of the Y-shaped tube connector and secured with adhesive, and the Toughsilon gel tube was connected to construct 9 types of the AVF model, each simulating a different size of stenotic lesion on the outflow-vein side downstream from the anastomosis site.

To measure the simulated shunt murmur occurring in the outflow vein of the AVF model, the Toughsilon gel tube was implanted in a biological phantom (konjac jelly) to simulate biological acoustic impedance. The pulsatile flow of a multipurpose pulsation pump was set at a heart rate of 60 pulses/min with a duty rate of 35%, the ratio between heart systole and diastole. To simulate blood pressure values in a hemodialysis patient, the high and low outputs in the pulsatile flow were adjusted to obtain maximum and minimum pressures of 120 mmHg and 80 mmHg, respectively, in the tube upstream of the Y-shaped tube connector. During the experiment, the maximum and minimum pressures were monitored constantly with a biological information monitor, and the flow rate Q_0 [ml/min] of water circulating at each stenosis rate in the AVF model was measured with a graduated cylinder.

An appropriate amount of US gel was applied to the surface of the biological phantom at 20 mm from the end of the Y-shaped tube connector, an acceleration sensor was next mounted on the surface, and the simulated shunt murmur at that position was then measured for 10 sec with a bio sound analyzer (BSA). The simulated shunt murmur signal obtained with each stenosis-rate model type was analyzed with WaveletDisp and WaveletBitMapAnalyzer bio sound analysis software, with the simulated shunt murmur signal measured in the AVF model types, with stenosis rates of 0% and 10% or more as the reference data and the comparative data, respectively. The normalized cross-correlation coefficient R representing the degree of match between the images resulting from the time-frequency analysis results in the comparison between the reference data and the comparative data was determined for quantification of the change in the simulated shunt murmur with a stepwise increase in the stenosis rate.

2-2 Change over time in R determined from shunt murmur in hemodialysis patients

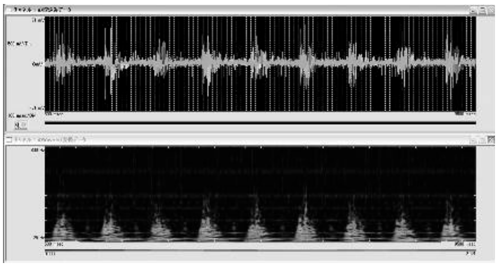
An acceleration sensor was mounted on subject A with a specialized double-sided tape at 3 positions: ① the anastomosis site; ② the puncture site on the blood removal side; and ③ the puncture site on the blood return side. Before initiation of therapy, the shunt murmur was measured with a BSA for 3 sec. Subject A was a 72-year-old man with diabetic nephropathy as the primary disease and VA with an AVF dialysis duration of 7 years and 3 months. With the anastomosis site taken as the reference (0 cm), ② the puncture site on the blood removal side was at a position just after the stenosis site approximately 7 cm from the anastomosis site on the central side, and ③ the puncture site on the blood-return side was at a position approximately 20 cm from the anastomosis site on the central side. On the 21st day after PTA, the blood removal flow rate was 250 mL/min, and VA function was judged as generally good, and it was taken as the reference date. The shunt murmur signal measured on the reference date was taken as the reference data, and the shunt murmur signal measured every week over time for approximately 6 months after the reference date was taken as the comparative data to investigate the change over time in R. R was calculated using the signal at ② the puncture site on the blood removal side, which among the shunt signal murmurs measured at the 3 positions ① to ③ most fully reflected the effect of stenosis. Measurement of the shunt murmur was performed after providing the subject with sufficient explanation and receiving his written consent.

III. Experimental results

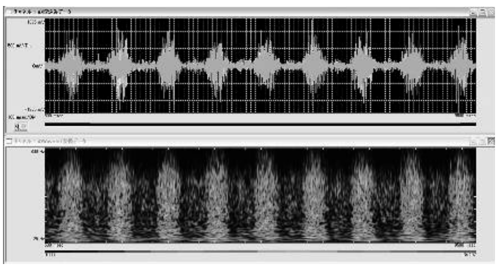
3-1 R calculated for simulated shunt murmurs measured in the AVF model with various stenosis rates

The upper part of ***Fig. 1(a)*** shows the simulated shunt murmur signal measured in the AVF model with a 0% stenosis rate, and the lower part shows the result of the wavelet transformation represented by the map colored blue to red in accordance with the size of the frequency spectrum. The lower part shows that the frequency composition of the simulated shunt murmur signal was distributed in the low-frequency domain of approximately 25 Hz to 150 Hz. The upper part of ***Fig.1(b)*** shows the results of the wavelet transformation for the simulated shunt murmur signal measured in the AVF model with an 80% stenosis rate, and the results in the lower part show that the frequency composition of the simulated shunt murmur signal was distributed in a broad range of approximately 25 Hz to 600 Hz.

Fig. 2 shows examples of R obtained with the

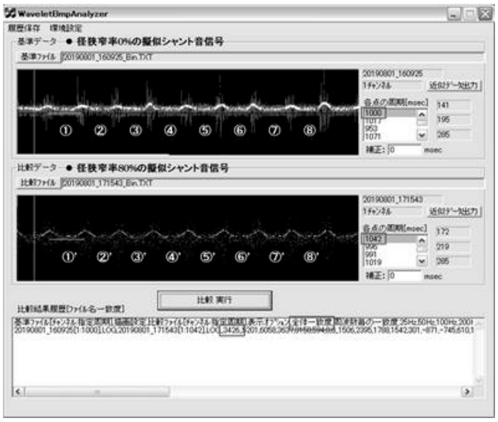


(a) stenosis rate of 0%

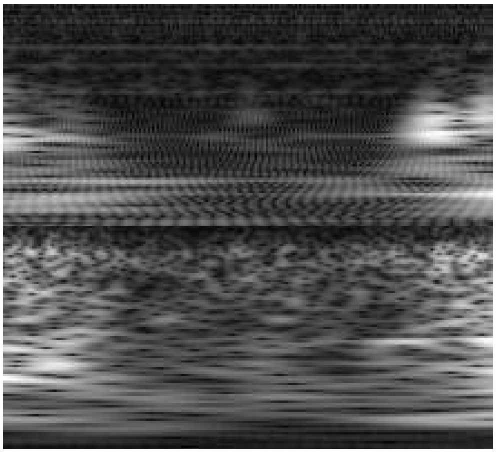


(b) stenosis rate of 80%

Fig.1 Simulated shunt murmur signalsmeasured in AVF models



(a) Calculation example of R



(b) Wavelet transformation results
(upper figure: stenosis rate of 0%,
lower figure: stenosis rate of 80%)

Fig.2 Calculation method of R with analytical software for simulated shunt murmur signals

analytical software for the simulated shunt murmur signals obtained in the AVF model with a stenosis rate of 0% shown in the upper part of ***Fig.2(a)*** as the reference data and stenosis rates of 10% to 90%, with that of 80% shown in the lower part as comparative data. Also shown in the box labeled Time Period of Each Point are the time periods of the amplitude peak of the simulated shunt murmur signal; in these examples, the 8 periods are from ① to ⑧. For the simulated shunt murmur signal of the 0% stenosis rate in ***Fig.2(a)***, the amplitude peak time period of period ① was 1,000 ms. When this was selected, then, in the signal waveform, a yellow straight line appeared between the amplitude peaks in the related waveform. Similarly, the 8 periods ①' to ⑧' were obtained for the simulated shunt murmur signal measured in the model with an 80% stenosis rate shown in the lower part. The results of wavelet transformation obtained for the reference data ① and for the comparative data ①' are shown in ***Fig.2(b)***. The calculated R values represent the degree of match between these two images and are shown in the box labeled Comparison Result History. The degree of match found in this case was R=3,426. For the combinations of the 8 reference-data periods and the 8 comparative-data periods that resulted in a total number of 64, calculating R for each and obtaining the mean values yielded the changes in R relative to stenosis rate (%) shown in ***Fig.3***. As shown by these results, R remained nearly constant at approximately 6,500 with rising stenosis rates up to 40%, but it decreased in nearly a straight line as stenosis rates rose above 50%; Q_0 similarly followed a nearly straight-line decrease.

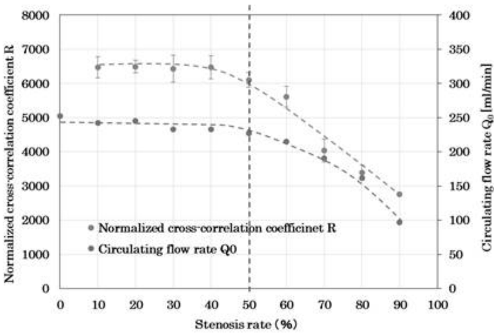
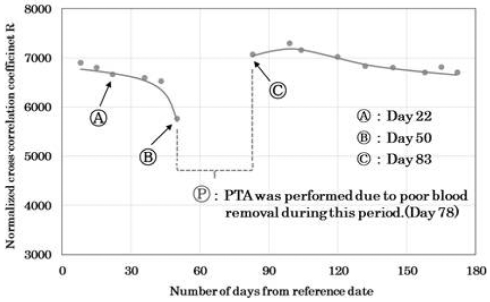


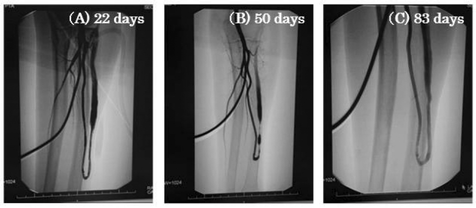
Fig.3 Change of normalized cross-correlation coefficient R and circulation flow rate Q_0 to stenosis rate

3-2 Calculated R values of the shunt murmur measured in a hemodialysis patient

Fig.4(a) shows the shunt murmur signal measured at ② the puncture site on the blood removal side of subject A at the time of good VA function after PTA as reference data and, as comparative data, the subsequent temporal course of the mea-



(a) Change over time in normalized cross-correlation R



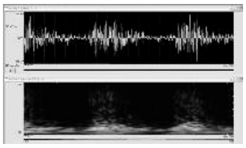
(b) Angiography results

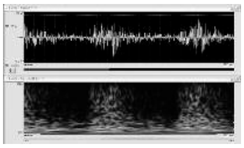
Fig.4 Relationship between number of days from reference date and normalized cross-correlation coefficient R

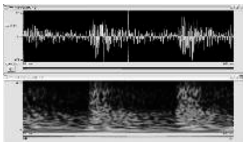
sured shunt murmur signal found by monitoring the change over time in R for a period of approximately 6 months. The VA function was initially found to be good following the PTA, with R maintaining a value of approximately 7,000, but it decreased gradually from (A) 22 days after the reference date (43 days after the PTA date) to less than 5,000 by (B) 50 days after the reference date (71 days after the PTA date). This was accompanied by a gradual decrease in the blood removal rate from Q = 250 mL/min at the time of reference data measurement to an insufficient level of 100 to 150 mL/min at approximately 50 days after the reference date. ***Fig.4(b)*** shows the angiography results of subject A (A) before PTA at approximately 22 days, (B) before PTA at approximately 50 days, and (C) after PTA at approximately 83 days. These angiograms show stenosis of approximately 5 cm from just after the anastomosis site toward the central side and thus permit confirmation of a stenotic lesion ② just before the puncture site on the blood removal side. PTA was then performed again at 78 days after the base date (99 days after the PTA date), followed by improvement in the stenotic lesion and recovery in R to the level found on the day of the reference measurement.

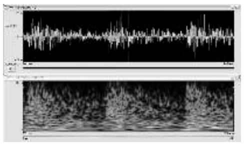
IV. Discussion

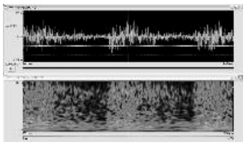
R as calculated from the simulated shunt murmur measured in the AVF model with various stenosis rates was found to closely resemble the change over time in R calculated from the shunt murmur measured in the hemodialysis patient who showed gradual progress in a stenotic lesion after PTA and underwent PTA again. ***Fig. 5(a)*** shows the results of analysis of the measured shunt murmur for subject A at ② the puncture site on the blood removal side (1) just after PTA and (2) 8, (3) 22, (4) 36, and (5) 50 days after the reference date. At (1) just after PTA, the stenotic lesion improved, and the improvement in the blood removal state resulted in the finding of a continuous shunt murmur known as a low-pitch murmur with a frequency composition of approximately 25 to 150 Hz. In subject A, repeated stenosis of approximately 5 cm occurred from just after the anastomosis site toward the central side, and the stenotic lesion progressed in the course of time after PTA from (2) to (5). The intermediate to high frequency compositions of approximately 200 to 800 Hz, which were not observed at (1), therefore gradually increased, and an apparent change in shunt murmur from low pitch to an intermittent high pitch with a high frequency composition can be confirmed. The results of the simulated shunt murmur analysis in the AVF model with various stenosis rates shown in ***Fig.5(b)*** indicate stenosis rates of (1) 0%, (2) 20%, (3) 40%, (4) 60%, and (5) 80%. Comparison of ***Fig.5(a)*** and ***(b)*** shows that the change in images accompanying the time course from PTA in the hemodialysis patient resembles the change in images accompanying the increase


(1) just after PTA

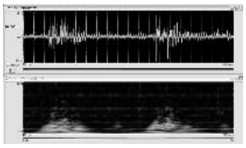

(2) 8 days

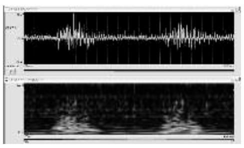

(3) 22 days

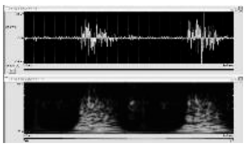

(4) 36days

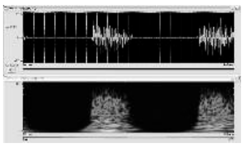

(5) 50 days

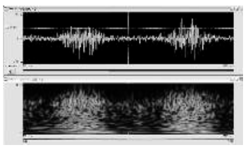
(a) Analysis results of shunt murmurs measured in a hemodialysis patient


(1) 0%


(2) 20%


(3) 40%


(4) 50%


(5) 80%

(b) Analysis results of simulated shunt murmurs measured in AVF model

Fig.5 Comparison of analysis results of simulated shunt murmur and shunt one measured in a hemodialysis patient

in stenosis rate in the AVF model. With the blood vessel diameter a in the angiography results shown in ***Fig.4(b)*** approximately (C) 83 days after PTA taken as the reference, the stenosis rate ($\frac{a-b}{a}\times100$ [%]) calculated from the blood vessel diameter b at (A) approximately 22 days after the reference date was 41.9%, which closely approximates (3) the stenosis rate of 40% in ***Fig.5(b)***. Similarly, the stenosis rate calculated from blood vessel diameter b at (B) approximately 50 days in ***Fig.4(b)*** was 80.5%, and, thus, it also closely approximates (5) the stenosis rate of 80% in ***Fig.5(b)***. These results show that the progress in the stenotic lesion can be quantitatively assessed by monitoring the change over time in R calculated from the shunt murmur obtained from the hemodialysis patient, and that the stenosis rate can be fairly though approximately estimated.

Conditions for VA stenosis therapy should include a stenosis rate of 50% or more together with at least one of the following clinical medical abnormalities: (1) blood flow decline, swelling formation, (2) elevated venous pressure, (3) abnormally high BUN value or elevated recirculation rate, (4) unpredictable dialysis rate decline, or (5) abnormal physical finding. ***Fig.3*** shows that both R and Q_0 decrease linearly when the stenosis rate in the AVF model exceeds 50%. The investigation of use of the constructed AVF model thus also shows that a stenosis rate cutoff value of 50% can be obtained and serve as an indicator, and that 6,000 can be taken as the R cutoff value. Accordingly, observation of the change over time in R in a hemodialysis patient in ***Fig.4(a)*** shows that when R declines to less than 6,000 at Ⓑ, the stenosis rate rises to 80% and closely matches the clinical result of subsequent PTA.

This method appears to permit simple calculation of R from a recording of the shunt murmur using an acceleration sensor, electronic stethoscope, or other such device and can accordingly be performed with no major expenditure of labor, effort, or time. In addition, elucidation of the R cutoff value will enable the use of this method in screening for stenotic lesions and in comprehensively determining, along with other physical findings, the need for further more careful examination in cases of R decreasing below the cutoff value. It can also presumably be used for early detection of VA dysfunction at a stage of slight stenosis and contribute to effective VA management for long-term VA patency.

V. Summary and further studies

Comparison between the analytical images of the shunt murmur of a hemodialysis patient with progress in stenotic lesion and those of the simulated shunt murmur measured in the AVF model clearly showed that image changes with an increasing stenosis rate closely resemble the image changes observed in the course of time after PTA. This finding shows that, by monitoring the change in R in shunt murmur after the VA in a hemodialysis patient, it will be possible to quantitatively assess the progress of a stenotic lesion and perform a fair though approximate estimation of the stenosis rate. Further studies will include measurement of the brachial arterial flow rate (FV) and the vascular resistance index (RI) under stepwise changes in the stenosis rate in the AVF model, and investigation of the relevance of VA function assessment by R.

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