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Original Article

Evaluating the Need for and Effect of Percutaneous Transluminal Angioplasty on Arteriovenous Fistulas by Using Total Recirculation Rate per Dialysis Session ("Clearance Gap")

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The functioning of an arteriovenous fistula (AVF) used for vascular access during hemodialysis has been assessed mainly by dilution methods. Although these techniques indicate the immediate recirculation rate, the results obtained may not correlate with Kt/V. In contrast, the clearance gap (CL-Gap) method provides the total recirculation rate per dialysis session and correlates well with Kt/V. We assessed the correlation between Kt/V and CL-Gap as well as the change in radial artery (RA) blood flow speed in the fistula before percutaneous transluminal angioplasty (PTA) in 45 patients undergoing continuous hemodialysis. The dialysis dose during the determination of CL-Gap was 1.2 to 1.4 Kt/V. Patients with a 10% elevation or more than a 10% relative increase in CL-Gap underwent PTA ($n = 45$), and the values obtained for Kt/V and CL-Gap before PTA were compared with those obtained immediately afterward. The mean RA blood flow speed improved significantly (from 52.9 to 97.5 cm/sec) after PTA, as did Kt/V (1.07 to 1.30) and CL-Gap (14.1% to −0.2%). A significant correlation between these differences was apparent ($r = -0.436$ and $p = 0.003$). These findings suggest that calculating CL-Gap may be useful for determining when PTA is required and for assessing the effectiveness of PTA, toward obtaining better dialysis.

Key words: hemodialysis, recirculation, clearance gap, vascular access, percutaneous transluminal angioplasty

Percutaneous transluminal angioplasty (PTA) is often performed to treat stenotic lesions in an arteriovenous fistula (AVF) that is used for vascular access for hemodialysis. However, there are no clearly established criteria for judging when PTA is indicated or its effect on the adequacy of dialysis. Previously, it was often assumed that decreasing the rate of stenosis occurrence was the most important goal of PTA; thus, morphologic evaluations done radiologically were considered the primary assess-

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ments for determining whether PTA was necessary or effective, and changes in stenosis were regarded as indications that PTA was required or had improved the efficiency of dialysis efficiency [1, 2].

The dialysis rate, or Kt/V, was recently suggested to be a more objective evaluation method for an AVF [3-6]. Kt/V, however, is associated with multiple factors; in addition to urea clearance, the length of dialysis and quantity of blood flow (QB) can affect Kt/V values. Because QB depends on the condition of the vascular access, adequate Kt/V values cannot be obtained unless the access is functioning well. Moreover, it is difficult to obtain such values when there is a high recirculation rate, even when QB is sufficient. Therefore, it is necessary to include the recirculation rate as a factor when performing a comprehensive functional evaluation of an AVF. Various methods for determining the recirculation rate have been proposed, but there is no standard technique [7-9].

Recirculation rate and access function are closely correlated, and it can be assumed that improvements in recirculation rate and dialysis efficiency parallel each other. Thus, the use of recirculation rates in evaluation of the indications for and effects of PTA could be expected to contribute to an objective assessment method. There are 2 types of recirculation rate: the immediate recirculation rate, which is determined by using a hematocrit dilution technique [7, 8], and the total recirculation rate per dialysis session, which is reflected by the urea clearance gap (CL-Gap) [9]. It is not known whether the immediate recirculation rate correlates with Kt/V. However, to assess the functional evaluation of vascular access hematologically and to assess the recirculation rate and dialysis efficiency at the same time, the determination of the total recirculation rate per dialysis session may be the more appropriate choice.

In this study, we used the clearance gap (CL-Gap) method to evaluate the need for and results of PTA, focusing on the recirculation rate.

Patients and Methods

All patients provided informed consent to their participation in this study, and the study protocol was approved by the institutional review board of Shigei Medical Research Hospital.

Forty-five patients in our unit underwent creation of a radiocephalic AVF. These patients met the following criteria: they were without heart failure; they had a B-type natriuretic peptide (BNP) level < 283 pg/mL; and they did not fall under New York Heart Association (HYHA) category subsequently required PTA because of a stenotic lesion between April and December 2011. Before and after PTA, the Kt/V was set at 1.2 to 1.4 and the recirculation rate was calculated by the CL-Gap method.

The CL-Gap represents the difference between the expected dialysis efficiency and the actual dialysis efficiency; therefore, it is indicated by the difference between the theoretical clearance value (tCL) on the dialysis membrane side and the effective clearance (eCL) from the patient. The method for calculating CL-Gap is detailed in Fig. 1 and is summarized as follows: CL-Gap (%) $= (\text{tCL} - \text{eCL})/\text{tCL} \times 100$. The eCL was calculated as $K = V/T \times Kt/V$ [10], where K indicates clearance (mL/min), T indicates the length of dialysis (minutes) and V is body fluid volume (mL). V is calculated by using the Watson formula [11] + weight gained; for a man, this is $(2.447 - 0.09516 \times \text{age} + 0.1074 \times \text{height in cm} + 0.3362 \times \text{dry weight in kg} + \text{weight gained in kg}) \times 1{,}000$ mL; for a woman, this is $(-2.097 + 0.1069 \times \text{height in cm} + 0.2466 \times \text{dry weight in kg} + \text{weight gained in kg}) \times 1{,}000$ mL. There is a limitation in calculating tCL: urea clearance *in vitro*, based on each dialyzer membrane, is within 200 mL/min. The calculation sheet for the CL-Gap formula is available at http://juns.cool.ne.jp (Fig. 1).

PTA was performed when a 10% absolute increase in CL-Gap or a 10% relative increase was observed. The blood flow speed in the radial artery (RA) was measured by angiography with iodine-positive contrast medium for patients without an iodine allergy, or with carbon dioxide gas-negative contrast medium for patients with an iodine allergy, and the values for Kt/V and CL-Gap were calculated both before and after PTA. The same dialysis conditions, routes of blood removal and transmission, and puncture position were used before and after PTA.

The carbon dioxide angiographic examination used a cardiac catheter test device (Philips Electronics Japan, Tokyo, Japan), and carbon dioxide was supplied by a carbon dioxide injector, GASTER (Gadelius Medical, Tokyo, Japan). When carbon

CL-Gap(%)=(tCL-eCL)/tCL*100

$eCL=K=V/t*ln(Urea_{pre}/Urea_{post})$

K	: urea clearance per hemodialysis (ml/min)
V	: patient's total body water(ml)$_{watson\ formula}$
t	: dialysis time(min)
$Urea_{pre}$	: urea concentration at predialysis(mg/dl)
$Urea_{post}$	: urea concentration at postdialysis(mg/dl)

$ln(Urea_{pre}/Urea_{post})=Kt/V_{sinzato\ formula}$

$tCL=E_{(in\ vivo)}*QB_{(in\ vivo)}$

$E_{(in\ vivo)}$	: expected dialysis effectiveness in vivo
$QB_{(in\ vivo)}$	: quantity of blood volume in vivo(ml/min)

$E_{(in\ vivo)}=[1-exp\{N_{UTU}(1-Z_{(in\ vivo)})\}]/[Z_{(in\ vivo)}-exp\{N_{UTU}(1-Z_{(in\ vivo)})\}]$

N_{UTU}	: urea transfer unit
$Z_{(in\ vivo)}$	: $QB_{(in\ vivo)}/QD_{(in\ vivo)}$
$QD_{(in\ vivo)}$	: quantity of dialysis solution volume in vivo(ml/min)

$N_{UTU}=K_{TUTI}*(A_{SADM}*10000)*60/QB_{(in\ vivo)}$

K_{TUTI}	: total urea transfer index
A_{SADM}	: surface area of each dialyzer membrane(m^2)

$K_{TUTI}=(QB_{(in\ vitro)}/60)(A_{SADM}*10000)(1-Z_{(in\ vitro)})*ln\{(1-E_{(in\ vitro)}Z_{(in\ vitro)})/(1-E_{(in\ vitro)})\}$

$QB_{(in\ vitro)}$	: quantity of blood volume in vitro(ml/min)=200(ml/min)
$QD_{(in\ vitro)}$	: quantity of dialysis solution volume in vitro(ml/min)=500(ml/min)
$Z_{(in\ vitro)}$	: $QB_{(in\ vitro)}/QD_{(in\ vitro)}$=200(ml/min)/500(ml/min)=0.4
$E_{(in\ vitro)}$	: dialysis effectiveness in vitro =

Urea clearance in vitro based on each dialyzer membrane(ml/min)/$QB_{(in\ vitro)}$=
Urea clearance in vitro based on each dialyzer membrane(ml/min)/200(ml/min)

Fig. 1 Methods for calculating theoretical clearance (tCL), effective clearance (eCL), and clearance gap (CL-Gap) in patients undergoing hemodialysis.

dioxide gas is manually injected into a vessel during angiography, the direction of the gas influences the flow speed in the RA; thus, a difference in flow speed between the upward and downward direction develops. To reduce this difference, the brachial artery is punctured at the cubital fossa with a 22-ga. elaster needle (which is left in place), and the carbon dioxide is injected at 4 mL per sec (8–10 mL per injection). Bubble flow caused by the gas injection is depicted at 30 frames/sec. The bubble flow rate was measured at the straight segment of the RA and was considered to be the RA blood flow speed in the AVF. The same method was used for the iodine angiography. Iodine contrast medium, Iomeprol, equivalent to 300 mg of iodine (Brocco-Eizai Co., Tokyo, Japan) was diluted to half concentration with saline, and injected at 4 mL/sec (8–10 mL per injection).

Differences between pre-PTA and post-PTA values for RA blood flow speed, Kt/V, and CL-Gap were assessed by using box-and-whisker plots in the 45 patients who underwent PTA. Lastly, the correlation between RA blood flow speed improvement and CL-Gap improvement after PTA was analyzed by a scatterplot to judge PTA efficacy immediately after the PTA. All of the analyses were conducted by PASW version 18.0J (SPSS Japan Inc. Tokyo, Japan), and p-values less than 0.05 (two-sided) were considered as significant.

Results

Forty-five patients were studied: 28 men and 17 women; mean [± SD] age, 63 ± 11 years; mean dialysis duration, 58 ± 63 months; diabetes, 20 patients [44.4%]. The mean (± SD) blood flow speed in the RA in the 45 patients who underwent PTA increased from 52.9 ± 27.8 cm/sec before PTA to 97.5 ± 29.7 cm/sec after PTA ($p < 0.001$, Fig. 2); thus, the speed after the procedure was 2.33 times greater than that beforehand. The mean value for Kt/V increased from 1.07 ± 0.24 to 1.30 ± 0.15 ($p < 0.001$, Fig. 3), and the mean value for CL-Gap (%) decreased from 14.1

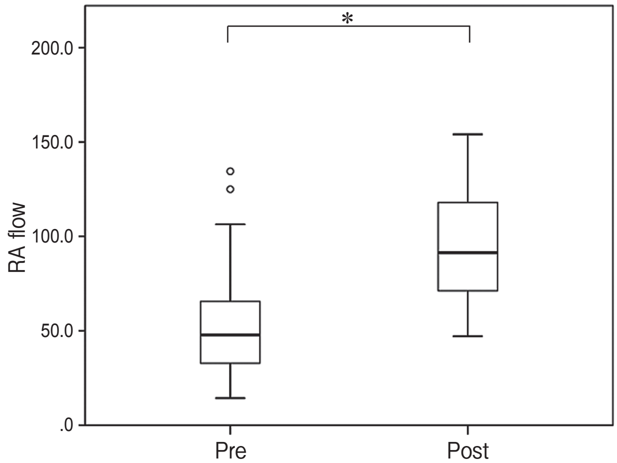

Fig. 2 Box-and-whisker plots of pre-PTA and post-PTA values for RA blood flow speed (n = 45). RA: radial artery. $^{*}p < 0.001$

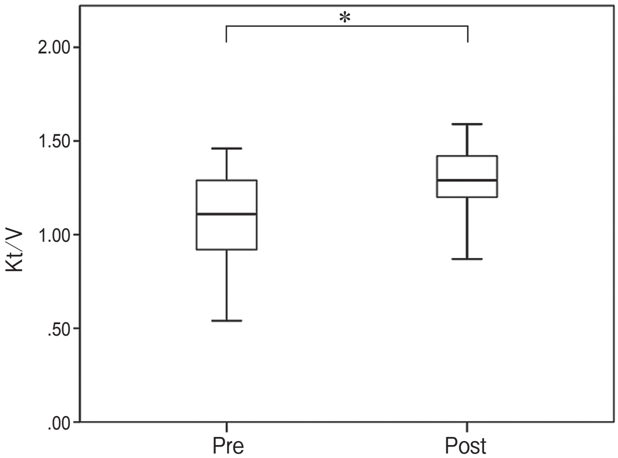

Fig. 3 Box-and-whisker plots of pre-PTA and post-PTA values for Kt/V (n = 45). $^{*}p < 0.001$

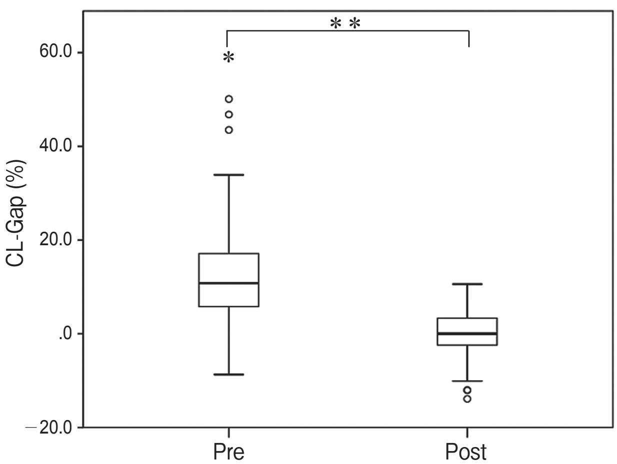

Fig. 4 Box-and-whisker plots of pre-PTA and post-PTA values for CL-Gap (n = 45). $^{**}p < 0.001$

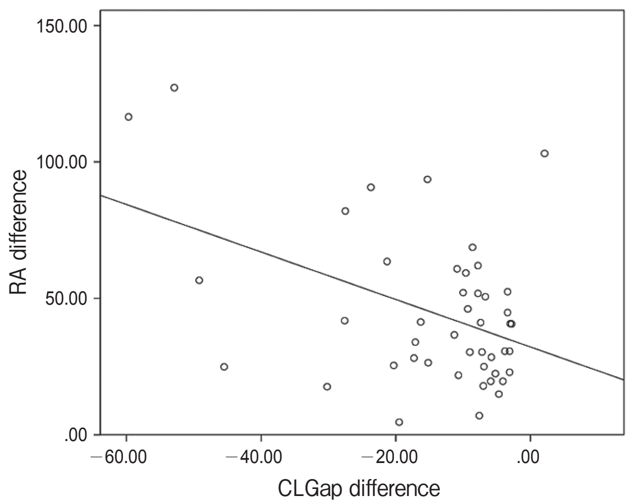

Fig. 5 A scatterplot between improvements of RA blood flow speed and CL-Gap (n = 45). RA: radial artery.

$\pm 14.6\%$ to $-0.2 \pm 5.4\%$ ($p < 0.001$, Fig. 4). And, a correlation between these differences was apparent ($r = -0.436$ and $p = 0.003$, Fig. 5).

In the 45 patients who underwent PTA, the procedure was considered necessary because their Kt/V and CL-Gap values indicated a possible deterioration in recirculation rate. Angiography showed that all these patients had stenosis, which was resolved by PTA in all cases.

Discussion

Although PTA treatment of stenosis in a vascular access helps to increase the duration of access patency, PTA therapy is often performed without evaluating whether the stenosis is actually causing a deterioration in recirculation rate. However, if the purpose of PTA is to improve dialysis efficiency, it is important to assess the extent to which it is likely to fulfill this aim before the procedure is done and thereby limit PTA treatment to patients with an inadequate recirculation rate. The results of the present study suggest that a hematologic functional evaluation of the access that is based on Kt/V and CL-Gap should be performed. It is also important to determine whether a PTA treatment has improved the recirculation rate and increased dialysis efficiency. If a comprehensive functional evaluation of a vascular access were reflected by the dialysis efficiency represented by Kt/V, the assessment would permit good access management based on the recirculation rate. However, because Kt/V depends on QB, it is difficult for an access with a high recirculation rate to obtain a sufficiently high Kt/V, even if QB is sufficient. QB is considered to be maintained when the recirculation is evaluated adequately and accurately. Various methods for evaluating recirculation in a vascular access have been proposed [7, 8].

We previously showed that the CL-Gap, correlated with Kt/V, indicates the recirculation rate of an AVF. [9] In the present study, the CL-Gap value improved significantly after PTA, as did Kt/V and RA blood flow speed. Fig. 5 shows the correlation between the CL-Gap and RA difference in PTA. This analysis showed whether CL-Gap prescribed RA difference in PTA. The correlation index between the differences in CL-Gap and Kt/V pre- and post-PTA was $r = -0.436$ and was significant ($p = 0.003$). CL-Gap is measured after hemodialysis, so PTA efficacy by CL-Gap is judged several days after PTA. RA blood flow speed is measured at PTA, and RA blood flow speed improvement is judged immediately after PTA. The data in Fig. 5 suggest that the faster that the RA blood flow improved after PTA, the more the recirculation rate (CL-Gap) improved. Thus we were able to assess PTA efficacy immediately after the PTA by measuring the RA blood flow speed. We therefore suggest that PTA is necessary for AVFs that show at least a 10% increase in absolute CL-Gap or more than a 10% relative increase. This standard can be also used to assess the effectiveness of PTA.

We studied 45 patients who underwent PTA with BNP, because BNP is a risk factor for cardiac events in hemodialysis patients. Kuno *et al.* studied 395 patients with both BNP > 283 pg/mL and Troponin T > 0.08 ng/mL, and they reported that the patients group had a 41.1% risk of mortality and a 52.7% risk of cardiac events in the five-year period after starting hemodialysis [12].

In summary, we conclude that CL-Gap is a valid index of recirculation rate and that it also indicates the dialysis ability of an AVF for vascular access. Improvements in dialysis efficiency might be obtained by focusing on improving RA blood flow speed values by performing PTA.

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