Dear Editor,

Composition of regional muscle and fat masses are related to arteriosclerotic changes in the general population [1]. This study was aimed to clarify the association of muscle mass in the lower limbs and abdominal fat mass with arteriosclerotic parameters in patients on chronic hemodialysis (HD). We measured abdominal subcutaneous fat mass area (ASFA), abdominal visceral fat mass area (AVFA), and thigh muscle area (TMA) from computed tomography (CT) images and adjusted those by body mass index (BMI) in 124 HD patients (age 61±11 [37–79] years, time on HD 11±10 [0–36] years, male/female=84/40). Brachial-ankle pulse wave velocity (baPWV) and ankle brachial pressure index (ABI) were also measured together and automatically in CAVI-VaSera VS-1000 (Fukuda Denshi Co, Ltd, Tokyo, Japan) just before HD session.

A significant association was found between baPWV and TMA/BMI ratio in male \((r=-0.32, p<0.01)\). Male patients in the top tertile of baPWV had a significantly lower TMA/BMI ratio when compared with those in the middle tertile and those in the bottom tertile (Table 1).

TMA/BMI ratio was also correlated with ABI \((r=0.46, p<0.01)\) in female patients. There was a significantly lower TMA/BMI ratio in patients with the lowest ABI compared to those with the second and with the highest tertile (Table 2).

There was rather an inverse association between AVFA/BMI ratio with baPWV in women \((r=-0.38, p<0.05)\). A multiple linear regression analysis adjusted by conventional, nutritional, and anthropometric parameters revealed that TMA/BMI was independently associated with baPWV in male, while with ABI in female (Table 3). In contrast, there was no relationship between AVFA/BMI and ASFA/BMI ratios and arteriosclerotic parameters in men.

It has been demonstrated that skeletal muscle atrophy is associated with accelerated arteriosclerosis. TMA is inversely associated with baPWV in general subjects [2, 3]. A higher PWV is related to a more profound decline in sarcopenic index in older men [4]. Skeletal muscle mass to visceral fat area ratio is also inversely associated with baPWV [5]. In this study, we showed that TMA/BMI ratio was independently associated with baPWV in male, while with ABI in female HD patients, suggesting a possible association of muscle wasting with arteriosclerotic changes in HD patients.

Visceral adiposity is linked to arteriosclerosis. AVFA is positively correlated with baPWV and carotid-femoral PWV in general subjects [2, 6]. Visceral fat level was a predictor of carotid-femoral PWV in peritoneal dialysis patients [7]. A positive relationship between AVFA and baPWV was also observed in diabetic HD patients [8]. In this study, however, AVFA/BMI was rather negatively associated with baPWV in female HD patients. The reasons for this discrepancy are not known, but may be due to a well-preserved nutritional status in female patients with abdominal adiposity. An increased body fat mass volume is paradoxically associated with better outcomes in HD patients [9]. The protective role of accumulated trunk fat on subclinical vascular damage, assessed by carotid-radial PWV, was also observed in the elderly women [10].

In summary, we found that reduced TMA/BMI ratio was independently associated with increased baPWV in male, while with decreased ABI in female patients. The findings
### Table 1 Baseline characteristics according to the baPWV tertile

| Clinical parameters | Male ($n=84$) | Female ($n=40$) |
|---------------------|---------------|-----------------|
|                     | 1st tertile (<12.8) | 2nd tertile (12.8 ≤ 14.8) | 3rd tertile (14.8 ≤) | 1st tertile (<12.2) | 2nd tertile (12.2 ≤ 14.7) | 3rd tertile (14.7 ≤) |
| Age (years)         | 54±12         | 61±9*           | 67±10**         | 55±13         | 62±9*           | 70±6**         |
| HD duration (years) | 14±11         | 9±8             | 10±10           | 13±12         | 11±9            | 13±12          |
| Diabetes (%)        | 11            | 29              | 36              | 8             | 7               | 23             |
| Creatinine (mg/dL)  | 13.6±3.4      | 13.9±2.3        | 12.3±3.1*       | 11.1±3.4      | 11.5±1.7        | 9.2±1.7*       |
| Albumin (g/dL)      | 3.8±0.3       | 3.7±0.2         | 3.6±0.3         | 3.6±0.3       | 3.7±0.3         | 3.6±0.3        |
| Calcium (mg/dL)     | 9±0.1         | 9.2±0.8         | 9±0.9           | 9.3±0.7       | 9.6±0.8         | 8.8±1.0        |
| Phosphorous (mg/dL) | 5.7±1.3       | 6.1±1.4         | 5.6±1.5         | 5.8±2.1       | 5.4±1.9         | 5.2±1.3        |
| hs-CRP (mg/L)       | 6.5±23.9      | 8.5±29.8        | 6.6±19.5*       | 1.5±2.5       | 4.3±13.2        | 2.3±5.4        |
| Transferrin (mg/dL) | 33.1±8.6      | 30.2±6.4        | 26.5±7.5**      | 27.7±7.5      | 29.0±7.8        | 25.5±7.7       |
| Total cholesterol (mg/dL) | 159±41 | 145±31         | 142±29          | 183±32        | 182±48          | 154±33*        |
| HDL-C (mg/dL)       | 53±20         | 47±13           | 46±12           | 51±14         | 56±16           | 47±15          |
| Hemoglobin (g/dL)   | 11.2±1.3      | 10.5±1.4        | 11.1±1.1        | 11.2±1.1      | 10.5±0.8        | 10.1±1.2       |
| Total lymphocyte count (/µL) | 1320±510 | 1340±530       | 1100±510        | 1440±520      | 1270±510        | 1010±220       |
| BMI (kg/m²)         | 20.6±2.8      | 21.9±3.0        | 21.2±2.9        | 19.8±2.7      | 20.1±2.7        | 18.5±1.9       |
| ASFA/BMI            | 5.5±2.0       | 6.2±2.3         | 6.0±2.3         | 6.8±2.4       | 8.7±3.7         | 5.5±2.4*       |
| AVFA/BMI            | 3.6±2.6       | 5.1±3.0         | 4.2±2.8         | 4.2±3.1       | 3.8±2.5         | 1.8±0.9**      |
| TMA/BMI             | 10.1±1.9      | 9.8±1.7         | 8.7±2.3*        | 7.1±2.0       | 8.7±2.5         | 7.2±1.9        |
| Systolic blood pressure (mmHg) | 120±20 | 142±21**       | 161±27*         | 107±26        | 137±20**        | 148±21**       |

*HD* hemodialysis, *hs-CRP* highly sensitive C-reactive protein, *HDL-C* HDL cholesterol, *BMI* body mass index, *ASFA* abdominal subcutaneous fat area, *AVFA* abdominal visceral fat area, *TMA* thigh muscle area

*p < 0.05, **p < 0.01 vs. the lowest tertile; *p < 0.05 vs. the middle tertile

### Table 2 Baseline characteristics according to the ABI tertile

| Clinical parameters | Male ($n=84$) | Female ($n=40$) |
|---------------------|---------------|-----------------|
|                     | 1st tertile (<1.04) | 2nd tertile (1.04 ≤ 1.14) | 3rd tertile (1.14 ≤) | 1st tertile (<1.00) | 2nd tertile (1.00 ≤ 1.10) | 3rd tertile (1.10 ≤) |
| Age (years)         | 64±9          | 63±10           | 55±12**          | 69±11          | 59±11*           | 59±10*          |
| HD duration (years) | 11±10         | 10±9            | 12±10           | 17±13         | 10±10           | 11±9            |
| Diabetes (%)        | 30            | 31              | 14              | 8            | 7               | 21              |
| Creatinine (mg/dL)  | 12.2±2.4      | 13.8±2.6*       | 13.7±3.7        | 10.0±2.3      | 10.8±2.4        | 11.1±3.0        |
| Albumin (g/dL)      | 3.6±0.3       | 3.7±0.2         | 3.8±0.3         | 3.5±0.3       | 3.7±0.3         | 3.8±0.3*        |
| Calcium (mg/dL)     | 8.9±0.9       | 9.0±0.8         | 9.1±1.0         | 9.4±1.1       | 9.1±0.9         | 9.2±0.7         |
| Phosphorous (mg/dL) | 5.6±1.3       | 6.1±1.5         | 5.7±1.4         | 5.1±1.1       | 6.1±2.1         | 5.2±1.7         |
| hs-CRP (mg/L)       | 15.2±34.0     | 1.8±2.5         | 5.2±18.2        | 1.0±1.2       | 6.2±13.8        | 0.7±0.7         |
| Transferrin (mg/dL) | 26.8±6.9      | 29.9±7.3        | 32.3±8.6**      | 25.4±5.1      | 26.8±7.6        | 29.9±9.2        |
| Total cholesterol (mg/dL) | 146±26 | 143±43         | 158±33          | 183±41        | 163±30          | 174±48          |
| HDL-C (mg/dL)       | 52±19         | 45±14           | 49±12           | 52±11         | 52±18           | 51±16           |
| Hemoglobin (g/dL)   | 10.8±1.5      | 10.8±1.2        | 11.2±1.2        | 10.5±0.9      | 10.8±1.1        | 10.5±1.3        |
| Total lymphocyte count (/µL) | 1230±490 | 1190±480       | 1340±580        | 1170±390      | 1300±500        | 1240±510        |
| BMI (kg/m²)         | 20.7±2.1      | 21.4±2.7        | 21.5±3.2        | 19.1±2.5      | 19.2±2.7        | 20.1±2.3        |
| ASFA/BMI            | 5.7±2.1       | 5.7±2.3         | 6.2±2.2         | 6.9±2.7       | 6.3±2.7         | 7.8±3.7         |
| AVFA/BMI            | 4.0±2.9       | 4.5±2.8         | 4.6±2.9         | 3.7±2.2       | 2.7±2.6         | 3.4±2.8         |
| TMA/BMI             | 9.4±2.6       | 9.4±1.8         | 9.7±1.7         | 6.3±2.0       | 8.2±2.0*        | 8.3±2.3*        |
| Systolic blood pressure (mmHg) | 148±35 | 139±25         | 136±22          | 116±32        | 144±24          | 130±23          |

*HD* hemodialysis, *hs-CRP* highly sensitive C-reactive protein, *HDL-C* HDL cholesterol, *BMI* body mass index, *ASFA* abdominal subcutaneous fat area, *AVFA* abdominal visceral fat area, *TMA* thigh muscle area

*p < 0.05, **p < 0.01 vs. the lowest tertile
support a possible relationship between arteriosclerosis and thigh muscle atrophy even in the dialysis population.

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Table 3 Independent determinants of baPWV and ABI in male and female patients

| Gender | Parameters       | Standardized regression coefficient | F value | R² | P value |
|--------|-----------------|------------------------------------|---------|----|---------|
| Male   | Systolic blood pressure | 40.6                              | 63.5    | 0.44 | <0.01   |
|        | Age             | 30.9                              | 26.1    | 0.24 | <0.01   |
|        | Transthyretin   | 44.9                              | 11.4    | 0.13 | <0.01   |
|        | TMA/BMI ratio   | 13.1                              | 9.4     | 0.10 | <0.01   |
|        | Albumin         | 4.1                               | 5.0     | 0.06 | 0.03    |
|        | Total lymphocyte count | 1895.1                           | 4.5     | 0.05 | 0.04−   |
| Female | Systolic blood pressure | 56.2                              | 17.0    | 0.29 | <0.01   |
|        | Age             | 39.5                              | 7.9     | 0.17 | <0.01   |
|        | Total lymphocyte count | 2122.4                           | 7.1     | 0.16 | 0.01    |
|        | AVFA/BMI ratio  | 7.8                               | 6.3     | 0.12 | 0.02    |
|        | Hemoglobin      | 12.3                              | 4.4     | 0.10 | 0.04    |
| Male   | Transthyretin   | 17.6                              | 8.6     | 0.05 | 0.04−   |
| Female | TMA/BMI ratio   | 0.55                              | 10.2    | 0.21 | <0.01   |
|        | Age             | 88.3                              | 4.9     | 0.11 | 0.03    |
|        | Time on hemodialysis | 35.4                             | 4.1     | 0.10 | <0.05   |

We examined the determinants of baPWV and ABI with a stepwise multiple-regression analysis using the 15 parameters (age, time on HD, serum calcium, phosphorous, albumin, total cholesterol, HDL cholesterol, TTR, log-transformed hs-CRP, hemoglobin, total lymphocyte count, systolic blood pressure, AVFA/BMI, ASFA/BMI, and TMA/BMI)

BMI body mass index, AVFA abdominal visceral fat area, TMA thigh muscle area

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Sarcopenia and Muscle (von Haehling S, Morley JE, Coats AJS, Anker SD. Ethical guidelines for authorship and publishing in the Journal of Cachexia, Sarcopenia and Muscle. J Cachexia Sarcopenia Muscle. 2010;1:7–8). Akihiko Kato, Takako Takita, and Hiromichi Kumagai declare that they have no conflict of interest. This study was approved by the appropriate ethics committee (Maruyama Hospital, Hamamatsu, Japan) and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.