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	作成者: 片橋, 一人
	メールアドレス:
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Flow dynamics of type II endoleaks can determine sac expansion after endovascular aneurysm repair using four-dimensional flow-sensitive magnetic resonance imaging analysis

Kazuto Katahashi, MD,[a] Masaki Sano, MD, PhD,[a] Yasuo Takehara, MD, PhD,[b] Kazunori Inuzuka, MD, PhD,[a] Masataka Sugiyama, MD,[c] Marcus T. Alley, PhD,[d] Hiroya Takeuchi, MD, PhD,[a] *and* Naoki Unno, MD, PhD,[a,e] *Hamamatsu and Nagoya, Japan; and Palo Alto, Calif*

ABSTRACT

Objective: The objective of this study was to investigate the hemodynamic parameters of type II endoleaks (T2ELs) to predict sac expansion using four-dimensional flow-sensitive magnetic resonance imaging (4D-flow MRI) analysis.

Methods: Patients who underwent endovascular aneurysm repair (EVAR) and were diagnosed with a T2EL were included in the study. Using 4D-flow MRI at 7 days, the peak flow velocity and amplitude of dynamics of blood flow per minute were measured in each T2EL vessel. The peak flow velocity was defined as the maximum of the absolute value of the blood flow velocity. The amplitude of dynamics of blood flow in the tributary arteries was defined as the sum of the absolute values of the inflow and outflow volume in each vessel. The amplitude of dynamics of blood flow in the tributary arteries per sac was calculated in each sac. The aneurysm sac diameter was measured by computed tomography (CT) at 1 year. The patients were divided into two groups according to the presence or absence of sac expansion.

Results: Of 155 patients who underwent EVAR, both CT angiography and 4D-flow MRI were performed in 107 patients at 7 days after EVAR. Among them, 39 (36.4%) were found to have a T2EL, of whom 28 were re-evaluated with CT angiography and 4D-flow at 1 year; 7 patients had expanding sacs (expanding group), whereas 21 had nonexpanding sacs (not-expanding group). At 7 days, 28 patients had 80 T2EL vessels detected by 4D-flow MRI, of which 39 vessels (48.8%) had stopped flowing at 1 year (transient vessels); 41 vessels (51.3%) had sustained flow (persistent vessels). The persistent vessels had significantly larger peak flow velocity and amplitude of dynamics of blood flow. The comprehensive analysis of T2EL vessels per sac identified that the amplitude of dynamics of blood flow in the tributary arteries per sac was significantly higher in the expanding group than in the not-expanding group. A receiver operating characteristic curve analysis revealed that the sensitivity and specificity of sac enlargement at a cutoff value of 3750 mm^3/min were 85.7% and 76.2%, respectively.

Conclusions: The fate of aneurysm sacs with T2ELs after EVAR has remained difficult to predict. A comprehensive analysis of concurrent multiple T2EL vessels using 4D-flow MRI analysis may enable prediction of the sac expansion after EVAR. (J Vasc Surg 2018;■:1-10.)

Keywords: Aortic aneurysm; Endoleak; Hemodynamics; Stent graft; Magnetic resonance imaging

Endovascular aneurysm repair (EVAR) has become a viable alternative to conventional surgical open repair owing to its perioperative survival benefit.[1-3] However, EVAR is associated with a unique complication called endoleak (EL), which continues to perfuse and pressurize the aneurysm sac and cause aneurysm enlargement and rupture. Among the various types of ELs, type II ELs (T2ELs) are due to patent aortic branch vessels, such as the inferior mesenteric artery (IMA) and lumbar arteries (LAs). Although T2ELs often disappear spontaneously,[4,5] some persistent T2ELs are associated with the enlargement and rupture of aneurysms.[5-7] The decision for conservative vs invasive management for T2ELs depends on the enlargement of the aneurysm sac. However, it is difficult to anticipate which aneurysm having a T2EL will lead to sac shrinkage or enlargement.

From the Second Department of Surgery,[a] Department of Radiology,[c] and Department of Vascular Surgery,[e] Hamamatsu University School of Medicine, Hamamatsu; the Department of Fundamental Development for Advanced Low Invasive Diagnostic Imaging, Nagoya University, Graduate School of Medicine, Nagoya[b]; and the Department of Radiology, Stanford University, Palo Alto.[d]

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Correspondence: Naoki Unno, MD, PhD, Division of Vascular Surgery, Hamamatsu Medical Center and Hamamatsu University School of Medicine, 1-20-1 Handayama, Higashi-ku, Hamamatsu 431-3192, Japan (e-mail: unno@hama-med.ac.jp).

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We previously reported the usefulness of four-dimensional flow-sensitive magnetic resonance imaging (4D-flow MRI) to distinguish each type of EL, except for type V ELs, after EVAR.[8] Based on a hemodynamic analysis with 4D-flow MRI, T2ELs are classified into two distinct subtypes: type IIA (with a to-and-fro biphasic flow pattern) and type IIB (with a monophasic flow pattern).[8] The objective of this study was to analyze each T2EL vessel hemodynamically using 4D-flow MRI and comprehensively assess each sac with multiple T2EL vessels to determine the hemodynamic parameters that can predict aneurysm sac enlargement.

ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective single-center study of prospectively collected data
- **Key Findings:** Comprehensive and hemodynamic analysis of type II endoleak vessels at 7 days identified that the amplitude of blood flow dynamics in tributary arteries per sac was higher in the expanding group than in the not-expanding group at 1 year.
- **Take Home Message:** The authors suggest using four-dimensional flow-sensitive magnetic resonance imaging analysis to measure amplitude of blood flow dynamics in tributary arteries per sac that may enable prediction of sac expansion after endovascular aneurysm repair.

METHODS

Ethical considerations. This study's experimental protocol and informed consent were approved by the Institutional Review Board of the Hamamatsu University School of Medicine Ethics Committee of Clinical Research (approval No. E 14-001-1). The patients provided written informed consent to participate in the study and for publication of the report and any accompanying images.

Study population. This was a single-center retrospective analysis of prospectively collected data. The study included patients who underwent elective EVAR for treatment of infrarenal abdominal aortic aneurysms (AAAs) between January 2013 and December 2016. Computed tomography angiography (CTA) and magnetic resonance angiography (MRA) were performed in all patients at 7 days and evaluated for the presence of ELs. Patients with T2ELs at 7 days after EVAR were enrolled in this study and 4D-flow analysis was performed. CTA and MRA were performed in all patients at 1 year after EVAR. The exclusion criteria were as follows: use of non-nitinol stent devices (because of metallic artifacts in MRI), those with type I or type III ELs, those with a contraindication to 4D-flow MRI (such as an allergy, estimated glomerular filtration rate [eGFR] <30 mL/min/1.73 m^2, or claustrophobia), and those who did not provide written informed consent. The interpretations of CTA, MRA, and 4D-flow were performed in a blinded manner for comparison, and at least two physicians independently read the images of each modality and compared the results.

Data of patients' demographics and comorbid conditions (age, sex, smoking history, hypertension, diabetes mellitus, coronary artery disease, chronic obstructive pulmonary disease [COPD], hypercholesterolemia, stroke, eGFR, aneurysm diameter, device type, and number of T2EL vessels) were recorded. The definition of each condition was as follows: smoking history, present or past smoking history; hypertension, medication for hypertension or a systolic blood pressure >140 mm Hg or a diastolic blood pressure >90 mm Hg; diabetes mellitus, present or past medication for diabetes; coronary artery disease, present medication, past percutaneous coronary intervention, or coronary artery bypass grafting history; COPD, medication for COPD or a forced expiratory volume in 1 second <70%; hypercholesterolemia, medication for hypercholesterolemia or a total serum cholesterol concentration >220 mg/dL; and stroke, a history of stroke. Age and eGFR were reported as means ± standard deviations. The aneurysm diameter was determined by radiologists as a hospital routine work using the minor axis at the site of the largest cross section on computed tomography (CT) images without contrast agent.

The patients were divided into two groups according to the aneurysm sac status at 1 year after EVAR, in which the maximum short diameter of the sac was measured on noncontrast-enhanced CT images by unspecified radiologists. Patients whose aneurysm sac diameter was enlarged by ≥5 mm compared with that at 7 days after EVAR were assigned to the expanding group. The rest of the patients, that is, those with an aneurysm diameter that either was reduced or did not change, were assigned to the not-expanding group.

Assessment using 4D-flow analysis. Before 4D-flow analysis, contrast-enhanced three-dimensional MRA was performed using a 3.0T scanner (Discovery MR 750 and 32-channel torso array coil; GE Healthcare, Waukesha, Wisc) after a bolus injection of gadolinium chelate at a standard dosage of 0.1 mmol/kg, according to the previously reported protocol.[8] Under the protocol,[8] the 4D-flow analysis was performed using a retrospective electrocardiography-gated technique. Detailed information about the parameters is described in the Supplementary Methods (online only).

Analysis of T2EL vessels. Using 4D-flow MRI, we classified T2ELs into two subtypes according to the flow patterns of the aortic side branches: type IIA and type IIB.[8] Type IIA ELs had a to-and-fro biphasic flow vector in which the aortic side branches (ie, the LAs or IMA)

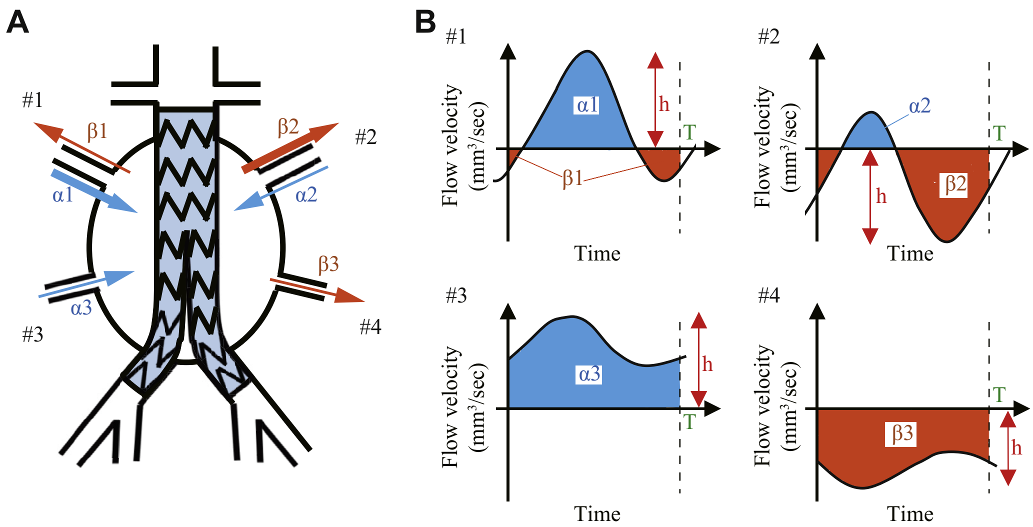


Fig 1. Subclassification of type II endoleak (T2EL) and definition of hemodynamic parameters. **A,** Schema of an aneurysm with four different types of T2EL vessels: *#1*, an inflow (α1)-dominant and to-and-fro biphasic flow pattern (type IIA); *#2*, an outflow (β2)-dominant and to-and-fro biphasic flow pattern (type IIA); *#3*, a constant-inflow (α3), monophasic pattern (type IIB); and *#4*, a constant-outflow (β3), monophasic pattern (type IIB). **B,** Change in the flow velocity per one heartbeat in each T2EL vessel (*#1*, *#2*, *#3*, *#4* in Fig 1, *A*). α, Inflow volume; β, outflow volume; *h*, peak flow velocity, *T*, one heartbeat. The balance of flow-volume through #1 = |α1 + β1|. The amplitude of dynamics of blood flow through #1 = |α1| + |β1|. The balance of flow-volume through #4 = The amplitude of dynamics of blood flow through #4 = |β3|. The total balance of flow-volume per sac = |α1 + β1+ α2 + β2 + α3 + β3|. The amplitude of dynamics of blood flow in the tributary arteries = |α1| + |β1| + |α2| + |β2| + |α3| + |β3|.

showed periodic blood flow changes from retrograde to antegrade (Fig 1, *A*, *#1* and *#2*). On the contrary, type IIB ELs had a monophasic flow vector in which the flow direction of the aortic side branches was constantly one way (either retrograde [Fig 1, *A*, *#3*] or antegrade [Fig 1, *A*, *#4*]). The 4D-flow MRI showed the inflow phase volume (α1 and α2), outflow phase volume (β1 and β2), and peak flow velocity (h) in one heartbeat in type IIA EL vessels (Fig 1, *B*, *#1* and *#2*). In type IIB EL vessels, 4D-flow MRI showed either the inflow phase volume (α3; Fig 1, *B*, *#3*) or outflow phase volume (β3; Fig 1, *B*, *#4*) and peak flow velocity (h; Fig 1, *B*, *#3* and *#4*) in one heartbeat.

The peak flow velocity (|h|) was defined as the maximum of the absolute value of the blood flow velocity in one heartbeat. The balance of flow-volume was defined as the balance of the inflow volume (α) and outflow volume (β) in the T2EL vessels during one heartbeat (balance of flow-volume = |α + β|). The amplitude of dynamics of blood flow was defined as the total of the absolute value of the inflow volume (|α|) and outflow volume (|β|) in the T2EL vessels during one heartbeat (amplitude of dynamics of blood flow = |α| + |β|; Fig 1, *B*). Most of the patients had multiple, concomitant T2EL vessels. Therefore, to comprehensively assess the T2EL vessels for each sac, we also measured the amplitude of dynamics of blood flow in the tributary arteries per sac ($|\alpha_1|+|\beta_1|+|\alpha_2|+|\beta_2|+|\alpha_3|+|\beta_3|$; Fig 1, *A*). Both the balance of flow-volume and the amplitude of dynamics of blood flow were expressed as volume per minute, which was calculated from heart rate per minute. For example, there is a post-EVAR sac with one T2EL vessel (eg, IMA), which is a to-and-fro type, and the bidirectional blood flow to each direction is 5 mL/min. In this case, the absolute value of the to-and-fro blood flow (ie, amplitude of dynamics of the blood flow) is 10 mL/min. In the next case, there is also a sac with one T2EL vessel, similarly a to-and-fro type. However, the bidirectional blood flow to each direction is 20 mL/min. In this case, the absolute value of the to-and-fro blood flow (ie, the amplitude of dynamics of the blood flow) is 40 mL/min. Although the balance of the T2EL blood flow in both is zero per sac, the amplitude of the dynamics is four times higher in the latter case.

At 1 year after EVAR, the T2EL vessels were divided into two groups according to whether the EL was transient or persistent, which was determined using 4D-flow MRA.

Statistical analyses. Differences in categorical variables (sex, smoking history, hypertension, diabetes mellitus, coronary artery disease, COPD, hypercholesterolemia, stroke, device type, out of instructions for use, patent IMA on preoperative CT, preoperative hypogastric artery embolization or occlusion, and preoperative antiplatelet agents) between the expanding group and not-expanding group were analyzed using Fisher exact test. The differences in age, eGFR, and aneurysm diameter between the expanding and not-expanding groups were analyzed using a *t*-test. The differences in the amplitude

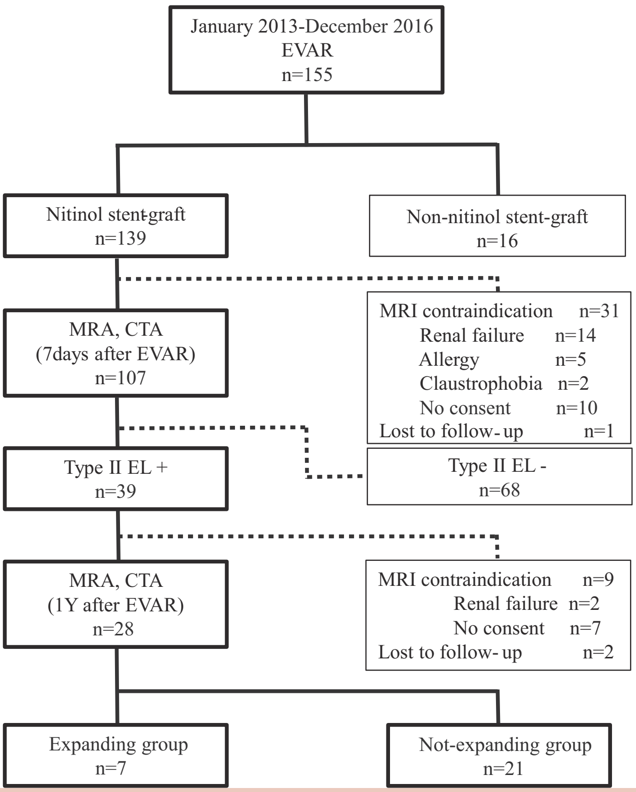


Fig 2. Trial profile. *CTA,* Computed tomography angiography; *EL,* endoleak; *EVAR,* endovascular aneurysm repair; *MRA,* magnetic resonance angiography; *MRI,* magnetic resonance imaging.

of dynamics of blood flow in the tributary arteries per sac between the expanding and not-expanding groups, peak flow velocity, balance of flow-volume, and amplitude of dynamics of blood flow between the transient T2EL vessel group and the persistent T2EL vessel group were analyzed using *t*-test on log-transformed data. The predictive factors for sac enlargement were analyzed using a multivariate logistic regression analysis. Receiver operating characteristic (ROC) curves were used to select cutoff values for aneurysm enlargement. All statistical analyses were performed using SPSS statistical software version 23 (IBM Corp, Armonk, NY). Statistical significance was defined as $P < .05$.

RESULTS

Selection of patients. Between January 1, 2013, and December 31, 2016, we performed elective EVAR in 155 patients with infrarenal AAAs (Fig 2). Sixteen patients were excluded from this study because they used non-nitinol stent devices. Among the 139 patients with nitinol-based stent grafts, Endurant stent grafts (Medtronic, Minneapolis, Minn) were employed in 60 and Excluder stent grafts (Gore Medical, Flagstaff, Ariz) were employed in the other 79. Thirty-two patients had contraindications to 4D-flow MRI (14 had renal failure, 5 had an allergy, 2 had claustrophobia, and 10 did not consent) and were lost to follow-up. Hence, only 107 patients underwent 4D-flow MRI at 7 days after EVAR, during which 39 patients (36.4%) were found to have T2ELs.

One year later, 11 more patients were excluded from this study (2 for renal failure, 7 for lack of consent, and 2 for loss to follow-up). Therefore, a total of 28 patients were finally enrolled in this study (Fig 2). Using 4D-flow MRI, we identified 80 EL vessels in these 28 patients at 7 days after EVAR (type IIA, 59; and type IIB, 21). At 1 year after EVAR, 41 EL vessels were identified as persistent and the remaining 39 had ceased (Table I). No delayed T2EL occurred because of the new appearance of vessels during the study period. Among 18 IMA ELs at postoperative day 7, there were 14 (78%) persistent IMAs at 1 year. On the contrary, only 27 of 62 LAs (44%) were persistent at 1 year after EVAR. Therefore, IMA ELs were more persistent than LAs (Table I).

Sensitivity and specificity of detecting sac tributary arteries. We compared the findings of MRA with those of catheter angiography. In this study, we had seven cases with sac expansion at 1 year after EVAR. We performed catheter angiography in all seven cases to consider the possibility of embolization of T2EL tributary vessels. Using the images of catheter angiography, we compared them with MRA to assess the sensitivity and specificity of detecting sac tributary arteries. The sensitivity and specificity of detecting the vessels with MRA were both 100%.

Subclassification of T2EL vessels into type IIA and type IIB. Fig 3, *A* to *E* shows a typical case of a type IIA EL vessel in a 70-year-old man who underwent EVAR with an Endurant stent graft. CTA (Fig 3, *A*), catheter angiography (Fig 3, *B*), and MRA (Fig 3, *C*) also showed the T2EL vessels. A 4D-flow MRI analysis identified that the direction of the blood flow in the EL vessel changed periodically from retrograde to antegrade (a to-and-fro, biphasic flow pattern; Fig 3, *D* and *E*), and the EL was classified as a type IIA EL (Video 1, online only).

Fig 3, *F* to *K* shows a typical case of a type IIB EL in a 60-year-old man who underwent EVAR with the Excluder stent graft. CTA (Fig 3, *F*), catheter angiography (Fig 3, *G*), and MRA (Fig 3, *H*) identified the T2EL vessel. Using 4D-flow MRI, we identified that the direction of the blood flow in the T2EL was constantly one way (a monophasic flow pattern; Fig 3, *I-K*). Therefore, this EL was classified as type IIB (Video 2, online only).

Comparison of hemodynamics between transient and persistent EL vessels. The 4D-flow MRI showed 80 EL vessels (type IIA, 59; type IIB, 21) at 7 days after EVAR in 28 patients. Among these EL vessels, 39 disappeared (transient vessels) and 41 remained persistent (persistent vessels) at 1 year after EVAR. Among the 28 cases, a new EL did not develop between 7 days and 1 year after EVAR. Table I shows the hemodynamic comparisons between the transient EL group (n = 39) and persistent EL group

Table I. Comparison of type II endoleak (*T2EL*) vessels and four-dimensional flow-sensitive (4D-flow) analysis between transient vessels and persistent vessels

	Transient vessels (n = 39)	Persistent vessels (n = 41)	*P* value
No. of T2ELs			.015
IMA	4	14	
LA	35	27	
Subclassification of T2ELs			.801
Type IIA	28	31	
Type IIB	11	10	
Peak flow velocity,[a] geometric mean, mm^3/s	24.4	52.4	<.01
Balance of flow-volume,[a] geometric mean, mm^3/min	420.9	500.4	.529
Amplitude of dynamics of the blood flow,[a] geometric mean, mm^3/min	701.5	1528.6	<.01

IMA, Inferior mesenteric artery; *LA*, lumbar artery.
[a]The data were derived from 4D-flow analysis done at 7days after endovascular aneurysm repair (EVAR).

(n = 41) at 7 days after EVAR. The peak flow velocity (Fig 4, *A*) was significantly higher in the persistent EL vessel group than in the transient EL vessel group (Table I). There were no significant differences in the balance of flow-volume between the two groups (Table I; Fig 4, *B*); however, the amplitude of dynamics of blood flow was also significantly higher in the persistent EL vessel group than in the transient EL vessel group (Fig 4, *C*). We also performed interobserver data comparison and measured the correlation. As a result, the interobserver correlations in values of peak flow velocity and amplitude of dynamics of blood flow in each tributary vessel were strong ($R^2 = 0.979$ [$P < .01$] and $R^2 = 0.968$ [$P < .01$], respectively).

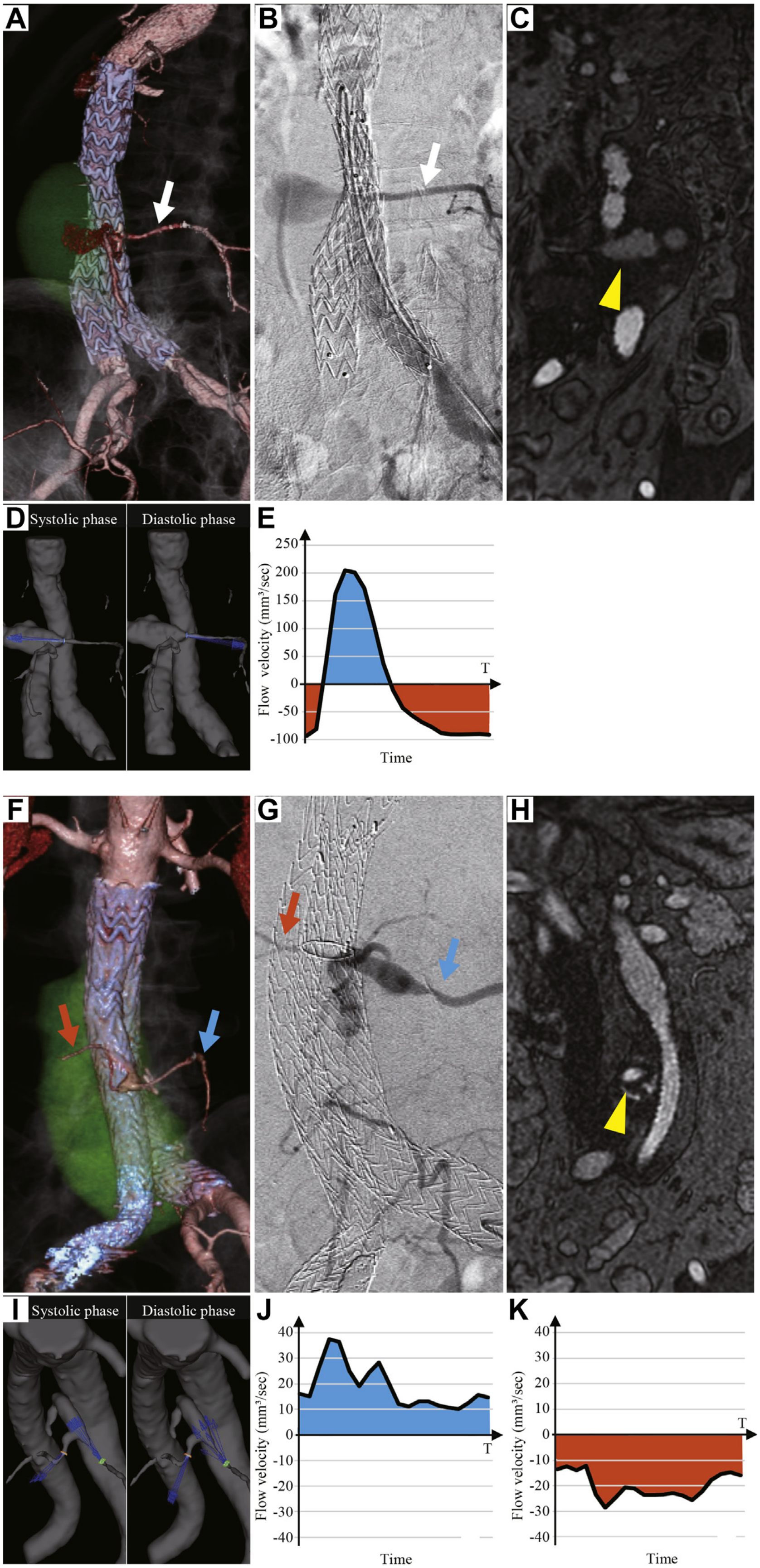
Comparison between the expanding group and not-expanding group. One year after EVAR, the diameter of the aneurysm sac enlarged by 5 mm or more in 7 of 28 patients in this study (Fig 2). The results of comparison of baseline characteristics, comorbidities, number of EL vessels, and amplitude of dynamics of blood flow in the tributary arteries per sac at 7 days after EVAR were compared between the expanding group (n = 7) and not-expanding group (n = 21; Table II). Statistically significant differences between the two groups were identified in the number of T2EL vessels at 7 days after EVAR ($P = .031$) and the amplitude of dynamics of blood flow in the tributary arteries per sac ($P < .01$) at 7days after EVAR. There were no significant differences between the groups in terms of other background characteristics and comorbidities. The amplitude of dynamics of blood flow in the tributary arteries per sac was significantly higher in the expanding group (6563.0 mm^3/min) than in the not-expanding group (2188.3 mm^3/min; $P < .01$; Fig 5).

Multivariate analysis of aneurysm sac expansion. Using the logistic regression model, the variables of amplitude of dynamics of blood flow in the tributary arteries per sac, number of T2EL vessels at 7 days, and history of coronary artery disease were selected. In the multivariate analysis, the amplitude of dynamics of blood flow in the tributary arteries per sac significantly increased the risk of aneurysm expansion (odds ratio, 42.787 [1.256-1463.57]; $P = .037$; Table III).

ROC analysis. To assess the value of the amplitude of dynamics of blood flow in the tributary arteries per sac as prediction of aneurysm expansion, a ROC curve was then constructed for the amplitude of dynamics of blood flow in the tributary arteries per sac. The area under the ROC curve for the amplitude of dynamics of blood flow in the tributary arteries per sac was 0.84. When the amplitude of dynamics of blood flow in the tributary arteries per sac of 3750 mm^3/min was set up as threshold, the positive predictive value was 85.7% and the negative predictive value was 76.2%.

DISCUSSION

ELs have been described as the Achilles heel of EVAR.[9] Although a consensus has been reached on the management of type I and type III ELs, the management of T2EL remains a controversial subject without clear-cut guidelines, so that decision-making is totally up to the surgeon's and patient's preferences.[4] The incidence rate of T2EL was reported to be between 16% and 34%,[4,5,7,10] and T2EL vessels often stop flowing spontaneously.[4,5] However, some T2ELs might result in enlargement or rupture of aneurysms, and persistent T2ELs are associated with late adverse outcomes.[6,7,10,11] Some physicians selectively treat T2EL with sac enlargement >5 mm[4,12]; others recommended less aggressive management to observe T2EL.[13] AAA sac expansion after EVAR >5 mm at 1 year was reported to be an independent predictor of late mortality regardless of the presence or absence of EL.[14] Several studies reported that intraoperative or preoperative IMA embolization, LA embolization, and aneurysm sac embolization before EVAR were associated with a reduced occurrence of T2ELs or greater shrinkage of the aneurysm sac's diameter.[15,16] However, adverse events, such as colonic infarction and death that are related to the embolization of the aortic branches, were also reported.[17,18] Additional costs and these risks prevent pre-EVAR embolization from being a standard procedure in most vascular centers. Considering that most T2EL vessels stop flowing spontaneously, selective embolization of the T2EL vessels responsible for enlarging sacs as a prophylactic procedure is desirable, if possible.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Flow velocity (mm³/sec)
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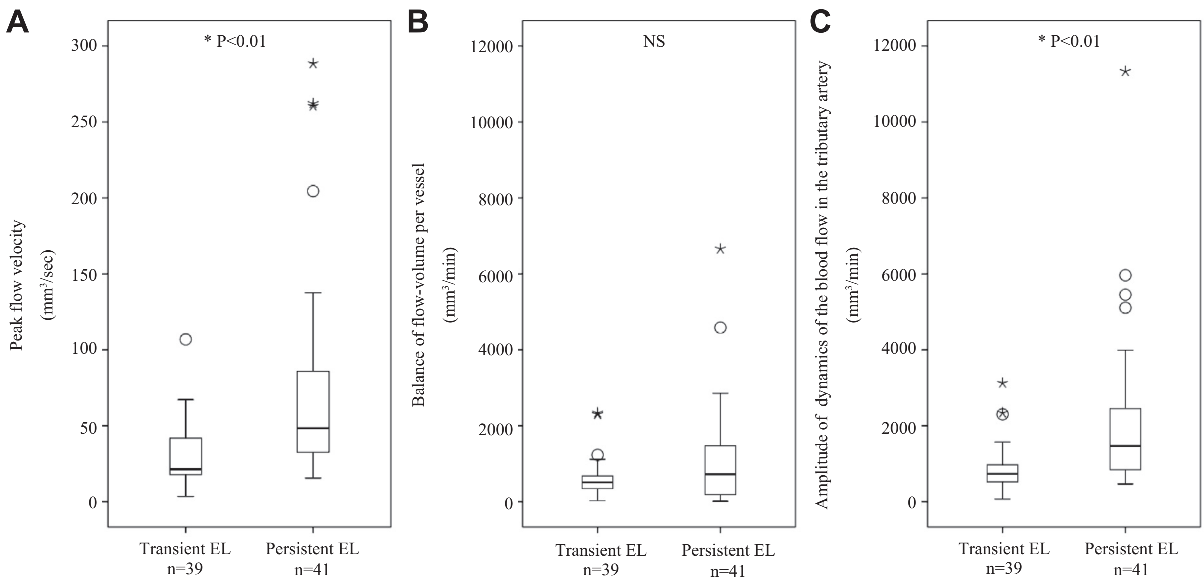

Fig 4. Comparison of hemodynamic parameters between the transient and persistent endoleak (*EL*) vessel groups. The peak flow velocity **(A),** balance of flow-volume per vessel **(B),** and amplitude of dynamics of blood flow per vessel **(C)** between the transient (n = 39) and persistent (n = 41) EL vessel group. Significant differences were found in the peak flow velocity ($P < .01$) and amplitude of dynamics of blood flow per vessel ($P < .01$).

Regarding the risk factors leading to persistent T2ELs and aneurysm enlargement, the patent IMA as well as an increase in the number of patent LAs and the diameter of the T2EL vessels have been reported to be positive risk factors.[19,20] This explains the rationale for embolizing the branch vessels.

Although CTA was considered the "gold standard" for postoperative evaluation of EVAR,[21] CTA may not be the best modality for evaluating T2ELs because it is difficult for CTA to assess each branch vessel's hemodynamics. On the contrary, MRI has a higher sensitivity than CTA for detecting T2ELs.[22,23] Recently, 4D-flow MRI has emerged as a novel technique to evaluate blood flow parameters, such as the flow vector, rate, and volume.[8,24-26] With this technique, T2EL vessels can be classified into type IIA and type IIB according to their flow patterns.[8] To evaluate the hemodynamics of T2EL, color duplex ultrasound imaging has also been used not only for detecting ELs but also for assessing hemodynamics of T2EL.[27,28] Beeman et al[28] reported that a bidirectional to-and-fro flow pattern in T2EL vessels (ie, type IIA in this study) might be associated with sac enlargement, whereas Monastiriotis et al[29] reported that a low-resistance, high-flow or to-and-fro T2EL has higher chances of sac enlargement. However, our study demonstrated that most of the sacs had multiple T2EL vessels with different flow patterns simultaneously, as seen in Fig 1, *A*, so that comprehensive assessment of all T2EL vessels may be more reasonable to predict the fate of an aneurysm sac.

Regarding the persistency of each T2EL vessel, 4D-flow MRI showed significant differences between the persistent and transient T2EL vessels in the peak flow velocity and amplitude of dynamics of blood flow but no difference in the balance of flow-volume and flow patterns (ie, type IIA or type IIB). The balance of flow-volume represents the balance of the amount of blood flow into the aneurysm sac through the T2EL vessel per minute. In contrast, the amplitude of dynamics of blood flow represents the absolute quantity of the blood flow moving through the T2EL vessel per minute. These results suggested that the absolute quantity of the blood flow

Fig 3. Typical cases of the type IIA and type IIB endoleaks (ELs). **A-E,** A type IIA EL in a 70-year-old man that was detected using **(A)** computed tomography angiography (CTA), **(B)** catheter angiography (*arrow*, EL vessel—lumbar artery [LA]), **(C)** and magnetic resonance angiography (MRA; *arrowhead*, EL). A four-dimensional flow-sensitive (4D-flow) analysis of the EL vessel in the systolic phase and diastolic phase (**D;** *arrow*, flow vector) and a graph of flow velocity in the type IIA EL vessel (**E;** *blue area*, retrograde flow-volume; *orange area*, antegrade flow-volume; Video 1, online only). **F-K,** A type IIB EL in a 60-year-old man that was detected with **(F)** CTA, **(G)** catheter angiography (*blue arrow*, EL vessel with retrograde flow [LA]; *orange arrow*, EL vessel with antegrade flow [LA]), and **(H)** MRA (*arrowhead*, EL). A 4D-flow analysis of the EL vessel in the systolic phase and diastolic phase (**I;** *arrow*, flow vector) and graphs of retrograde flow velocity **(J)** and antegrade flow velocity **(K)** in the type IIB EL vessel (*blue area*, retrograde flow-volume; *orange area*, antegrade flow-volume; Video 2, online only).

Table II. Comparison of baseline characteristics, comorbidities, and endoleak (EL) vessels between the expanding and not-expanding group

	Not-expanding group (n = 21)	Expanding group (n = 7)	*P* value
Age, years	75.3 ± 6.6	74.4 ± 7.7	.779
Sex			1.00
Male	20	7	
Female	1	0	
Smoking history	17 (81)	3 (43)	.142
Hypertension	16 (76)	7 (100)	.290
Diabetes mellitus	6 (29)	1 (14)	.639
Coronary artery disease	8 (38)	0 (0)	.075
COPD	9 (43)	3 (43)	1.00
Hypercholesterolemia	10 (48)	1 (14)	.191
Stroke	3 (14)	1 (14)	1.00
eGFR, mL/min/1.73 m^2	62.3 ± 15.8	56.8 ± 4.8	.377
Aneurysm diameter, mm	54.8 ± 10.8	50.8 ± 3.0	.353
Graft type			.646
Excluder	15	4	
Endurant	6	3	
Outside of IFU	7 (33)	3 (43)	.674
Patent IMA on preoperative CT	18 (86)	7 (100)	.551
Preoperative hypogastric artery embolization or occlusion	6 (29)	3 (43)	.646
Preoperative antiplatelet agents	8 (38)	1 (14)	.371
No. of T2EL vessels at 7 days postoperatively, median	2	4	.031
Amplitude of dynamics of blood flow in the tributary arteries per sac, geometric mean, mm^3/min	2188.3	6563.0	<.01

COPD, Chronic obstructive pulmonary disease; *CT,* computed tomography; *eGFR,* estimated glomerular filtration rate; *IFU,* instructions for use; *IMA,* inferior mesenteric artery; *T2EL,* type II endoleak.
Categorical variables are presented as number (%). Continuous variables are presented as mean ± standard deviation.

movement (ie, amplitude of dynamics of blood flow) significantly influenced the persistence of the T2EL vessels.

The hemodynamic parameters of each T2EL vessel allowed us to comprehensively assess multiple T2EL vessels by combining the amplitude of dynamics of blood flow of each T2EL vessel per sac. Multivariate analysis revealed that the amplitude of dynamics of blood flow of the T2EL vessels per sac significantly predicted the expansion of the aneurysm sac. We would like to emphasize that the fate of the sac was determined not by the inflow-outflow balance of blood flow in sacs but by the amplitude of the dynamics of the blood flow of the tributary vessels. The ROC curve of the amplitude of dynamics of the blood flow of the T2EL vessels per sac revealed that the cutoff value was 3750 mm^3/min for sac expansion at 1 year after EVAR. Therefore, the value that was obtained with 4D-flow MRI at 7 days after EVAR may predict expansion of an aneurysm sac 1 year later, which would help us not only select patients who require early reintervention but also select EL vessels to be embolized.

This study has some limitations. First, the sample size was small, and the follow-up period was relatively short. Hence, a prospective study with larger cases would help increase the reliability of the threshold value and improve both positive and negative values. Second, the analysis of 4D-flow MRI depends on spatial and temporal resolutions of 2 mm^3 and 40 mm seconds, respectively. Therefore, smaller aortic branches might go undetected and escape assessment. Moreover, although interobserver differences in the data analysis using 4D-flow were small, the process of combining the value of all tributary vessels' data might have a large margin of error. Third, the assessment using 4D-flow MRI was applied only to the T2EL vessels that were present at 7 days after EVAR. As several studies indicated, recurrent or delayed T2ELs during follow-up, which did not occur in the 28 cases in this study, also affect the fate of the sac.[7,10] Further studies are needed to assess the new appearance of T2EL vessels. In contrast, although 4D-flow MRI analysis may be useful to assess the sac fate, the technique also has several limitations. First, 4D-flow MRI

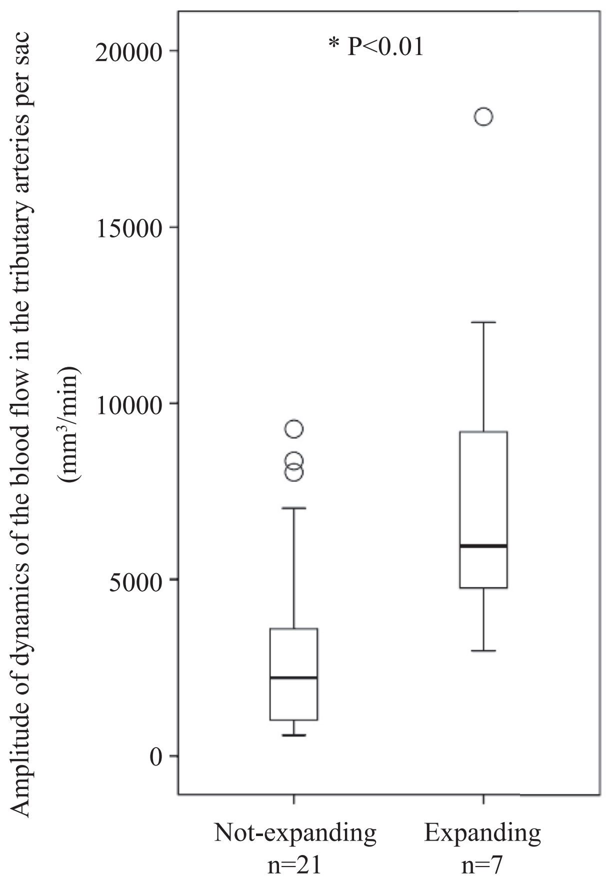

Fig 5. Comparison between the expanding group and not-expanding group with four-dimensional flow-sensitive (4D-flow) analysis. Comparison of the amplitude of dynamics of blood flow in the tributary arteries per sac between the expanding group (n = 7) and not-expanding group (n = 21; $P < .01$).

Table III. Results of the multivariate logistic regression analysis of the predictor of sac expansion

Variables	*P* value	Odds ratio	95% Confidence interval
Amplitude of dynamics of blood flow in the tributary arteries per sac	.037	42.797	1.256-1463.57
No. of T2EL vessels at 7 days postoperatively	.339	1.519	0.645-3.573
Coronary artery disease	.999	0.000	0.000

T2EL, Type II endoleak.

could not be used in patients with a stainless steel-based stent graft. Second, it is difficult to use a gadolinium contrast agent in patients with chronic kidney disease (eGFR <30 mL/min/1.73 m^2) or those on dialysis because there is an increased risk of the potential occurrence of nephrogenic, systemic fibrosis. Therefore, 4D-flow MRI may be suited not to T2EL screening but to selection of patients requiring early reintervention.

CONCLUSIONS

Hemodynamic analyses of each T2EL vessel using 4D-flow MRI were useful to detect persistent ELs. By combining the hemodynamic parameters of each T2EL vessel, a comprehensive analysis of concurrent multiple T2EL vessels may enable us to predict expansion of an aneurysm sac after EVAR.

AUTHOR CONTRIBUTIONS

Conception and design: NU
Analysis and interpretation: KK, MS, YT, KI, MS, MA, HT, NU
Data collection: KK, MS, KI
Writing the article: KK, MS, NU
Critical revision of the article: KK, MS, YT, KI, MS, MA, HT, NU
Final approval of the article: KK, MS, YT, KI, MS, MA, HT, NU
Statistical analysis: KK, MS, YT
Obtained funding: YT, NU
Overall responsibility: NU

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SUPPLEMENTARY METHODS (online only).

Time-resolved contrast-enhanced three-dimensional (3D) magnetic resonance angiography. The contrast agent was used to increase the definition of the arterial wall boundary for postprocessing and also to increase the signal to noise ratio in four-dimensional flow-sensitive (4D-flow) measurement. A coronal 3D fast spoiled gradient echo sequence was used with the following parameters: repetition time (TR)/echo time (TE)/flip angle (FA)/number of excitations (NEX), 2.6 ms/0.8 ms/15 degrees/1; field of view (FOV) of 34 to 48 × 33.6 cm; partition thickness of 2 mm; slice zero fill interpolation of 2; overlaps of 2 mm; matrix of 224 × 224; receiver band width of 83.3 kHz; array spatial sensitivity encoding technique with eduction factor of 2; 60 partitions × 6; and scan time of 35 seconds. The best arterial-phase 3D data set was selected from the six phases and was used for segmenting the boundary of aortic wall or stent graft by maximum intensity projection algorithm.

Time-resolved two-dimensional (2D) phase-contrast magnetic resonance imaging (MRI). Electrocardiography-gated, respiratory-compensated, axial time-resolved 2D phase-contrast MRI was also performed to optimize velocity encoding for 4D-flow. The cross section was placed in the abdominal aorta using the following parameters: TR/TE/FA/NEX, 29 ms/auto (5 ms)/30 degrees/2; receiver band width, 32 kHz; FOV, 16 cm; thickness, 4 mm; matrix, 160 × 160; R-R phase, 30; and velocity encoding, 150 cm/s in all directions.

4D-Flow. A 4D-flow analysis was conducted with the following parameters: TR/TE/FA/NEX, 4.5 to 5.0 ms/1.6 to 2.0 ms/15 degrees/1; FOV, 34 to 48 cm; matrix, 224 to 256 × 160 to 224; partition thickness, 1 to 2 mm; 40 to 60 partitions; 12 phases; approximate imaging time, 5 to 7 minutes; and reduction factor of 2 for an autocalibrating reconstruction for Cartesian sampling. The velocity encoding was determined on the basis of the maximum flow velocity value measured with 2D phase-contrast cine MRI, to which a safety margin of 10 cm/s was added.

Postprocessing of the 4D-flow data. The 4D-flow and MRA data sets were transferred to a personal computer (Intel Core i7 CPU, 3.2 GHz, 12 GB RAM, Microsoft Windows 7; Microsoft Corp, Redmond, Wash) in Digital Imaging and Communications in Medicine format, and they were postprocessed by using flow analysis software (Flova; Renaissance Technology, Hamamatsu, Japan). The application consisted of two processes of extraction and analysis. First, time-resolved images of the 3D velocity vector fields were generated to overview the blood flow within the abdominal aorta. Then, 3D streamlines were generated by using 4D data sets.

Contrast-enhanced computed tomography. For Aquilion 64 (Toshiba, Tokyo, Japan), 120 kV, 442 to 480 mA was used; for SOMATOM Definition Flash (Siemens Healthcare, Hoffman Estates, Ill), 120 kV, 222 to 342 mA was used. Typical FOV was 40 × 43 cm, pitch factor was 0.8 with rotation speed of 0.3 to 0.5 second, and the matrix was 512 × 512. Iodinated contrast media used were 350 to 370 mgI/mL (Iopamiron 370 [Bayer Pharma, Berlin, Germany], Omnipaque 350 [Daiichi Sankyo, Tokyo, Japan], and Iomeron 350 [Bracco Eisai, Tokyo, Japan]). Contrast medium (2 mL/kg body weight) was injected at a rate of 4 mL/s followed by a chaser bolus of 20 mL of saline solution using an autoinjector (Dual Shot GX; Nemoto Kyorindo, Tokyo, Japan). Timing scan was combined for arterial-phase data acquisitions. Pre-contrast-enhanced and three phases of post-contrast-enhanced acquisitions were made.