

Association of the incidence of venous air embolism on coronary computed tomography angiography with the intravenous access route preparation process

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Abstract

Venous air embolism (VAE) can be observed in the right heart system on contrast-enhanced computed tomography (CT), following injection of contrast media with a power injector system. Although most VAEs are mostly asymptomatic, they may result in paradoxical air embolism (PAE).

To evaluate whether the incidence of VAE on coronary CT angiography is associated with the process of preparation of the intravenous access route.

We retrospectively evaluated 692 coronary CT examinations at 3 institutions. Trained CT nurses placed an intravenous cannula in the forearm. Tubes connected to the cannula were prepared in the following ways: A, using an interposed three-way cock and a 20-mL syringe filled with normal saline to collect air contamination in the tube; B, through direct connection to the power injector system without the interposed 3-way cock; and C, using an interposed three-way cock and a 100-mL normal saline drip infusion bottle system to keep the tube patent. The incidence and location of VAE and preparation of intravenous injection were assessed.

The overall incidence of VAE was 55.3% (383/692), most frequently observed in the right atrium (81.5%, 312/383). Its incidence varied significantly across the 3 techniques (A: 21.6% (35/162), B: 63.2% (237/375) and C: 71.6% (111/155); $P < .001$). No patient demonstrated any symptom associated with VAE.

Using a 3-way cock with syringe demonstrated the lowest incidence of VAE on coronary CT angiography. It is thus recommended to reduce potential complication risks related to intravenous contrast media injection.

Abbreviations: aOR = adjusted odds ratio, CI = confidence interval, CT = computed tomography, ECG = electrocardiogram, LA = left atrium, LV = left ventricle, PA = pulmonary artery, PACS = picture archiving and communication system, PAE = paradoxical air embolism, PFO = patent foramen ovale, RA = right atrium, RV = right ventricle, SD = standard deviation, VAE = venous air embolism.

Keywords: contrast media, coronary computed tomography angiography, intravenous access preparation, venous air embolism

1. Introduction

Despite meticulous preparation, venous air embolism (VAE) can be observed in the right heart system on contrast-enhanced computed tomography (CT), following injection of contrast

media with a power injector system.^[1] Generally, small air bubbles represent minimal VAE, and are of no clinical significance.^[2,3] VAE during a contrast-enhanced CT scan is reported as a non-fatal event.^[4,5] Although most VAEs are asymptomatic, they carry the potential risk of paradoxical air embolism (PAE). The reported incidence of VAE associated with the injection of contrast media for CT scan is 7% to 23%.^[4,6-8] Lee et al reported a case of PAE through a patent foramen ovale (PFO), in the distal right coronary artery identified by coronary CT angiography.^[9] Patients with conditions, such as right-to-left intracardiac shunt and pulmonary arteriovenous malformation, are reported to be at higher risk for neurological deficits from even small amounts of venous air.^[4,6]

Only a few studies have reported the incidence of VAE after contrast-enhanced CT examination using power injectors,^[8] although they are routinely used in the current-day clinical settings. Furthermore, to our knowledge, there has been no report regarding the incidence of VAE in coronary CT angiography with high-spatial resolution and minimal motion artifacts.

There are several possibilities for air contamination during the preparation of the intravenous access route. However, the process of preparation differs among institutions. Therefore, we hypothesized that the varied incidence of VAE reported in previous studies might be associated with the preparation of the

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intravenous access route. We also hypothesized that the electrocardiogram (ECG)-gated coronary CT angiography would be suitable for minimizing false negative results of VAE that may attribute to the reported incidence.

The purpose of our study was to evaluate the incidence of VAE on coronary CT angiography across different preparation processes for intravenous contrast media infusion.

2. Materials and methods

This retrospective study was conducted at three institutions (institution A [Tohoku University Hospital, Sendai, Japan], an academic hospital with 1262 beds, institution B [Japan Community Health Care Organization Hokkaido Hospital, Sapporo, Japan] and C [Sapporo Shiroishi Memorial Hospital, Sapporo, Japan], private hospitals with 358 and 108 beds, respectively) and approved by their ethics committees. Informed consent from subjects was waived.

A total of 692 coronary CT examinations acquired at the 3 institutions between May and July 2014 were included. CT scanners used for the examinations were SOMATOM Definition Flash (Siemens Healthineers, Forchheim, Germany) and Aquilion ONE ViSION Edition (Canon Medical Systems, Otawara, Japan) in institution A, Aquilion ONE ViSION Edition in institution B, and Discovery CT 750 HD (GE Healthcare, Milwaukee, Wisconsin, USA) in institution C. All three institutions used the same power injector system, Dual Shot GX 7 (Nemoto Kyorindo co., Ltd., Tokyo, Japan). Table 1 describes the detailed scan protocols as well as patient demographics.

2.1. Preparation of intravenous access route

Trained CT nurses placed an intravenous cannula in the forearm. Tubes connected to the cannula were prepared in the following ways: A, using an interposed three-way cock and 20-mL syringe filled with normal saline to collect air contamination in the tube (Fig. 1A); B, through direct connection to the power injector system without the interposed 3-way cock (Fig. 1B); and C, using

an interposed 3-way cock and 100-mL normal saline drip infusion bottle system to keep the tube patent (Fig. 1C).

2.2. Image analysis

The CT examinations were independently reviewed by 1 reviewer from each institution. The studies were reviewed with picture archiving and communication system (PACS) in each institution. Images were initially reviewed at a window level of 100 HU and window width of 500 HU. In all cases, reviewers were allowed to adjust window/level settings and magnification for the assessment of the intravascular air.

The location of VAE was assessed using thin-slice volume data with ECG-gated coronary CT angiography images. Recorded locations included the right atrium (RA), right ventricle (RV), pulmonary artery (PA), left atrium (LA), and left ventricle (LV).

2.3. Statistical Analysis

Descriptive statistics are presented as means ± standard deviations (SDs) or medians with interquartile ranges for continuous variables, and as numbers of cases and percentages per group for categorical variables. Pearson chi-square test was used to evaluate whether the differences in the incidence of VAE among the 3 institutions were significant and the location of each VAE incidence. Bonferroni correction for multiple comparison tests was performed as a post-hoc analysis, if necessary. The injection rates and volumes were compared between 2 groups with the presence and absence of VAE using the two-tailed Student *t* test. Then, a multivariate logistic regression analysis was used to evaluate whether the preparation process and injection rates were independently associated with the incidence of VAE; adjusted odds ratios (aOR) with 95% confidence intervals (CI) were calculated. *P* < .05 was used to designate statistical significance. All statistical calculations were performed using JMP (version 14.0.0, SAS Institute, Cary, NC).

Table 1
Summary of the institutions, medical instruments, and study population.

Institutions	A		B	C
	Academic hospital 1262 beds		Private hospital 358 beds	Private hospital 103 beds
CT machine	Definition Flash	Aquilion ONE	Aquilion ONE	Discovery CT 750HD
Tube voltage (kVp)	120	120	120	120
Tube current	Quality ref. mAs 250	SD 25	SD 25	Variable mA according to BMI [†]
Kernel	I36f	FC 13	FC 04	STND
IR* level	SAFIRE 3	AIDR weak	AIDR mild	ASIR 50%
Thickness	0.6 mm	0.5 mm	0.5 mm	0.625 mm
Injector			Dual Shot GX 7	
Contrast media			Iohexol (350 mg/ml)	
Fractional dose	22 mg/kg/s		23.3 – 31.4 mg/kg/s	26 mg/kg/s
Injection time	12 s		7–12 s	12 s
Saline flush	30 mL		30 mL	30 mL
Number of cases	162		375	155
Male	117		198	82
Female	45		177	73
Ave. age	59.3 y.o.		67.3 y.o.	69.0 y.o.

* IR: iterative reconstruction.

† BMI: body mass index.

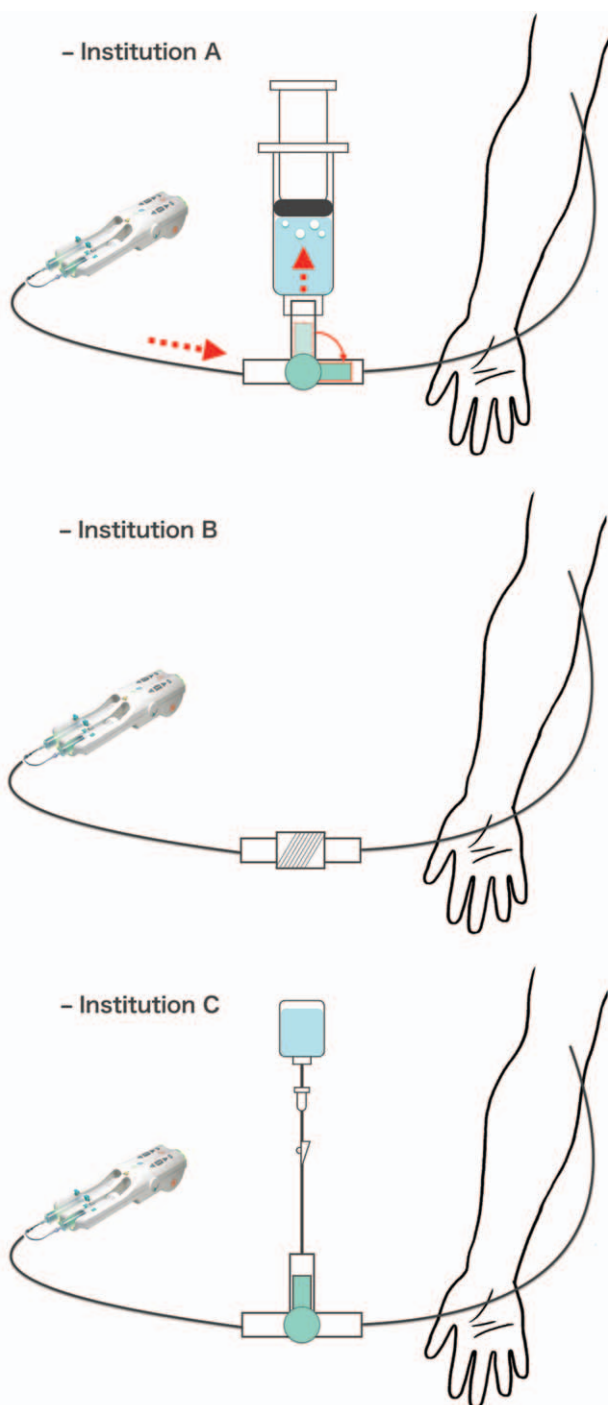


Figure 1. Illustration of intravenous access routes among 3 institutions. (A) Institution A: An interposed three-way cock and 20-mL syringe filled with normal saline was used to collect air contamination in the tube. (B) Institution B: Direct connection to the power injector system without an interposed 3-way cock. (C) Institution C: An interposed 3-way cock and 100-mL normal saline drip infusion bottle system to keep the tube patent.

3. Results

No patient demonstrated any symptom associated with VAE. The overall incidence of VAE was 55.3% (383/692). The incidence differed significantly among the 3 methods of preparation (institution A: 21.6% (35/162), B: 63.2% (237/

375), and C: 71.6% (111/155)) (Fig. 2). All air embolisms were observed in the right heart system. They were most frequently observed in the RA (81.5%, 312/383), followed by the PA (47.3%, 181/383) and RV (39.2%, 150/383). Table 2 shows the details of the location of VAE in each institution. In institutions B and C, VAEs were observed in the RA, RV, and PA simultaneously in 21.1% and 12.6% of the cases, respectively; on the other hand, institution A showed no incidence of the above case (chi-square test, $P < .05$).

Table 3 compares the injection rate and the volume of contrast media between the 2 groups with the presence or absence of VAE. In institution A, the group with the presence of VAE showed significantly lower injection rate and volume than the other; in the other 2 institutions, no significant differences were observed for either the injection rate or volume between the two groups. For multivariate regression analyses to evaluate associations with the presence of VAE, we defined preparation methods as independent categorical variables with the reference category of institution A and injection rate/volume as continuous variables. In the multivariate regression analyses, neither the injection rate (aOR for 1 mL/second increase, 0.89; 95% CI, 0.75, 1.06; $P = .21$) nor injection volume (aOR for 10 mL increase, 0.84; 95% CI, 0.70, 1.00; $P = .05$) were significantly associated with the incidence of VAE. When the preparation method of institution A was set as the reference category, aOR and 95% CI of institutions B and C were as follows: institution B, aOR with injection rate as confounder, 7.3; 95% CI, 4.6, 11.8; $P < .01$ and aOR with injection volume as confounder, 5.6; 95% CI, 3.6, 8.9; $P < .01$; institution C, aOR with injection rate as confounder, 10.3; 95% CI, 6.0, 17.8; $P < .01$ and aOR with injection volume as confounder, 11.5; 95% CI, 6.5, 20.1; $P < .01$.

4. Discussion

The key findings of our study were

- (1) the lowest incidence of VAE in the right heart system with use of a 3-way cock and syringe, and
- (2) no significant association of injection rate/volume with the incidence of VAE.

Orebaugh noted that 3 elements must be present for the air to be administered into the venous system:

- (1) a source of the air (the atmosphere),
- (2) a connection between the vascular system and the air source, and
- (3) a pressure gradient that favors air entry.^[10]

The last element can occur under conditions, such as the presence of a negative intravascular pressure relative to air pressure, resulting in air being pushed into the vessels. Power injectors induce high pressure and thus easily push the contaminated air into the veins. Since the use of a power injector is mandatory to acquire CT coronary angiography with diagnostic image qualities, the aforementioned three elements are hard to avoid. Therefore, it is critical to reduce the amount of air bubbles contaminating the tube before initiation of the injection. Groell et al reported that contaminated air can enter during catheter insertion and while connecting the cannula to the injection tube before contrast media injection.^[6] Based on our results, collection of air bubbles in the tube with a syringe is an effective method to minimize VAE. A 3-way cock with a syringe can collect air bubbles in the intravenous access route, including

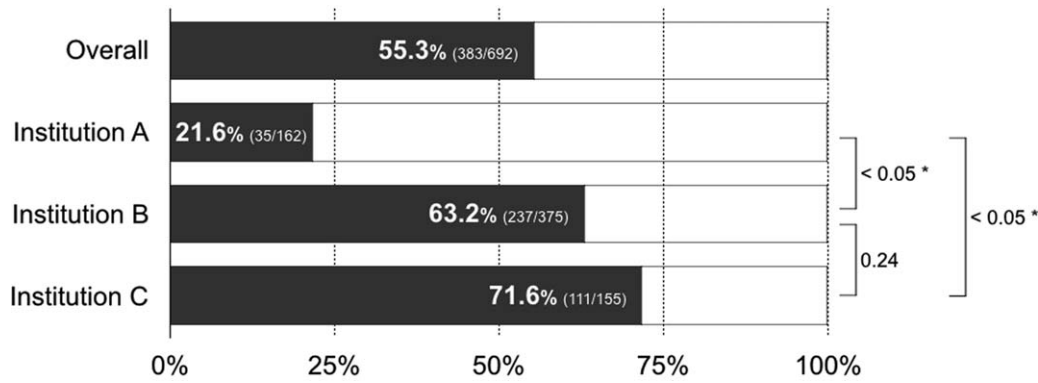


Figure 2. Incidence of VAE. The overall incidence of VAE was 55.3%. The incidence at institution A was the lowest. VAE=venous air embolism.

the canula, tubes, cock, syringes, and their connections. The air in the upstream system can be pushed into the syringe through the three-way cock by the power injector, whereas the air in the downstream system can be aspirated into the syringe.

In institutions B and C, VAEs observed in the RA, RV, and PA simultaneously in 21.1% and 12.6% of the cases, respectively; on the other hand, institution A showed none of the above incidence. The differences may be related to the volume of the VAE that may be introduced into the vascular system. Combining the above with the results of the overall incidence of VAE, the methods in institution A contributed to a reduction in the amount of contaminated air in the tube.

Although we did not record the intra-tube pressure automatically measured by the power injector system, the pressure generally increases with the injection rate. Therefore, we assumed that the injection rate generating a pressure gradient between the tube and vein was positively associated with the incidence of VAE. However, the association was not significant, except for a negative association in institution A. We could not elucidate the reason for the negative association. Nevertheless, our results indicate that preparation of the tube system is more significantly associated with VAE as compared to the injection rate.

The incidence of VAE associated with contrast-enhanced CT has been reported as 7- 23%.^[4,6-8] Our incidence (overall,

55.3%) was higher than in these reports; even the lowest incidence in institution A exceeded 20%. The high incidence was probably because we evaluated ECG-gated coronary CT angiography. None of the earlier studies have evaluated ECG-gated thin-slice images for the incidence of VAE. Therefore, it is reasonable that motion artifacts and partial volume effects underestimated the presence of small air bubbles contaminating the right heart system. Smaller reconstructed field-of-view dedicated for CT coronary angiography, rather than general body imaging, may also have attributed to the identification of small air bubbles in our study.

Complications of VAE include increased pulmonary vascular resistance, increased right ventricular pressure, hypoxemia, myocardial infarction, and stroke.^[11] A massive VAE (200-300mL air) is considered to be fatal.^[12] On the other hand, a small air embolism does not usually require any intervention other than observation because it does not interfere with cardiopulmonary circulation.^[13] Most of the time, small emboli are absorbed in the blood or the alveoli of the lungs without any inadvertent consequence, and the patients remain asymptomatic.^[14] However, we should be aware that even small VAEs can cause serious complications if a right-to-left shunt is present. PFO is a common type of shunt in general populations, with an estimated prevalence of 25% to 35%, based on autopsy

Table 2
Details of the location of venous air embolism at each institution.

	Institution A	Institution B	Institution C	P value			
				χ^2	A vs B	B vs C	C vs A
RA only	37.1% (13 / 35)	25.7% (61 / 237)	46.8% (52 / 111)	<0.01*	.68	<.01*	1
RV only	11.4% (4 / 35)	4.2% (10 / 237)	3.6% (4 / 111)	0.14	-	-	-
PA only	34.3% (12 / 35)	9.7% (23 / 237)	7.2% (8 / 111)	<0.01*	<.01*	1	<.01*
RA + RV	5.7% (2 / 35)	16.9% (40 / 237)	14.4% (16 / 111)	0.22	-	-	-
RV + PA	2.9% (1 / 35)	3.4% (8 / 237)	0.9% (1 / 111)	0.40	-	-	-
PA + RA	8.6% (3 / 35)	19.0% (45 / 237)	14.4% (16 / 111)	0.23	-	-	-
RA + RV + PA	0% (0 / 35)	21.1% (50 / 237)	12.6% (14 / 111)	<0.01*	.017*	.24	.18

PA=pulmonary artery, RA=right atrium, RV=right ventricle.

Table 3
Degree of presence of venous air embolism and the injection rate and volume of contrast media.

	Presence	Absence	P value
Injection rate (mL/s)			
Institution A	3.4±0.7	3.9±0.8	<.01*
Institution B	4.9±1.1	4.9±1.0	.76
Institution C	4.8±0.5	4.9±0.7	.21
Overall	4.7±0.1	4.5±0.1	<.01*
Injection volume (mL)			
Institution A	41.3±8.6	47.2±9.5	<.01*
Institution B	37.5±10.1	37.7±9.6	.88
Institution C	57.4±6.0	58.9±7.9	.20
Overall	43.6±12.6	44.7±11.8	.26

studies.^[15] Holding the breath during deep inspiration on CT examination can induce elevation of intrathoracic pressure and RA pressure, resulting in right-to-left shunt across the PFO.^[7] This may allow venous air bubbles to enter the arterial circulation, increasing the risk.^[16,17] Lee et al reported a case of PAE in the distal right coronary artery identified by coronary CT angiography, the underlying cause of which was considered to be PFO.^[9]

This study has 2 important limitations. First, protocols that depended on clinical routine settings were not uniform across institutions in the retrospective observational study. Therefore, there may be a confounding bias apart from how to connect tubes, such as ranges in the skills of expert nurses, preparation time, and total examination time, depending on the institution. A randomized prospective study would have been favorable to minimize these biases. However, based on our results, a future randomized study would not be tolerated considering patient safety. In fact, both institutions B and C have already changed their preparation methods to that used by institution A following our results. Second, no complication related to the VAE was observed in any examination. Therefore, we could not demonstrate whether the preparation methods were associated with significant clinical complications, such as stroke and myocardial ischemia. However, considering patient safety, no contamination of non-physiological air in the vascular system is clinically desired.

In conclusion, using a three-way cock with syringe demonstrated the lowest incidence of VAE on coronary CT angiography. The most important management for iatrogenic VAE is prevention.^[16,18–20] Therefore, it is recommended to reduce potential risks of complication related to intravenous contrast media injection in daily practice.

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