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LABORATORY INVESTIGATION

Influence of Contrast Agent Dilution on Ballon Deflation Time and Visibility During Tracheal Balloon Dilation: A 3D Printed Phantom Study

Min Tae Kim[1] · Jung-Hoon Park[1,2] · Ji Hoon Shin[1] · Namkug Kim[1,3] · Sunghyun Daniel Kim[4] · Jiaywei Tsauo[1] · Kun Young Kim[1] · Guk Bae Kim[2] · Ho-Young Song[1]

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Abstract
Purpose To determine the effect of contrast medium dilution during tracheal balloon dilation on balloon deflation time and visibility using a 3-dimensional (3D) printed airway phantom.
Materials and Methods A comparison study to investigate balloon deflation times and image quality was performed using two contrast agents with different viscosities, i.e., iohexol and ioxithalamate, and six contrast dilutions with a 3D printed airway phantom.
Results Compared to 1:0 concentration, 3:1, 2:1, 1:1, 1:2, and 1:3, contrast/saline ratios resulted in a 46% (56.2 s), 59.8% (73.1 s), 74.9% (91.6 s), 81.7% (99.8 s), and 83.5% (102 s) reduction for iohexol, respectively, and a 51.8% (54.7 s), 63.8% (67.6 s), 74.7% (79.2 s), 80.5% (85.3 s), and 82.4% (87.4 s) reduction for ioxithalamate, respectively, in the mean balloon deflation time, although at the expense of decreased balloon opacity (3.5, 6.9, 11.1, 12.4, and 13.9%, for iohexol, respectively, and 3.2, 6, 9.6, 10.8, and 12.4%, for ioxithalamate, respectively).
Conclusions Use of a lower viscosity contrast agent and higher contrast dilution is considered to be able to reduce balloon deflation times and then simultaneously decrease visualization of balloons. The rapid balloon deflation time is likely to improve the safe performance of interventional procedures.

Keywords Deflation time · Balloon catheter · Tracheal Stricture · Obstruction

Introduction

Tracheal balloon dilation is an accepted initial therapeutic option for patients with benign tracheobronchial strictures. This procedure is not only less invasive than surgery, but is also associated with lower morbidity and mortality rates, although recurrence is more common [1–5]. In order to reduce the risk of recurrence, many physicians have recommended balloon inflation for at least one full minute [6–8]. However, balloon inflation can temporarily obstruct the trachea and thus impair air exchange. Therefore, if the balloon is inflated for an extended period of time, major life-threatening complications, such as respiratory failure, cardiac arrest, and brain injury, could occur [9]. Various contrast agents are currently available with different viscosities, osmolalities, and charge (ionic vs. non-ionic) [10–12]. Higher viscosity may prolong balloon deflation times, which could be critical during balloon dilation [12]. The viscosity of the contrast agent and its flow rate within

Min Tae Kim and Jung-Hoon Park have contributed equally to this work.

✉ Ji Hoon Shin
jhshin@amc.seoul.kr

✉ Namkug Kim
namkugkim@gmail.com

[1] Departments of Radiology and Research Institute of Radiology, Asan Medical Center, University of Ulsan College of Medicine, 388-1, Poongnap 2-dong, Songpa-gu, Seoul, Republic of Korea

[2] Biomedical Engineering Research Center, Asan Medical Center, University of Ulsan College of Medicine, 388-1, Poongnap 2-dong, Songpa-gu, Seoul, Republic of Korea

[3] Department of Convergence Medicine, Asan Medical Center, University of Ulsan College of Medicine, 388-1, Poongnap 2-dong, Songpa-gu, Seoul, Republic of Korea

[4] Seoul National University College of Medicine, 103, Daehak-ro, Ihwa-dong, Jongno-gu, Seoul 110-799, Republic of Korea

the balloon catheter are important factors for reducing the deflation time during the procedure [13]. Manufacturers of balloon catheters commonly recommend a mixture of contrast and saline in a 1:1 ratio. However, whether this contrast agent dilution is optimal for tracheal balloon dilation still remains unknown and the optimal contrast agent dilution for tracheal balloon dilation has not yet been investigated. We hypothesized that optimal contrast agent dilution could reduce temporal tracheal obstruction time during balloon dilation. Therefore, the purpose of this study was to determine the effect of contrast medium dilution during tracheal balloon dilation on balloon deflation time and visibility in a 3-dimensional (3D) printed airway phantom.

Materials and Methods

The deflation time and image quality of iohexol (Omnipaque 300; General Electric Healthcare Company, Shanghai, China) and ioxithalamate (Telebrix 300; Guerbet Aulnay-Sous-Bois, Paris, France), two commonly used contrast agents, in six dilutions (contrast/saline ratios, 1:0 [100%], 3:1 [75%], 2:1 [66.6%], 1:1 [50%], 1:2 [33.3%], and 1:3 [25%]) were investigated. Non-ionic monomer iohexol has an osmolality of 672 mOsm/kg H_2O and a viscosity of 6.3 cPs at 37 °C, whereas ionic monomer ioxithalamate has an osmolality of 1500 mOsm/kg H_2O and a viscosity 5.2 cPs at 37 °C. Both contrast agents were preheated to 37 °C before the experimental study.

Fabrication of a 3D Airway Phantom

In order to estimate average morphological airway information and anatomical geometry, medical images of CT, ultrasonography, and endoscopy in patients with normal anatomy and the human anatomy atlas were utilized. The 3D simulation model using two open source programs [MeshLab (http://meshlab.sourceforge.net/) and MeshMixer (http://www.meshmixer)] consisted of three parts of airway tissue, cartilage, and stricture (Fig. 1). A 3D printed phantom for the airway was created using a 3D printer (Connex3 Objet500; Stratasys Corporation, Rehovot, Israel). Airway tissue of the phantom was made of 100% rubber-like material (TangoTM Family); the cartilage was made of a mixture of 70% rubber-like material and 30% blue-colored, hard material (Vero Color blue); and the stricture was made of a mixture of 35% rubber-like material and 65% red-colored, hard material (Vero Color red).

The trachea was 120 mm in length and 21 mm in diameter, the bronchi were 60 mm in length, the left bronchus was 14.6 mm and right bronchus 15.8 mm in diameter, the angle formed by the right and left bronchi was 90°, the cartilage was 3.5 mm thick at the trachea and 2.4 mm thick at the bronchus. The cartilage rings were separated by 6 mm in the trachea, by 4.6 mm in the left bronchus, and by 5 mm in the right bronchus. The stricture part was 20 mm long and 10 mm in diameter and was located at the position of 70 mm from the top of the trachea.

Deflation Time Assessment

A 0.035-inch × 180 cm guide wire (Radiofocus M; Terumo, Tokyo, Japan) was passed through the trachea into the left or right bronchus. Then, a 18 mm × 4 cm balloon catheter (shaft length, 75 cm, XXL balloon dilatation catheter, Boston Scientific Watertown, MA, USA) was placed across the stricture in the 3D printed airway phantom and inflated to exactly 5 atm using a pressure gauge

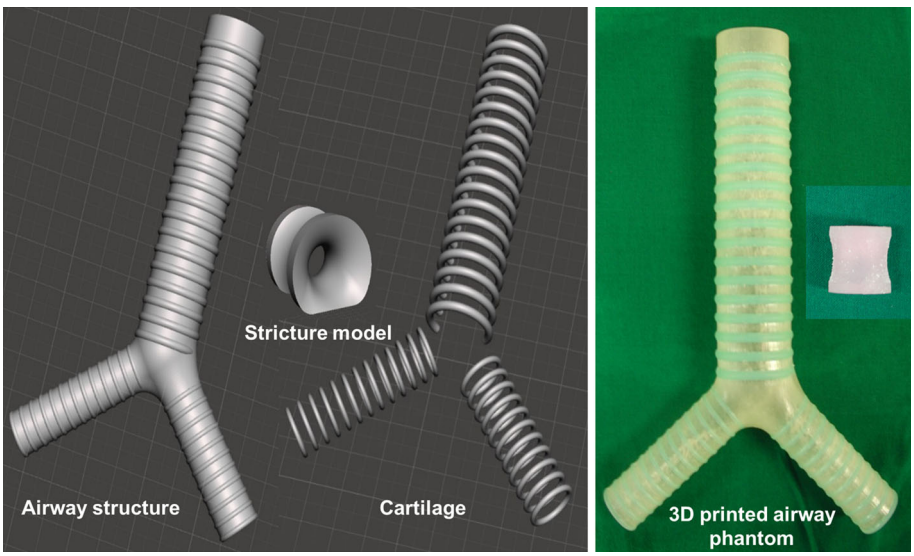

Fig. 1 The images show the 3D design of the simulation models (*left*) and a 3D printed phantom (*right*) including an airway structure, cartilage, and a stricture. The trachea was 21 mm in diameter and the stricture part was 10 mm in diameter

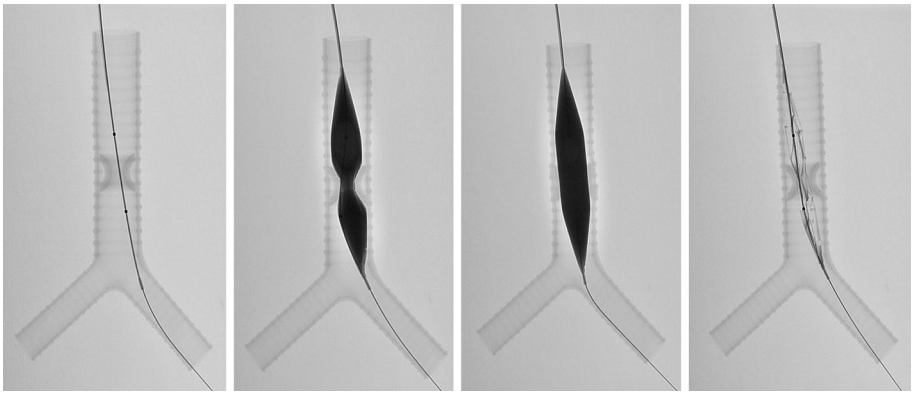

Fig. 2 Fluoroscopic images show the balloon dilation procedure performed to evaluate the deflation time in a 3D printed airway phantom. An 18 mm × 4 cm balloon catheter and two contrast agents with different viscosities, i.e., iohexol and ioxithalamate, and six contrast dilutions were used for balloon inflation

monitor (Genoss Inflator; Genoss, Suwon, Korea) with iohexol or ioxithalamate. Balloon deflation time was recorded (Fig. 2). If air was identified into the balloons after inflation under fluoroscopy, the balloon preparation was repeated. The balloon catheter was then deflated by applying 15 mL of negative suction, and the time until 10 mL of contrast agent had been aspirated into the syringe was recorded. A single balloon catheter was used in each group. The experiment was repeated ten times using different contrast agent dilutions.

Image Quality Assessment

Image quality was assessed using a flat-panel detector angiographic system (Artis Zee Multipurpose; Siemens, Muenchen, Germany).

The signal-to-noise ratio (SNR) was measured in order to evaluate the image quality. All measurements were performed on a workstation. Circular region of interests (ROIs) (10–10 mm^2) were drawn at the middle portion (ROI 1) of the balloon catheter and signal attenuation and background image outside in the balloon catheter (ROI 2) (Fig. 3). The SNR is defined $\mathrm{SNR} = \frac{\mathrm{BG}-\mathrm{ROI}}{\sqrt{\mathrm{STD}^2_{\mathrm{ROI}}+\mathrm{STD}^2_{\mathrm{BG}}/2}}$ [14], where BG is the mean value of the pixel contained in the ROI 2 outside the balloon catheter, and ROI the mean value of the pixel contained in the ROI 1 in the balloon catheter; STD the corresponding standard deviation for the pixel content in the selected ROIs inside and outside the balloon catheter. Three measurements were made for ROIs in the balloon catheter and outside the balloon catheter. SNR values reported for each image are mean values from the three corresponding calculations.

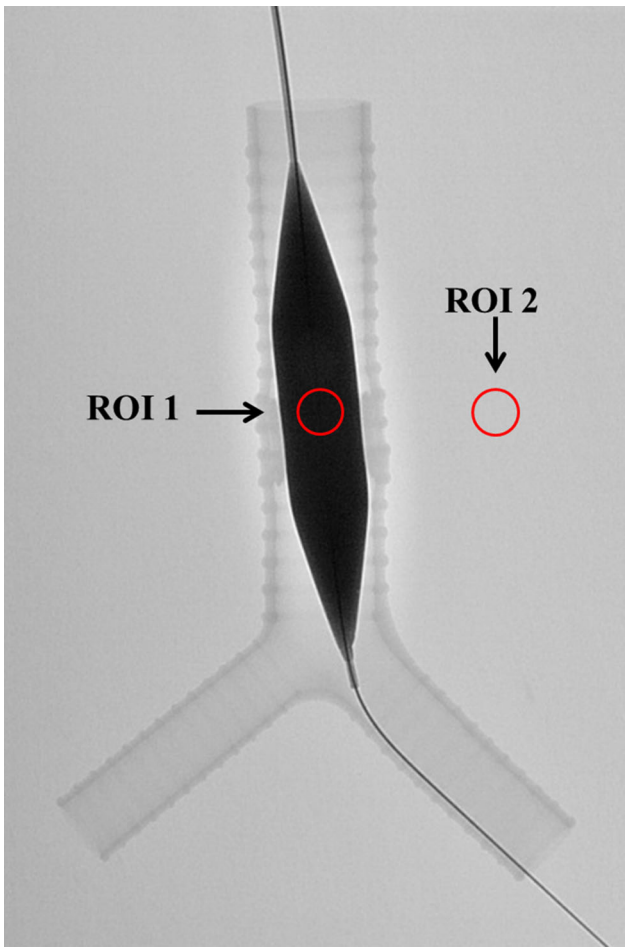

Fig. 3 Radiographic image obtained during balloon dilation in 3D printed phantom study

Statistical Analysis

Descriptive statistics, including the median and standard deviation, were calculated for each of the all groups. Non-parametric, Kruskal–Wallis, multiple-comparison tests were used to assess the differences in balloon deflation time and the SNR. Mann–Whitney *U* tests were used to compare between iohexol and ioxithalamate. Statistical significance was defined as $P < 0.05$. All statistical analyses were performed using SPSS version 22.0 (SPSS, Chicago, IL, USA).

Table 1 Comparison of the deflation time and image quality between the two contrast agents and among the six contrast dilutions

Contrast: saline ratio	Contrast agents	Deflation time (s)	*P* value*	*P* value**	*P* value^{+}	Image quality (Mean SNR)	*P* value*	*P* value**	*P* value^{+}
1:3	Iohexol	20.17 ± 0.52			<0.001	2.23 ± 0.01			<0.001
	Ioxithalamate	18.61 ± 0.40				2.18 ± 0.02			
1:2	Iohexol	22.29 ± 0.40			<0.001	2.27 ± 0.01			<0.001
	Ioxithalamate	20.70 ± 0.29				2.22 ± 0.02			
1:1	Iohexol	30.57 ± 0.39			<0.001	2.30 ± 0.01			<0.001
	Ioxithalamate	26.83 ± 0.54	<0.001	<0.001		2.25 ± 0.01	<0.001	<0.005	
2:1	Iohexol	49.04 ± 1.06			<0.001	2.41 ± 0.02			<0.001
	Ioxithalamate	38.39 ± 1.12				2.34 ± 0.02			
3:1	Iohexol	65.90 ± 1.51			<0.001	2.50 ± 0.01			<0.001
	Ioxithalamate	51.30 ± 1.06				2.41 ± 0.01			
1:0	Iohexol	122.13 ± 1.80			<0.001	2.59 ± 0.01			<0.001
	Ioxithalamate	106.00 ± 1.16				2.49 ± 0.01			

Data are mean ± standard deviation (SD)

* Comparison of the iohexol/saline ratio using the non-parametric Kruskal–Wallis multiple-comparisons test

** Comparison of the ioxithalamate/saline ratio using the Kruskal–Wallis multiple-comparisons test

$^{+}$ Comparison of the iohexol/saline ratio with the ioxithalamate/saline ratio using the Mann–Whitney *U* test

Results

The mean deflation time of iohexol was significantly longer than that of ioxithalamate (122.13 ± 1.80 vs. 106.01 ± 1.16 s, $P < 0.001$) with a 13.2% reduction. However, the mean SNR of iohexol was significantly greater than that of ioxithalamate (2.46 vs. 2.38, $P < 0.001$) and with a 3.3% reduction. The results of the phantom outcomes are summarized in Table 1.

The mean deflation time and the SNR of iohexol and ioxithalamate gradually decreased according to the increased saline ratio. Compared to 1:0 concentration, 3:1, 2:1, 1:1, 1:2, and 1:3, contrast/saline ratios resulted in a 46% (56.2 s), 59.8% (73.1 s), 74.9% (91.6 s), 81.7% (99.8 s), and 83.5% (102 s) reduction for iohexol, respectively, and a 51.8% (54.7 s), 63.8% (67.6 s), 74.7% (79.2 s), 80.5% (85.3 s), and 82.4% (87.4 s) reduction for ioxithalamate, respectively, in the mean balloon deflation time, although at the expense of decreased balloon opacity (3.5, 6.9, 11.1, 12.4, and 13.9%, for iohexol, respectively, and 3.2, 6, 9.6, 10.8, and 12.4%, for ioxithalamate, respectively) (Fig. 4). Compared to iohexol, the deflation time of ioxithalamate in all of the dilution ratios was rapid, although the balloon opacity inversely decreased.

Discussion

Our study demonstrates that the contrast/saline ratios have a significant impact on balloon deflation and image quality. Reduction in the balloon deflation times could be achieved with further saline dilution; however, visualization was then also reduced. Our experimental results can be extended to balloon dilation procedures for benign strictures involving non-vascular luminal organs. Mogabgab et al. reported that lower contrast viscosity and higher contrast dilution significantly reduced the coronary balloon deflation times [12]. However, visualization of the opacity according to different viscosities was not evaluated. Furthermore, as the balloon deflation time was measured from the onset of deflation until the last visible contrast passed the more proximal radiopaque marker, it was relatively uncertain compared with our method for measuring the time. In our study, in order to determine the optimal contrast/saline ratio for tracheal balloon dilation, we evaluated the deflation time in a 3D printed airway phantom with stricture and visualization of the balloon catheter in a rat tracheal model.

A more practical method of assessing image quality is the use of psychophysical measurements in which an observer must recognize visual stimuli, such as bar patterns or circular objects, using different contrast agents [15]. The 3D printed airway phantom does not replicate actual patient anatomy. As a result, the variations in gray values of a balloon catheter observed on images of contrast-detailed phantoms are typically much lower than those of actual patients. In fact, from a practical viewpoint, our 3D printed phantom model should predict changes in image quality. In the current study, image quality was assessed by measurement of the SNR and the subjective overall quality score using images obtained during balloon dilation of a rat trachea. However, the required image quality in the clinical

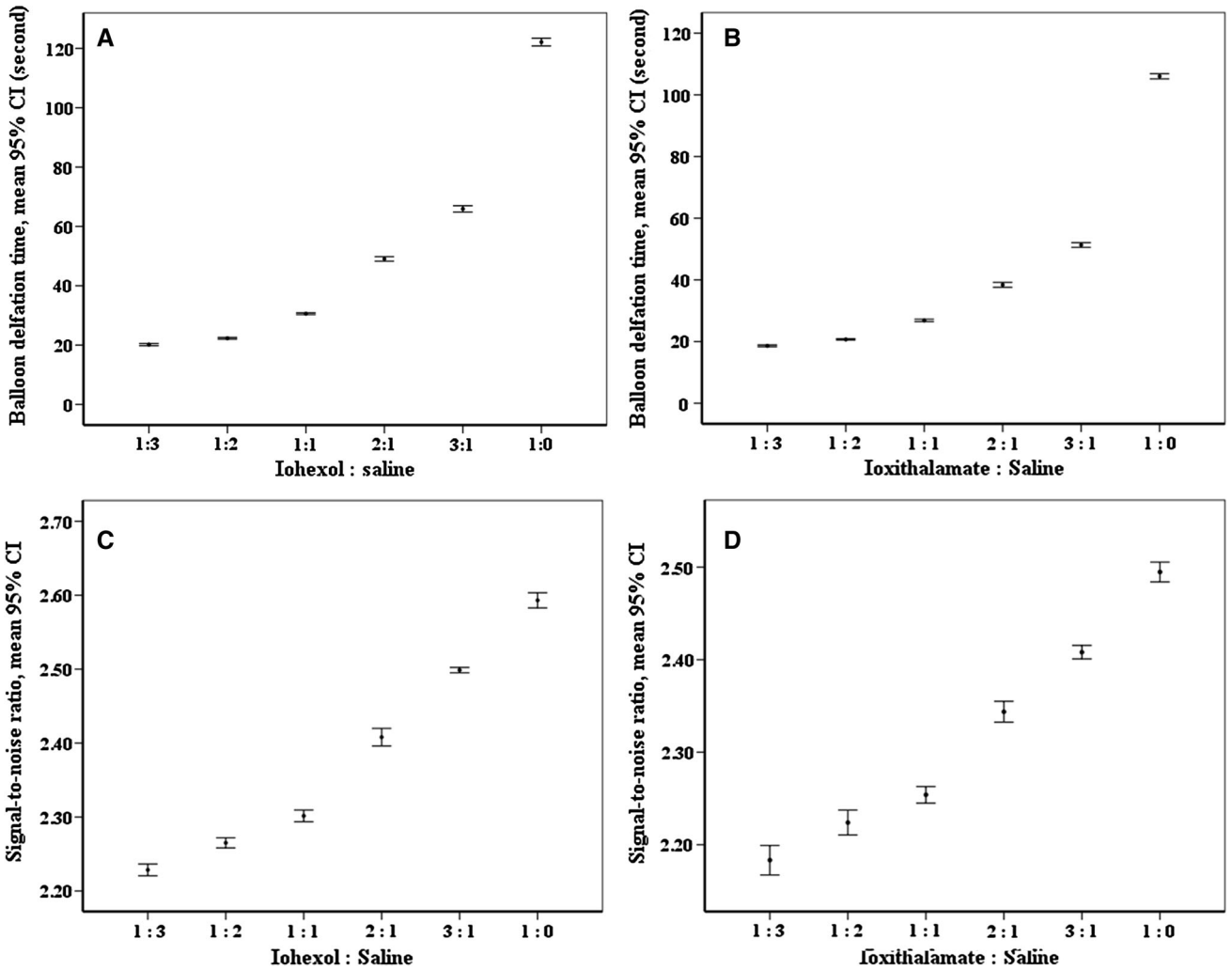

Fig. 4 Results of balloon deflation time and signal-to-noise ratio. **A** Balloon deflation time was shown according to iohexol/saline ratio. **B** Balloon deflation time was shown according to ioxithalamate/saline ratio. **C** SNR was shown according to iohexol/saline ratio. **D** SNR was shown according to ioxithalamate/saline ratio

setting may differ considerably depending on the human anatomic region under investigation. Based on our findings, further research should be performed in order to ascertain the optimal contrast/saline ratio for patients who have undergone tracheal balloon dilation.

3D printing technology has been used in various medical fields, including personalized treatment, medical research, and premedical education, for both soft and hard tissue [16–18]. The recently commercialized, 3D printable multi-materials with transparent, full-colored, and flexible properties accelerate its applications to more extensive medical fields [19–21]. In our study, quantitative morphological airway information was evaluated using medical images to develop a 3D printed airway phantom with a stricture. The 3D printed airway phantom was developed by simple modification in order to simulate balloon dilation. To obtain physical properties similar to those of real airway tissue, each part of the airway structure, cartilage, and stricture were made of different materials.

Our study has several limitations. The principal limitation is its small sample size which basically decreases its statistical power, although significant differences were observed between the all groups. Secondly, the shape and materials of the 3D printed phantom used in this study were based on known criteria of rigidity and size, but not enough to mimic real airway properties, and which is due to the present technical limitations of the current 3D printing technology. We also did not specifically address the influence of currently available balloon catheters; and furthermore, a single balloon catheter was used in this study. Although differences in balloon deflation times and visualization were observed according to six contrast/saline ratios and two kinds of contrast agents, these results may not apply to other clinical practices and need to be verified

in further studies or in comparison studies. Finally, checking of the aspirated contrast medium volume into the syringe is not only impractical but also may give incorrect information.

In conclusion, the use of a lower viscosity contrast agent and higher contrast dilution could reduce balloon deflation times and decrease visualization of balloons. The rapid balloon deflation time is likely to improve the safe performance of interventional procedures.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

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