

Intracardiac Shunts Among Patients Undergoing Oil-Based Contrast Lymphangiography: Prevalence and Rate of Systemic Arterial Embolic Complications

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Abstract

Objective: To determine the prevalence of systemic embolic complications after oil-based contrast lymphangiography.

Patients and Methods: A retrospective medical record review of all patients undergoing oil-based lymphangiographic procedures from January 1, 2000, to December 31, 2021 was performed to identify the following: (a) the rate of systemic embolic complications after the procedure; (b) the presence of preprocedure echocardiographic assessment for right-to-left shunting; and (c) the presence of right-to-left shunting after a systemic embolic complication.

Results: A total of 350 patients (200 male, 57%) underwent 400 oil-based lymphangiographic procedures. A total of 2 systemic embolic complications occurred for a prevalence of 0.5% (2/400). Preprocedure echocardiography was performed in 226 patients (226/350, 65%). Identification of a right-to-left shunt was made in 25 patients (25/226, 11%, with the majority reporting shunting at rest (23/25, 92%). Of the patients with systemic embolic complications, one had multifocal systemic oil contrast emboli, and one had a large territorial cerebrovascular infarct without the presence of oil-based contrast noted. Both cases underwent preprocedure echocardiography reporting a structurally normal heart with no evidence of a shunt through color flow Doppler evaluation, but neither case had undergone a true shunt study. Both patients were identified to have a right-to-left shunt during the dedicated echocardiographic shunt study postprocedure.

Conclusion: Risk of a systemic embolic complication after oil-based contrast lymphangiography is rare but can be catastrophic. A standardized assessment for patients undergoing the procedure may be necessary to identify those at risk and to allow for appropriate preventive strategies to be employed.

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From the Department of Radiology (W.N., E.B., C.R., E.T., S.T.), Department of Pediatrics, Division of Pediatic Cardiology (J.A.), Mayo Clinic, Rochester, MIN; and Department of Radiology, Section of Interventional Radiology, University of Wisconsin, Madison, WI (E.K.K.); and Department of Surgery, Division of Pediatric Surgery (S.P.), Mayo Clinic, Rochester, MN. thiodized oil (Lipiodol) contrast fluoroscopic lymphangiography may be performed by transpedal, transnodal, transhepatic, transmesenteric, or retrograde thoracic duct approach for both diagnostic and therapeutic purposes.^{1,2} An example would include lymphangiography to identify thoracic duct leak as an etiology of chylothorax, with the ability to perform thoracic duct embolization as a treatment strategy.³ The increasing demand of oil-based lymphangiography for both diagnostic and interventional purposes

underscores the need to have a clear understanding of the complication rates, with the most feared complication being systemic embolization of the oil-based contrast.⁴

The rate of systemic embolic complications during oil-based contrast lymphangiography is not well understood in the modern literature, likely because of the rarity of these complications and limited use of fluoroscopic lymphangiography for diagnostic purposes for several decades. A survey study from 1968 utilizing questionnaire data from proceduralists who performed oil-based contrast lymphangiograms reported a rate of cerebral disorder complications in 9 out of 32,000 lymphangiograms (0.028%).⁵ The accuracy and generalizability of these data are limited, owing to recall bias and incomplete reporting. A more recent estimation of systemic embolic complications during oil-based contrast use can likely be extrapolated from conventional transarterial chemoembolization with ethiodized oil. A large study analyzing 7855 transarterial chemoembolization procedures reported 8 cerebral ethiodized oil embolic complications (0.10%).⁶ Nonetheless, these findings from hepatic transarterial delivery of ethiodized oil may not be generalizable to intralymphatic administration. Although the rate of cerebral or systemic ethiodized oil embolization appears rare, its occurrence may have considerable morbidity and mortality.

Risk factors for cerebral ethiodized oil embolism are not well understood. A general predisposition for this complication would be the presence of a right-to-left shunt, thus leading the manufacturer to label the presence of intrapulmonary or intracardiac right-to-left shunting as a contraindication. Unfortunately, there have been case reports of cerebral ethiodized oil embolization in the absence of a documented shunt⁴ but this may also reflect that the shunt was undiagnosed by the assessment performed. There is no standard recommendation on how individuals should be screened for the presence of a right-to-left shunt before oil-based lymphangiography.

As such, the aim of the present study was to determine the prevalence of systemic embolic complications after oil-based contrast lymphangiography, with the goal of utilizing these data to guide a practice-based model of preprocedure risk evaluation.

PATIENTS AND METHODS

The study was approved by the local institutional review board and a waiver of written informed consent was granted as the institutional review board determined the research involved no more than minimal risk to patients; the research could not be carried out practicably without the waiver; and the waiver would not adversely affect the rights and welfare of the patients. In this study, a retrospective medical record review was conducted to determine all patients that underwent oil-based lymphangiographic procedures from 2000 to 2021. Demographic characteristics, clinical (medical/surgical history), and procedural data were collected. The presence of an echocardiogram (transthoracic or transesophageal) before the lymphangiogram procedure was determined and report reviewed. The presence or absence of a shunt via color flow Doppler or via shunt study was recorded. If multiple previous echocardiograms had been performed, then all were reviewed to assess these variables. A shunt study was defined as administration of intravenous agitated saline with and without valsalva maneuver during the echocardiogram to evaluate for the presence of right-to-left shunting of the contrast medium or saline bubbles. Shunt grade was not assessed, and the presence of any microbubbles in the left heart structures was deemed a positive test.

Lymphangiogram Procedure

The anesthetic approach included local analgesia, moderate sedation, monitored anesthesia care or general anesthesia depending on the procedure. Fluoroscopic lymphangiography with diagnostic \pm therapeutic intent was performed via a pedal and/or inguinal nodal approach using standard methods.^{7,8} Briefly, the pedal approach involved cannulating the dorsal pedal lymphatics followed by injection of ethiodized oil (Lipiodol).² The nodal approach involved needle access of lymph nodes, most commonly inguinal, under direct ultrasound guidance and injecting ethiodized oil directly into that node. After ethiodized oil injection, the lymphatics were imaged fluoroscopically. The number of lymphangiograms per patient, lymphatic access approach used, intervention if performed, ethiodized oil volume, and complications were collected. Complications were defined using the Society of Interventional Radiology Classification System for Complications by Outcome.⁷ Procedure related complications were defined as occurring within 30 days of the procedure.

Data Analyses

Study data were collected and managed using REDCap electronic data capture tools.^{9,10} Data were analyzed using JMP 16.2.0 (Raleigh) and Prism 9.0 (GraphPad Software,

Inc). Descriptive statistics (means, percentages, etc.) were used to summarize the data. Statistical analyses between groups was performed utilizing Fischer Exact Test. A *P*-value of <.05 was considered significant for all calculations.

RESULTS

The number of cases performed per year from 2000 to 2021 are summarized in Figure 1. Demographic characteristics and clinical data for all cases are summarized in Tables 1 and 2.

The mean ethiodized oil volume (ml) administered was 11.6 ± 5.1 ml (median 11 ml; range of 1-20 ml). The lymphangiogram approach was pedal in 239 cases (239/400, 60%) and nodal in 151 cases (151/400, 38%). A combined approach was used for 10 cases (10/400, 2%) In 137 lymphangiograms, intervention was attempted the same day (137/400, 34%). Systemic embolic complications were present in 2 cases (2/400, 0.5%). Specific details for each case are as follows:

Case 1—Ethiodized Oil Emboli to the Cerebral, Renal, and Splenic Circulation

In Figure 2, an 83-year-old male with recurrent chylothorax underwent diagnostic lymphangiography using 20 ml of ethiodized oil under general anesthesia. On waking from anesthesia, the patient had altered mental status with slurred speech. A head computed tomography was obtained reporting multifocal ethiodized oil emboli in the brain. Subsequent imaging confirmed oil-based contrast present in the kidney and spleen as well. A transesophageal echocardiogram was performed with shunt study reporting a patent foramen ovale with inducible right-to-left shunt. The patient clinically deteriorated and died 8 days later.

Case 2—Large Territory Middle Cerebral Artery Cerebrovascular Accident

An 80-year-old female with ovarian malignancy and chylothorax underwent diagnostic lymphangiography using 7 ml of ethiodized oil under local anesthetic. She became hypoxic immediately after the procedure with a change in her oxygen saturation from a normal baseline to 70%-79% on room air concerning for a pulmonary embolism. The following day she developed expressive aphasia, and a head computed tomography was obtained, reporting a left middle cerebral artery ischemic stroke. No focus of intracranial ethiodized oil was visualized on subsequent imaging. A transesophageal echocardiogram was performed with shunt study reporting a small extracardiac right-to-left shunt consistent with a pulmonary arteriovenous malformation.



TABLE 1. Demographic Characteristic Data of 350 Patients who Underwent Oil-Based Contrast Fluoroscopic Lymphangiography From 2000-2021

Age (y)	55.6±18.6 (range, 0.4-94.6)
Sex	
Male	200 (57)
Female	150 (43)
Height (cm)	169.3±17.4
Weight (kg)	78.2±25.1
BMI	26.6±6.9

BMI, body mass index.

Data are presented as mean \pm SD or n (%).

Echocardiography

Preprocedure echocardiography was present in 226 patients (226/350, 65%). Of those that underwent preprocedure echocardiography, the majority were assessed for the presence of a right-to-left shunt by color flow Doppler assessment only, 157 patients (157/226, 69%). A total of 2 patients had undergone a dedicated shunt study with administration of intravenous agitated saline with and without valsalva maneuvers (2/226, 0.9%). Identification of a right-to-left shunt was made in 25 patients (25/226, 11%) with the majority present at rest (23/25, 92%). The presence of a shunt was more common in those with congenital heart disease (4/7, 57.1% vs, 21/150, 14.1%; P=.01). These cases still underwent lymphangiography with no evidence of a systemic embolic complication. Of the 2 cases with systemic embolic complications denoted above, both had undergone preprocedure echocardiography. Color flow Doppler evaluation was used to assess for a shunt in both cases, and both presumed to be negative. Neither had undergone a dedicated shunt study and only after the complications occurred, a postprocedure shunt study was performed, confirming the presence of a right-to-left shunt.

DISCUSSION

Although case reports exist of systemic arterial embolic complications after ethiodized oilbased lymphangiography, no modern study has systematically evaluated the rate of these complications and association with intracardiac shunt status and history of congenital heart disease. As such, there are limited or no data to guide clinical decision-making as

TABLE 2. Past Medical and Surgical History of 350 Patients who Underwent Oil-Based Contrast Fluo- roscopic Lymphangiography From 2000-2021		
Past Medical History (n=350 patients)	n (%)	
Congenital heart disease	(3)	
Plastic bronchitis	4 (.)	
Fibrosing mediastinitis	l (0.3)	
Lymphoma	17 (4.9)	
Lymphatic malformation	35 (10)	
Prior cerebrovascular accident	9 (2.6)	
Other solid organ malignancy	153 (43.7)	
Obstructive sleep apnea	36 (10.3)	
Pulmonary arterial hypertension	8 (2.2)	
Congestive heart failure	33 (9.5)	
Past Surgical History (n=350 patients)		
Neck	35 (10)	
Congenital heart	12 (3.4)	
Acquired heart	37 (10.6)	
Esophageal	44 (12.6)	
Thoracic lung	83 (23.7)	
Other mediastinal	12 (3.4)	
Hepatopancreaticobiliary	31 (8.8)	
Gastric	31 (8.8)	
Intestinal	75 (21.4)	
Retroperitoneal	55 (15.8)	
Pelvic	77 (22.1)	
Data are presented as n (%).		

to which patients may or may not be at higher risk for such complications. In the present study, the prevalence of a systemic arterial embolic complication during ethiodized oilbased contrast lymphangiography was rare, occurring in 0.5% of cases (2/400), but can be catastrophic as evidenced by the cases presented herein. Only 1 case (1/400, 0.25%) truly reported evidence of cerebral ethiodized oil embolism. Nonetheless, ethiodized oilbased contrast lymphangiography is most often an elective procedure. As such, all efforts should be made to minimize the risk of morbidity and mortality, particularly systemic arterial embolic complications from the ethiodized oil-based contrast. In the present series, the degree of practice variability at a single center for preprocedure assessment of rightto-left shunt risk is notable. This found that there is no standardized preprocedure assessment nor guidance for either the clinician on



FIGURE 2. Multifocal ethiodized oil-based contrast emboli in an 83-year-old male following lymphangiography. (A) Coronal CT of the abdomen without intravenous contrast reports multifocal peripheral wedge-shaped hyperattenuating foci in the left kidney (yellow arrowhead) and spleen (yellow arrow), which represent ethiodized oil-based contrast emboli. (B-D) Axial non-contrast CT of the brain reports diffuse hyperattenuating foci (yellow arrows) are seen along the cerebral cortex at the gray-white junction, deep gray matter, and cerebellum, which represent ethiodized oil-based contrast emboli. The patient died of the cerebral ethiodized oil emboli. CT, compued tomography.

how these patients should be assessed to determine risk.

The 2 cases described with systemic arterial embolic complications were evaluated by echocardiography without a dedicated shunt study before lymphangiography and presumed to be negative for the presence of a shunt. Consequently, these cases may give the false impression that echocardiography would not be of utility before performing oil-



contrast lymphangiography.

based lymphangiography. Thus, it may be paramount to develop a structured approach that could be incorporated with ease into standard practice to help identify those patients at risk of paradoxical systemic embolic complications. A starting point for this approach could be extrapolated from the neurology and cardiology collaboration for evaluating poststroke patients.

Current practice standards for a patient with a stroke include an echocardiogram with a shunt study. The use of transthoracic vs transesophageal is often debated, but transthoracic studies allow for a proper valsalva maneuver to be performed. The sedation during a transesophageal study can limit this maneuver and result in a false negative study.¹¹ When a shunt is present, it can then be graded on a scale of I-IV based on the number of microbubbles in the left heart structures on a single echocardiographic frame. This evaluation has been developed to help identify those patients that may have experienced a paradoxical thromboembolic event leading to the stroke. It has been important to elaborate on the degree of shunt, as roughly 20% of the general population is reported to have a patent foramen ovale but usually without clinical significance.¹² Intracardiac shunting was reported preprocedurally in 25 patients in our study, and all these patients underwent oil-based lymphangiography without issue.

The difficulty is identifying those at highest risk for a paradoxical event allowing for proper preoperative counseling and maneuvers to reduce potential shunting. For example, in a patient with a patent foramen ovale and inducible right-to-left shunt, avoidance of valsalva like physiologic maneuvers (ie, heavy sedation with resultant airway obstruction) would be paramount to limiting the risk of shunting although the oil-based contrast is circulating. For large shunts, one may even consider temporary or permanent closure of the shunt to facilitate oil-based lymphangiography safely (Supplemental

Figure, available online at http://www. mcpiqojournal.org).¹³ Of note, both patients with cerebral arterial embolic complications in this study were octogenarians. Although age alone is unlikely to be an independent risk factor for cerebral ethiodized oil embolism, age associated cardiopulmonary or systemic co-morbidities such as pulmonary arterial hypertension, chronic heart failure, or chronic kidney disease with volume overload may increase right-sided cardiac or pulmonary arterial pressures, thereby increasing the risk of intracardiac or intrapulmonary right-to-left shunting. Preprocedure echocardiography, in addition to identifying intracardiac shunting, can help detect evidence of elevated rightsided heart pressures. In general, ethiodized oil contrast is contraindicated in patients with clinically significant pulmonary arterial hypertension as the more viscous contrast in the pulmonary arterial bed may theoretically exacerbate the underlying pulmonary disease. Furthermore, other co-morbidities that can lead to persistent (ie, central venous occlusions) or transient (ie, obstructive sleep apnea) increases in central venous or intra-thoracic pressure and subsequently right-sided heart pressures may be considered as potential risk factors for increased right-to-left shunting. In short, the combination of an intracardiac or intrapulmonary shunt and elevated rightsided heart pressures may be a risk factor for ethiodized oil cerebral or other systemic arterial embolism, particularly in older patients with multiple cardiopulmonary co-morbidities.

The development of a standardized preprocedural protocol may be useful to screen patients and guide management should a shunt be present. A screening protocol could be implemented in every patient undergoing elective lymphangiography but is most salient for patients with increased prevalence of rightto-left shunts, such as those with congenital heart disease. A candidate screening protocol may serve as a useful template for preprocedural lymphangiogram screening and management (Figure 3).

The candidate screening protocol described offers a template regarding screening, detection, and management of right-to-left shunts for patients potentially undergoing ethiodized-oiled based contrast lymphangiography. The protocol includes a standardized transthoracic echocardiogram involving an agitated saline contrast injection with and without a valsalva maneuver in addition to management guide-lines.¹⁴ Given roughly 20% of patients have a patent foramen ovale, shunt quantification is critical for risk stratification as contraindicating or requiring shunt closure in 20% of patients is not logistically feasible. Furthermore, as reported in our study, no patient with a preprocedural shunt had a major complication. This protocol may allow detection of high-risk shunts for risk mitigation although minimizing unneeded interventions in those with low-risk shunts or lymphangiography avoidance.

One could argue against the utility of implementing a screening and guidance protocol given the already low prevalence of systemic arterial embolic complications after the ethiodized-oiled-based contrast lymphangiography (2/400, 0.5%). Moreover, even with implementation of a screening protocol, it may be difficult to show a considerable risk reduction given for a small effect size without a very large sample population. However, a prospective screening protocol would not only help to better define risk on an individual patient level, thereby providing evidence for informed and shared decision-making, but also potentially identify the patients with the highest risk for systemic arterial complications for risk-minimizing measures such as shunt occlusion to facilitate lymphangiography.

There are limitations to the present study. This was a single center study with a relatively small sample size relative to complication rate and large amount of absent echocardiographic data applicable to shunt information. In addition, the overall rate of ethiodized oil embolization is likely underestimated because only symptomatic patients were further imaged. Moreover, these findings warrant validation from other centers performing a large volume of ethiodized oil-based lymphangiography and intervention.

CONCLUSION

In conclusion, symptomatic cerebral or other systemic arterial complications after ethiodized oil-based contrast lymphangiography are rare (2/400, 0.5%) but can be catastrophic. A standardized echocardiographic screening assessment with dedicated shunt study for patients before ethiodized-oiled-based contrast lymphangiography may be helpful both for identifying those at higher risk for systemic embolic complications and implementing tailored risk mitigation strategies. This screening protocol will require prospective clinical evaluation.

POTENTIAL COMPETING INTERESTS

Drs Anderson and Takahashi report participation on a Data Safety Monitoring Board or Advisory Board for Alucent Biomedical. Dr Koepsel reports as research consultant at Boston Scientific, funds paid to institution. Dr Thompson reports as research consultant at Boston Scientific, funds paid to institution, not individual; Advisory Board, Boston Scientific, funds paid to institution, not individual. The other authors report no competing interests.

ETHICS STATEMENT

The study was approved by the Mayo Clinic Rochester institutional review board and a waiver of written informed consent was granted as the institutional review board determined the research involved no more than minimal risk to patients; the research could not be carried out practicably without the waiver; and the waiver would not adversely affect the rights and welfare of the patients.

SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at http://www.mcpiqojournal.org. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

Data Previously Presented: These data were presented at Society of Interventional Radiology Annual Meeting, Boston, MA, June 11-16, 2022.

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