

Lung Scintigraphy for Suspected Pulmonary Embolism During Pregnancy: Fetal Radiation Dose and Pregnancy, Neonatal, and Childhood Outcomes

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Research Article

Keywords: pregnancy, pulmonary embolism, lung scintigraphy, ventilation/perfusion scanning, fetal radiation dose, neonatal outcomes, childhood outcomes

Posted Date: October 13th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-11156223/v1>

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Additional Declarations: No competing interests reported.

Abstract

Background

To evaluate lung scintigraphy findings, estimate fetal absorbed radiation doses in pregnant patients undergoing evaluation for suspected pulmonary embolism (PE), and describe subsequent pregnancy, neonatal, and childhood outcomes.

Methods

This retrospective, single-center cohort included 44 pregnant patients who underwent perfusion-only or ventilation/perfusion lung scintigraphy for suspected acute PE between July 2013 and May 2024. Clinical and imaging findings, administered radiopharmaceutical activity, estimated fetal absorbed dose, anticoagulant treatment, and available maternal, pregnancy, neonatal, and childhood outcomes were obtained from medical records and family telephone interviews.

Results

The mean gestational age at scintigraphy was 26.6 ± 7.4 weeks, and 26 examinations (59.1%) were performed in the third trimester. Most patients (38/44, 86.4%) received 1.0 mCi of technetium-99m macroaggregated albumin. The mean estimated fetal absorbed dose was 0.180 ± 0.046 mGy (range, 0.125–0.401 mGy). Scintigraphy findings were compatible with PE in eight patients (18.2%), indeterminate or suspicious in four (9.1%), and normal or not supportive of PE in 32 (72.7%). All patients with PE-compatible or indeterminate findings received anticoagulation. Maternal follow-up information was available for 31 patients (70.5%); no recurrent maternal venous thromboembolic events or maternal deaths were documented. Among the 31 pregnancies with available gestational-age data at delivery, seven (22.6%) resulted in preterm delivery, including three (9.7%) before 32 weeks. One case of preeclampsia and no stillbirths were documented. No major structural congenital anomalies were identified. Childhood health information was available for 30 children (68.2%), with a mean follow-up duration of 5.1 ± 3.4 years and a maximum of 10.3 years. No childhood malignancies were reported.

Conclusions

Lung scintigraphy, predominantly performed using a low-activity perfusion-only approach, was associated with a low estimated fetal absorbed radiation dose. Available pregnancy, neonatal, and childhood outcomes were generally reassuring; however, the small sample size, incomplete follow-up, and lack of an unexposed control group preclude definitive conclusions about long-term safety. Larger prospective multicenter studies with extended childhood follow-up are warranted.

Introduction

Venous thromboembolism (VTE) is a major cause of maternal morbidity and mortality during pregnancy and the postpartum period. Although deep vein thrombosis accounts for most cases, pulmonary embolism is responsible for most VTE-related deaths and accounts for 10–15% of maternal deaths in high-income countries [1, 2].

Physiological changes of pregnancy, including hypercoagulability, venous stasis, pelvic compression, and vascular damage, increase the risk of pulmonary embolism (PE) [3–6]. Diagnosing PE can be challenging because symptoms and signs such as dyspnea, sinus tachycardia, and lower-extremity edema are often present during pregnancy due to these changes [7]. The biomarker D-dimer has limited utility because its levels are physiologically elevated during pregnancy, peaking around delivery [8]. Current guidelines lack consensus on the role of D-dimer during pregnancy [9, 10].

Computed Tomography Pulmonary Angiography (CTPA) is the standard imaging modality for suspected PE in the nonpregnant population because it is widely available, provides rapid and accurate results, and can identify alternative thoracic conditions and signs of right ventricular dysfunction [10–13]. During pregnancy, both CTPA and Ventilation/Perfusion (V/Q) scintigraphy are acceptable options; however, several guidelines favor V/Q scintigraphy in patients with a normal chest radiograph, and a perfusion-only protocol may further reduce maternal and fetal radiation exposure. V/Q scintigraphy is also useful when iodinated contrast is contraindicated, although it is less suitable in patients with asthma, chronic lung disease, or an abnormal chest radiograph and cannot identify alternative diagnoses. Conversely, CTPA is generally preferred in these settings, despite its higher maternal breast radiation dose and the possibility of suboptimal vascular opacification during pregnancy, particularly in the second and third trimesters [12–14].

Despite extensive research on the diagnostic performance and radiation dosimetry of lung scintigraphy during pregnancy, clinical data on pregnancy, neonatal, and particularly long-term childhood outcomes after prenatal exposure remain limited [15]. Therefore, this study aimed to evaluate scintigraphic findings, estimate fetal radiation doses in pregnant patients undergoing evaluation for suspected PE, and describe subsequent pregnancy, neonatal, and childhood outcomes.

Methods

Study Design, Population, and Data Collection

Akdeniz University Hospital is a tertiary referral center for high-risk obstetric patients in the Mediterranean region of Türkiye. Approximately 400 lung scintigraphy examinations are performed annually in the Department of Nuclear Medicine. This retrospective cohort study included 44 pregnant patients who presented to the emergency department or were hospitalized in the Department of Obstetrics and Gynecology and were referred to the Department of Nuclear Medicine for lung scintigraphy to evaluate suspected acute PE, from July 14, 2013, to May 22, 2024. Patients were

identified through the hospital's electronic database and nuclear medicine records. The study protocol was approved by the Akdeniz University Clinical Research Ethics Committee (reference number: 427) on July 03, 2024.

Pregnant patients who underwent perfusion-only scintigraphy or combined ventilation/perfusion lung scintigraphy during the study period were eligible. Patients who underwent scintigraphy after delivery, and those in whom pregnancy at the time of imaging could not be confirmed, were excluded. Patients with incomplete pregnancy, neonatal, or childhood outcome data were retained in the cohort, and each outcome was analyzed using the available data.

Imaging requests, scintigraphy reports, nuclear medicine records, and obstetric medical records were reviewed to confirm eligibility and build the study dataset. De-identified data included available demographic and clinical characteristics, gestational age at imaging, administered radiopharmaceutical activity, estimated fetal absorbed radiation dose, imaging protocol, and scintigraphy findings. Results of additional diagnostic investigations performed during the evaluation of suspected PE, including chest radiography, D-dimer testing, compression ultrasonography, CTPA, and pulmonary angiography, were recorded when available. Information on anticoagulant treatment, subsequent maternal venous thromboembolic events, and pregnancy and neonatal outcomes was also obtained from the available medical records.

Lung Scintigraphy and Radiation Dosimetry

Lung scintigraphy was performed on a Siemens Symbia T-series SPECT/CT system (T2 or T16). Technetium-99m macroaggregated albumin (99mTc-MAA) was used for perfusion imaging, and 99mTc-Technegas (Cyclomedica Australia Pty Ltd, Kingsgrove, NSW, Australia) was used for ventilation imaging when required. Examinations were classified as perfusion-only scintigraphy or combined ventilation/perfusion (V/Q) scintigraphy based on the protocol documented in the nuclear medicine records. Administered radiopharmaceutical activities were obtained from patient records.

Fetal absorbed radiation doses were estimated using gestational-stage-specific fetal dose coefficients for 99mTc-MAA, as summarized by Stabin [16]. These coefficients, expressed in mGy/MBq, were derived from pregnant female computational phantoms and are provided for early pregnancy and at 3, 6, and 9 months of gestation. For each patient, a gestational-age-specific dose coefficient was calculated by linear interpolation between the two nearest tabulated gestational stages. This coefficient was multiplied by the administered activity of 99mTc-MAA to calculate the estimated fetal absorbed dose from the perfusion component, expressed in milligray (mGy). For combined V/Q examinations, the reported fetal dose estimates included only the contribution from 99mTc-MAA and excluded the additional contribution from inhaled 99mTc-Technegas.

Outcomes and Definitions

The primary outcomes were the estimated fetal absorbed radiation dose and lung scintigraphy findings. Secondary outcomes included results of additional diagnostic tests, anticoagulant treatment, subsequent maternal venous thromboembolic events, and pregnancy, neonatal, and childhood outcomes.

Scintigraphy findings were classified according to the conclusion of the original nuclear medicine report as PE-compatible, indeterminate or suspicious for PE, or normal/not supportive of PE. Pregnancy and neonatal outcomes included preeclampsia, pregnancy loss, stillbirth, gestational age and mode of delivery, preterm birth, birth weight, Apgar scores, and congenital anomalies. Gestational age at scintigraphy was categorized as first trimester (< 14 weeks), second trimester (14 to < 28 weeks), or third trimester ($\geq$ 28 weeks). Preterm birth was defined as delivery before 37 completed weeks, and very preterm birth as delivery before 32 completed weeks. Low birth weight was defined as a birth weight below 2500 g, and very low birth weight as a birth weight below 1500 g. Apgar scores were evaluated when a numerical score was available. Childhood outcomes included major ongoing health problems, documented medical or developmental conditions, and malignancy, as identified in available medical records or reported during telephone interviews with families.

Statistical Analysis

Continuous variables were summarized as mean $\pm$ standard deviation or as median, with ranges as appropriate. Categorical variables were presented as counts and percentages. Analyses were performed using the available data for each variable, without imputing missing values. Statistical analyses were conducted using SAS version 9.4 (Statistical Analysis Software SAS 9.4; SAS Institute).

Results

The study included 44 pregnant patients who underwent lung perfusion scintigraphy between July 2013 and May 2024. The mean gestational age at scintigraphy was 26.6 ± 7.4 weeks (range, 6–37 weeks). Four examinations (9.1%) were performed in the first trimester, 14 (31.8%) in the second trimester, and 26 (59.1%) in the third trimester (Table 1).

Table 1
Patient characteristics and lung scintigraphy findings

Characteristic	Result
Pregnant patients, n	44
Gestational age at scintigraphy, weeks, mean $\pm$ SD (range)	26.6 $\pm$ 7.4 (6–37)
First trimester, n (%)	4 (9.1)
Second trimester, n (%)	14 (31.8)
Third trimester, n (%)	26 (59.1)
Administered activity, mCi, mean $\pm$ SD	1.10 $\pm$ 0.28
Estimated fetal absorbed dose, mGy, mean $\pm$ SD (range)	0.180 $\pm$ 0.046 (0.125–0.401)
PE-compatible findings, n (%)	8 (18.2)
Indeterminate or suspicious findings, n (%)	4 (9.1)
Normal or PE-negative findings, n (%)	32 (72.7)
<i>Data are presented as mean $\pm$ standard deviation (with range where shown) or number (%). SD, standard deviation.</i>	

Presenting symptoms were available for 42 of 44 patients (95.5%). The most common symptoms, occurring alone or in combination, were dyspnea in 21 patients (50.0%), chest pain in 25 (59.5%), and back pain in six (14.3%). Pleuritic versus non-pleuritic characteristics of chest pain were not consistently documented. Before lung scintigraphy, chest radiography was performed in 31 of 44 patients (70.5%). Abnormal findings were identified in two of these patients (6.5%), including basal pulmonary infiltrates in one and elevation of the right hemidiaphragm in one. No findings of atelectasis, pulmonary vascular congestion, or pleural effusion were identified on chest radiography. Compression ultrasonography of the lower extremities was performed in 35 patients (79.5%), and all examinations were negative for deep vein thrombosis. Serial compression ultrasonography was not performed in any patient. D-dimer results were available for 38 patients (86.4%). According to the laboratory-specific reference ranges, D-dimer levels were elevated in 37 patients (97.4%) and within the reference range in one patient (2.6%). Computed tomography pulmonary angiography and conventional pulmonary angiography were not performed in any patient.

The mean administered activity was 1.10 $\pm$ 0.28 mCi; 38 of 44 patients (86.4%) received 1.0 mCi, four (9.1%) received 1.5 mCi, and one each received 1.8 and 2.5 mCi. The mean estimated fetal absorbed dose was 0.180 $\pm$ 0.046 mGy (range, 0.125–0.401 mGy) (Table 1).

Lung scintigraphy findings were compatible with pulmonary thromboembolism in eight patients (18.2%), indeterminate or suspicious for pulmonary thromboembolism in four patients (9.1%), and normal or not supportive of pulmonary thromboembolism in 32 patients (72.7%). Combined perfusion and ventilation

imaging was documented in nine patients. In four patients with indeterminate perfusion findings, ventilation imaging was recommended but not performed (Table 1).

Information on anticoagulant treatment was available for 42 of 44 patients (95.5%). Anticoagulation was administered at some point during the diagnostic episode in 36 patients (85.7%) and not administered in six (14.3%). All eight patients with PE-compatible scintigraphy findings and all four with indeterminate or suspicious findings received anticoagulation. Among patients with normal or PE-negative findings, 24 received anticoagulation, which had generally been initiated empirically before scintigraphy and was subsequently discontinued or reduced to a prophylactic dose after PE was excluded.

Maternal follow-up information was available for 31 of 44 patients (70.5%). No recurrent maternal venous thromboembolic events or maternal deaths were documented during follow-up. Of these 31 patients, 25 (80.6%) underwent cesarean delivery and six (19.4%) had a vaginal delivery. The mean gestational age at delivery was 37.2 ± 3.7 weeks (range, 24–41 weeks). Seven pregnancies (22.6%) resulted in preterm delivery before 37 weeks, including three (9.7%) before 32 weeks. Preeclampsia occurred in one pregnancy, and no stillbirths were documented among pregnancies with available outcome data. The mean birth weight was 2976 ± 697 g (range, 900–4090 g). Four neonates had a birth weight below 2500 g, including three below 1500 g. The median last recorded Apgar score was 9 (range, 4–10), and two neonates had a score below 7. No major structural congenital anomalies were identified. One child had a congenital cardiac defect that closed spontaneously (Table 2).

Table 2
Maternal, pregnancy, and neonatal outcomes

Outcome	Result
Maternal and delivery information available, n/44 (%)	31/44 (70.5)
Cesarean delivery, n/31 (%)	25 (80.6)
Vaginal delivery, n/31 (%)	6 (19.4)
Gestational age at delivery, weeks, mean $\pm$ SD (range)	37.2 $\pm$ 3.7 (24–41)
Preterm delivery < 37 weeks, n/31 (%)	7 (22.6)
Very preterm delivery < 32 weeks, n/31 (%)	3 (9.7)
Preeclampsia, n/31 (%)	1 (3.2)
Stillbirth, n/31 (%)	0 (0)
Birth weight, g, mean $\pm$ SD (range)	2976 $\pm$ 697 (900–4090)
Birth weight < 2500 g, n/31 (%)	4 (12.9)
Birth weight < 1500 g, n/31 (%)	3 (9.7)
Last recorded Apgar score, median (range)	9 (4–10)
<i>Data are presented as mean $\pm$ standard deviation (with range where shown), median (range), or number (%). Percentages are based on 31 pregnancies or neonates with available outcome data. SD, standard deviation.</i>	

Childhood health information was available for 30 children (68.2%). The mean follow-up duration was 5.1 ± 3.4 years (range, 0.5–10.3 years). One child (3.3%) had attention-deficit/hyperactivity disorder, and another (3.3%) had recurrent upper respiratory tract infections. No childhood malignancies were reported during the follow-up period.

Discussion

In this cohort, the mean estimated fetal absorbed dose from the perfusion component of lung scintigraphy was 0.180 mGy (range, 0.125–0.401 mGy). Most examinations were performed in the third trimester, and 86.4% of patients received 1 mCi. Scintigraphy findings were compatible with pulmonary embolism in 8 of 44 patients (18.2%). Among pregnancies with available outcomes, one case of preeclampsia was documented, and no stillbirths or major structural congenital anomalies were reported. Childhood health information was available for 30 children (68.2%), with follow-up extending to 10.3 years; no childhood malignancies were reported.

The mean estimated fetal absorbed dose in our study was 0.180 mGy, slightly lower than the 0.2–0.7 mGy range reported for V/Q lung scintigraphy in a previous systematic review and meta-analysis [17]. This relatively low dose may be attributable to the predominant use of perfusion-only imaging in our

cohort, which avoids the additional radiation exposure associated with the ventilation component in most patients, and to the low administered activity, as 86.4% of patients received only 1 mCi (approximately 37 MBq) of technetium-99m macroaggregated albumin.

In our study, scintigraphy findings were compatible with PE in 8 of 44 patients (18.2%). This imaging-positive rate was higher than the 5.5% reported by Tester et al., who similarly determined diagnostic yield from radiological report findings [18]. This difference may partly reflect the selected nature of our cohort, which consisted exclusively of pregnant patients referred for lung scintigraphy at a tertiary center, whereas Tester et al.'s study included both pregnant and postpartum women undergoing either CTPA or V/Q-SPECT. The relatively small sample size of our study and potential differences in patient selection, referral thresholds, and imaging protocols should also be considered when interpreting this higher rate.

Pregnancy and neonatal outcomes in our cohort were broadly comparable to those reported by Chan et al. [15]. The preterm birth rate in our study was 22.6%, similar to the 23.8% reported by Chan et al. Mean gestational age at delivery was also comparable (37.2 vs. 37 weeks), as was mean birth weight (2976 vs. 2914 g). Preeclampsia occurred in one of 31 pregnancies with available outcome data (3.2%), and no stillbirths were documented. In contrast, Chan et al. reported preeclampsia in 16.8% of pregnancies, spontaneous pregnancy loss in 2.5%, and infant death in 1.7%. The markedly higher cesarean delivery rate in our cohort (80.6% vs. 28.2%) likely reflects differences in referral characteristics, obstetric practice, and patient selection rather than an effect of scintigraphic exposure.

Regarding offspring outcomes, Chan et al. reported congenital anomalies in 3.6% and developmental abnormalities in 3.8% of children [15]. In our cohort, no major structural congenital anomalies were identified. Among the 30 children with available follow-up, one (3.3%) had attention-deficit/hyperactivity disorder and one (3.3%) had recurrent upper respiratory tract infections. Childhood outcome data were available for a smaller proportion of our cohort than in the study by Chan et al. (68.2% vs. 90.2%); however, our follow-up extended up to 10.3 years, compared with a mean child age of 20.5 months and a maximum of approximately 8.3 years in their cohort [15]. The developmental findings reported by Chan et al. were frequently associated with extreme prematurity or other maternal conditions; therefore, they are not directly comparable with the isolated neurobehavioral finding in our cohort.

No childhood malignancies were identified among the 30 children with available follow-up in our cohort. Chan et al. likewise reported no childhood cancer or leukemia among children with available pediatric data [15]. A population-based cohort study by Ray et al. found no statistically significant increase in childhood malignancy after major radiodiagnostic imaging during pregnancy, although its confidence intervals did not rule out a modest increase in risk [19]. Thus, although our findings provide reassuring real-world data on outcomes following prenatal exposure to lung scintigraphy, they cannot establish the absence of a small long-term risk.

The principal limitations of this study include its retrospective, single-center design; small sample size; nonconsecutive case identification; incomplete pregnancy and childhood outcome data; and the absence of an unexposed control group. Childhood outcomes were partially obtained through family

interviews and may therefore be subject to recall and reporting bias. Variable follow-up duration limited assessment of late-onset malignancies and neurodevelopmental conditions.

Conclusion

Lung scintigraphy for suspected pulmonary embolism during pregnancy was associated with a low estimated fetal absorbed radiation dose, especially when a low-activity, perfusion-only protocol was used. No major structural congenital anomalies or childhood malignancies were identified among offspring with available follow-up, which extended to 10.3 years. Although these findings offer reassuring real-world data, the small sample size, incomplete follow-up, and absence of an unexposed control group prevent definitive conclusions about long-term safety. Larger multicenter studies using standardized imaging protocols and prospective, long-term follow-up into childhood are needed to confirm these findings.

Abbreviations

PE Pulmonary embolism

VTE Venous thromboembolism

CTPA Computed tomography pulmonary angiography

V/Q Ventilation/perfusion

SPECT/CT Single-photon emission computed tomography/computed tomography

^{99m}Tc-MAA Technetium-99m macroaggregated albumin

SD Standard deviation

Declarations

Ethics approval and consent to participate

The study was approved by the Akdeniz University Clinical Research Ethics Committee (approval no. 874; July 03, 2024) and conducted in accordance with the Declaration of Helsinki. The ethics committee waived informed consent for the retrospective review of medical records. Verbal informed consent was obtained from parents or guardians before telephone interviews concerning childhood outcomes. Clinical data were analyzed in de-identified form.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no conflicts of interest related to the conduct, authorship, or publication of this study.

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Funding

The authors declare that no financial support was received for this study.

Author Contribution

E.S.B. and G.A.B. developed the study methodology and performed the data analysis; E.S.B. and T.A.T. collected the data; E.S.B. and G.A.B. drafted the manuscript; and E.S.B., G.A.B., and İ.İ.M. reviewed and edited it. All authors reviewed and approved the final manuscript.

Acknowledgement

The authors would like to thank all individuals who contributed to the successful completion of this study.

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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