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Cardiac photon-counting detector computed tomography in acute ischemic stroke: diagnostic accuracy for detection of left atrial appendage thrombus

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Annemarie Kirschfink*, Mohamed Elhalal*, Stefan Seidel, Stefanie Kammer, Dimah Hasan, Michael Frick, Nikolaus Marx, Jörg B. Schulz, Martin Wiesmann, Ertunc Altiok, Hani Ridwan, Arno Reich‡ and João Pinho‡

Abstract

Background: In up to one-third of ischemic stroke patients, no cause can be identified. Left atrial appendage (LAA) is the primary anatomical origin of cardiac embolism, yet it is often inadequately assessed in stroke etiological workup.

Objectives: The goal of this study was to analyze the diagnostic accuracy of cardiac photon-counting detector computed tomography (PCD-CT) integrated in the acute stroke imaging protocol for detection of LAA thrombus.

Design: Retrospective diagnostic accuracy study.

Methods: We selected consecutive patients with acute ischemic stroke or transient ischemic attack undergoing emergent cardiac PCD-CT and transesophageal echocardiography (TEE) between 2023 and 2025. Cardiac PCD-CT and TEE were assessed for the detection of LAA thrombus. Patients with and without LAA thrombus (defined by PCD-CT) were compared. Diagnostic performance metrics for cardiac PCD-CT for LAA thrombus detection were calculated using TEE as the gold standard.

Results: We included 101 patients, 42 were female (42%), median age was 59 years, 87 patients had acute ischemic stroke (86%). Median time between cardiac PCD-CT and TEE was 2 days. LAA thrombus defined by PCD-CT was present in 12 patients (12%). Patients with LAA thrombus were older (74 vs 58 years, $p < 0.001$) and more frequently had atrial fibrillation (83.3% vs 23.6%, $p < 0.001$). Diagnostic accuracy of PCD-CT was 96% (95% confidence interval (95%CI) = 90%–99%), sensitivity was 90% (95%CI = 56–100), specificity was 97% (95%CI = 91%–99%), positive predictive value was 75% (95%CI = 49%–90%), and negative predictive value was 99% (95%CI = 93%–100%).

Conclusion: Cardiac PCD-CT integrated as part of the acute stroke imaging protocol is a promising diagnostic tool that may reliably exclude the presence of LAA thrombus.

Plain language summary

Cardiac imaging in stroke patients for detection of thrombus in the heart

The cause of stroke remains unclear in up to one third of patients after careful evaluation. A new strategy to identify the cause of stroke is to perform a heart computed tomography (CT) imaging immediately after hospital admission. However, we are not sure if this strategy can reliably identify a thrombus in the hearts of stroke patients. In this study,

Correspondence to:
João Pinho
Department of Neurology, University Hospital RWTH Aachen, Pauwelsstr. 30, Aachen 52074, Germany
jferreiradep@ukaachen.de

Annemarie Kirschfink
Michael Frick
Nikolaus Marx
Ertunc Altiok
Department of Internal Medicine I (Cardiology), University Hospital RWTH Aachen, Aachen, Germany

Mohamed Elhalal
Dimah Hasan
Martin Wiesmann
Hani Ridwan
Department of Diagnostic and Interventional Neuroradiology, University Hospital RWTH Aachen, Aachen, Germany

Stefan Seidel
Stefanie Kammer
Arno Reich
Department of Neurology, University Hospital RWTH Aachen, Aachen, Germany

Jörg B. Schulz
Department of Neurology, University Hospital RWTH Aachen, Aachen, Germany

JARA-BRAIN Institute for Molecular Neuroscience and Neuroimaging, Forschungszentrum Jülich GmbH and Medical Faculty, RWTH Aachen University, Aachen, Germany

*These authors contributed equally to the work and share first co-authorship

‡These authors contributed equally to the work and share senior co-authorship

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we analysed if a special type of heart CT (photon-counting detector CT, integrated in the usual diagnostic work-up of ischemic stroke patients in the emergency department) is as good as the best currently available exam (transoesophageal sonography of the heart—TEE) to find a thrombus in the heart. We included in our study all of the stroke patients who, during a period of 2 years were treated in our hospital and had received both exams. We found that this heart CT had a good diagnostic performance, in comparison to TEE, especially in respect to exclusion of thrombus in the left atrial appendage of the heart. The main conclusion of our study is that performing cardiac CT early after hospital admission of stroke patients is a promising diagnostic tool to exclude heart thrombus as a possible cause for stroke.

Keywords: computed tomography, intracardiac thrombus, left atrial appendage, photon-counting detector, stroke, transesophageal echocardiography

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Introduction

In approximately one third of all patients with first ischemic stroke or transient ischemic attack (TIA), no cause is found after adequate investigation, and etiology is classified as cryptogenic. This is associated with a relatively high risk of recurrent stroke.[1] An occult cardiac embolic source is one of the main differential diagnoses to be considered in patients with cryptogenic embolic stroke.[2] Although the recognition of non-stenotic atherosclerotic large vessel disease as a potential cause of embolic stroke has gained more attention in recent years,[3] international guidelines recommend prolonged cardiac rhythm monitoring to increase detection of subclinical atrial fibrillation (AF) in patients with ischemic stroke or TIA of undetermined cause.[4,5] There is increasing evidence showing that early cardiac imaging integrated in the emergent evaluation of stroke patients increases the likelihood for detecting relevant aortic and cardiac sources of embolism.[6,7] The DAYLIGHT trial demonstrated that extending the computed tomography (CT) angiography to at least 6 cm below the carina as part of the diagnostic imaging for acute code-stroke patients improves detection of cardioaortic thrombi.[8] A meta-analysis of 43 studies reported a high sensitivity and specificity for the detection of intracardiac thrombus by cardiac CT in comparison to transthoracic (TTE) or transesophageal echocardiography (TEE).[9] However, only three of the studies performed cardiac CT as part of the acute code-stroke assessment,[6,7,10] and in more recent studies only a small proportion of patients underwent TEE.[11–15] In recent years, several studies analyzed the use of cardiac CT in the acute phase of ischemic stroke and showed a frequency of LAA thrombus between 4.0% and 12.4%.[7,11–14] However, the diagnostic accuracy of emergent cardiac CT in comparison to the current clinical gold standard (TEE) in acute ischemic stroke patients for detection of intracardiac thrombus is unknown. There are specific limitations and challenges for cardiac CT in the identification of major cardioembolic sources such as thrombus, vegetations, and tumors.[16] These limitations could be amplified in the setting of acute stroke because patients are frequently uncooperative, the majority of protocols do not include arm positioning, respiratory pause, or cardiac premedication, which are recommended and typically included in the protocols of elective cardiac CT. Recently, Sposato and Coutinho[17] summarized several open questions related to the use of cardiac CT in the acute phase of stroke, and one of them was the value of novel CT techniques, specifically of photon-counting detector CT (PCD-CT). These knowledge gaps in this specific field of research in stroke medicine constitute the rationale of the current study.

The aim of this study was to analyze the diagnostic accuracy of cardiac PCD-CT for the detection of left atrial appendage (LAA) thrombi in acute stroke patients.

Methods

We performed a retrospective single-center diagnostic accuracy study of consecutive adult patients with acute ischemic stroke or TIA who underwent cardiac PCD-CT as part of the code-stroke imaging protocol at admission and TEE as part of the routine stroke workup. Standard etiological workup in our comprehensive stroke center includes continuous 3-lead electrocardiogram (ECG) monitoring during stroke unit stay, imaging of cervical and intracranial arteries using at least two of the available methods (CT-angiography, ultrasound, magnetic resonance angiography, or digital subtraction angiography), 24- or 72-h ECG recording, echocardiography, blood tests, and brain imaging to detect acute infarcts (CT or magnetic resonance imaging (MRI)). Cardiac diagnostic (including TEE) in acute stroke patients is routinely performed by neurologists trained in cardiac diagnostic methods in the Department of Cardiology under the supervision of experienced cardiologists. There is a close cooperation with the Department of Cardiology for the discussion of selected cases. TEE is performed in all ischemic stroke or TIA patients younger than 60 years and in selected cases at the discretion of the treating physician, according to clinical characteristics of patients and results of initial etiological work-up. Since March 2023, cardiac imaging was incorporated into the routine CT imaging protocol for all adult patients with suspected acute ischemic stroke and TIA who developed symptoms within 24 h prior to hospital admission, with the goal of including all potential candidates for acute revascularization treatments (intravenous thrombolysis and/or mechanical thrombectomy). We use a PCD scanner (NAEOTOM Alpha®; Siemens Healthineers, Erlangen, Germany) located on the same floor as the emergency department during regular working hours on weekdays. Patients presenting outside this time window undergo CT imaging in a different scanner where no cardiac imaging is performed. No measurable delays in initiating hyperacute revascularization treatments occurred as a result of adding cardiac PCD-CT to the imaging protocol.

Patient selection and data collection

Among consecutive adult patients admitted in our comprehensive stroke center during the period between March/2023 and July/2025 who received a final diagnosis of acute ischemic stroke or TIA, we identified patients who underwent TEE. Among patients who underwent TEE, we selected patients who: (1) had performed emergent cardiac PCD-CT, (2) had complete TEE examination, and (3) had available TEE digital images. Performance of TEE later than 21 days after index hospital admission and previous LAA occlusion were considered exclusion criteria for this study. We collected demographic and clinical data from individual electronic patient records, including clinical severity of stroke at admission (National Institutes of Neurology Stroke Scale—NIHSS), vascular risk factors, comorbidities, anticoagulation before stroke, door-to-CT time, CT-to-TEE time, presence of large vessel occlusion, recanalization therapies, and final stroke etiology (according to the TOAST classification).[18]

Photon-counting detector computed tomography

The code-stroke imaging PCD-CT protocol consisted of: non-contrast enhanced brain CT, non-ECG-gated CT-angiography from the vertex to the level of the main pulmonary artery, cardiac CT from the aortic arch to the diaphragm, and optional CT perfusion of the brain (in this order). CT-angiography scanning was manually triggered upon contrast arrival in the internal carotid arteries. A nonionic low-osmolality contrast agent (300 mg iodine/mL, total volume of 100 mL) was used for the CT-angiography. Cardiac imaging was automatically triggered 8 s after the end of the CT-angiography (scan duration of about 1.5 s). We aimed to perform prospective ECG-triggering at 35% of the R–R interval in all patients. The cardiac PCD-CT parameters were the following: collimation: 144×0.4 mm; pitch: 3.2; rotation time: 0.25 s; tube voltage: 120 kV; ECG-gating: prospective, 35% phase, bandwidth quality level: 200. Images were reconstructed at 0.9 mm slice thickness at 40% RR interval.

One experienced neuroradiologist (M.E.) and one experienced vascular neurologist (J.P.) independently reviewed individual cardiac PCD-CT images for the detection of LAA thrombus, and were blinded for clinical information and for images of TEE. The two observers were allowed to use side-by-side comparisons of various reconstructions and orientations and identified LAA thrombi based on the presence of filling defects in the LAA. If a filling defect was found, Hounsfield units (HU) of regions of interest (ROI) deployed

manually within the filling defect were measured. ROIs of 100 mm^2 were manually placed in the left atrium (LA), LAA (without encompassing thrombi or trabeculae), aorta ascendens (AA), and aorta descendens (AD). Thrombi were defined as homogenous filling defects with a well-defined border, with ⩽100 HU and/or a filling defect/AA HU ratio ⩽0.19.[19,20] Disagreements were settled by consensus between the two observers. Image quality was quantified by calculating the signal-to-noise ratio (SNR, ratio of HU within a region of interest in the AD and standard deviation (SD) of HU within the same region of interest) and the contrast-to-noise ratio (CNR, ratio of the HU difference between the AD and subcutaneous pectoral fat issue and SD of HU of the subcutaneous pectoral fat tissue).[21] Radiation dose metrics were collected for individual patients: dose length product (DLP, mGy.cm) for the whole CT imaging and for cardiac imaging and volume CT dose index of cardiac imaging ($CTDI_{vol}$, mGy).

Transesophageal echocardiography

A comprehensive TEE examination was performed according to the current recommendations.[22,23] TEEs were carried out under conscious sedation using midazolam or a combination of midazolam and propofol by experienced echocardiographers. TEE studies were performed with one of two commercially available echocardiographic systems (GE HealthCare Vivid™ S70N; General Electric Vingmed, Horten, Norway; or Philips EPIQ 7c, Release 9.0.14; Philips Medical Systems, Andover, MA, USA) and corresponding transesophageal probes (6VT-D; General Electric Vingmed; or X7-2t; Philips Medical Systems). 3D-TEE imaging and ultrasound contrast were not routinely used. Special imaging software (GE HealthCare ViewPoint™ 6; General Electric Vingmed; or Vue PACS; Philips Medical Systems, Best, The Netherlands) was used for analysis of the TEE data.

One experienced cardiologist (A.K.) and one neurologist experienced in cardiac diagnostic (S.S.) independently reviewed individual TEE images for the detection of LAA thrombus, and were blinded for clinical information and for images of cardiac PCD-CT. A LAA thrombus was defined as an additional structure in the LAA which could be visualized in two different planes, with different echogenicity and mobility than the LAA. Disagreements were settled by consensus between the two observers. The two observers also assessed LAA morphology independently, visualized in different mid-esophageal 2D TEE views using additional biplane imaging. LAA measurements were performed at 45°–60°, 80°–100°, and 120°–135°. Maximum orifice diameter of the LAA (mm) as well as maximum LAA depth (mm) were measured. Maximum LAA depth was defined as the maximum diameter from the LAA orifice to the deepest point in the main lobe. Color flow Doppler and pulsed-wave Doppler were used for assessment of maximum LAA blood flow velocities (cm/s). LA dimensions were measured at 0°, where LA was largest. LA length was defined as the maximum measurement from midpoint of the mitral valve annulus to the farthest measurable LA point. LA width was measured from the interatrial septum to the lateral LA wall.

Statistical analyses

We used descriptive statistics to analyze the final study population. We compared baseline characteristics of patients with and without LAA thrombus, as defined in cardiac PCD-CT, using Fisher's exact tests or Mann–Whitney *U*-tests, as appropriate. We calculated interobserver agreement using Cohen's kappa. Statistical threshold for significance was set at an alpha value of 0.05. For the comparisons of TEE findings between the two groups, we applied a Bonferroni correction for multiple comparisons ($n = 9$), which redefined the statistical threshold for these analyses as an alpha value of 0.006. Using TEE as the gold standard for detection of LAA thrombus, we calculated accuracy, sensitivity, specificity, negative predictive value, positive predictive value, and positive likelihood ratio for emergent cardiac PCD-CT. Based on an expected sensitivity of 98%,[9] an expected prevalence of 6% of LAA thrombus,[5] a confidence level (CI) of 95%, and an expected drop-out rate of 0% we calculated the sample size as 101 patients.[24] As a sensitivity analysis, we calculated the same metrics of diagnostic performance for patients with a maximal time interval between cardiac PCD-CT and TEE of 3 days, to minimize the possibility of thrombus dissolution or new formation of thrombus. Additionally, we calculated and compared areas under the receiver operating characteristics curve (AUC) of cardiac PCD-CT with and without ECG-gating for the detection of LAA thrombus.

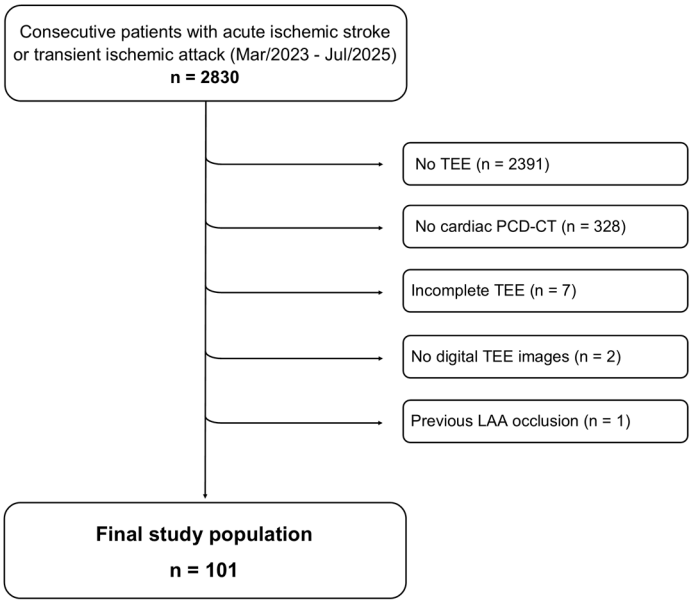


Figure 1. Patient flowchart.
LAA, left atrial appendage; PCD-CT, photon-counting detector computed tomography; TEE, transesophageal echocardiography.

No imputation of missing data was performed. Statistical analyses were performed using SPSS® version 28 (IBM Corp., Armonk, NY, USA) and MedCalc® Statistical Software v.20.111 (MedCalc Software Ltd., Ostend, Belgium). The study was approved by the ethics committee of the University Hospital RWTH Aachen, which waived the need for written informed consent because of the retrospective nature of the study. This report follows the Standards for Reporting of Diagnostic Accuracy Studies (STARD) 2015 guidelines (Supplemental Material).[25]

Results

During the study period, among 2830 patients with acute ischemic stroke or TIA admitted in our center, a total of 439 patients underwent TEE and a total of 573 patients underwent cardiac PCD-CT. We excluded patients from the initial population because of the following reasons: no TEE ($n = 2391$), no cardiac PCD-CT ($n = 328$), incomplete TEE examination ($n = 7$), no digital TEE images available ($n = 2$), previous LAA occlusion ($n = 1$; Figure 1). Patients who underwent TEE but had no cardiac PCD-CT had a similar sex distribution ($p = 0.648$) and were of similar age ($p = 0.349$) in comparison to the final study population. Patients who underwent cardiac PCD-CT but had no TEE had a similar sex distribution ($p = 0.184$) but were significantly older (median age 77 vs 59 years, $p < 0.001$) than the final study population. The final study population consisted of 101 patients, 42 patients were female (41.6%), median age was 59 years (interquartile range (IQR) 50–72), 14 patients had TIA as the final diagnosis (13.9%), median NIHSS was 4 (IQR = 1–8). Twenty patients suffered the ischemic event while taking oral anticoagulants (19.8%), 27 patients received intravenous thrombolysis after emergent CT (26.7%). Large vessel occlusion was present in 34 patients (33.6%), and 28 patients underwent mechanical thrombectomy (27.7%). Median door-to-CT time was 22 minutes (IQR = 16–33) and median CT-to-TEE time was 2 days (IQR = 1–4). ECG-gating was not achieved in 39.6% of cases due to technical problems with ECG-lead placement or problems with automatic ECG-signal recognition related to poor ECG-signal (low voltage or movement artifacts). Median DLP for the whole PCD-CT imaging was 3013 mGy.cm (IQR = 1424–3310) and for cardiac PCD-CT was 186 mGy.cm (IQR = 170–203), and median $CTDI_{vol}$ for cardiac PCD-CT was 8.9 (IQR = 8.9–8.9).

Interobserver agreement for detection of LAA thrombus in cardiac PCD-CT was excellent

($\kappa = 0.91$, standard error = 0.07, $p < 0.001$). Interobserver agreement for the detection of LAA thrombus in TEE was substantial ($\kappa = 0.63$, standard error = 0.13, $p < 0.001$).

Comparison of patients with and without LAA thrombus (defined by cardiac PCD-CT)

After consensus reading of cardiac PCD-CT, 12 patients with LAA thrombus were found (11.9%). Patients with LAA thrombus were older (median age 74 vs 58 years, $p < 0.001$), more frequently had AF (83.3% vs 23.6%, $p < 0.001$), more frequently suffered acute ischemic stroke or TIA while receiving oral anticoagulation (50.0% vs 15.7%, $p = 0.012$) and more frequently had cardioembolic etiology (100% vs 29.2%, $p < 0.001$; Table 1). Door-to-CT time (median 18 vs 23 min, $p = 0.068$) and CT-to-TEE time (median 2 vs 2 days, $p = 0.682$) were not different between the two groups of patients. Cardiac PCD-CT image quality assessed by SNR and CNR were similar in both groups ($p = 0.571$ and $p = 0.652$, respectively). Among the 12 patients with LAA thrombus in cardiac PCD-CT, 3 patients received intravenous thrombolysis after emergent CT imaging, and 4 were treated with anticoagulation before undergoing TEE (of which 2 had received intravenous thrombolysis). Patients with LAA thrombus had a larger LA width (median 44 vs 38 mm, $p = 0.002$), larger LAA orifice diameter measured at 120°–135° (median 19 vs 14 mm, $p < 0.001$), and greater LAA depth measured at all examined angles (Table 1). LAA blood flow velocity was significantly lower in patients with LAA thrombus (24 vs 55 cm/s, $p < 0.001$).

Diagnostic accuracy (TEE as gold standard)

A 2×2 contingency table describing the classification of the cases by cardiac PCD-CT and by TEE is presented (Table 2). The diagnostic accuracy of cardiac PCD-CT for detection of LAA thrombus was 96.0% (95%CI = 90.2%–98.9%), sensitivity was 90.0% (95%CI = 55.5–99.7), specificity was 96.7% (95%CI = 90.7%–99.3%), positive predictive value was 75% (95%CI = 49.2%–90.3%), negative predictive value was 98.9% (95%CI = 93.2%–99.8%), and positive likelihood ratio was 27.3 (95%CI = 8.8–84.7).

After exclusion of patients with time interval >3 days between cardiac PCD-CT and TEE ($n = 26$), the diagnostic accuracy was 98.7% (95%CI = 92.8–100), sensitivity was 88.9% (95%CI = 51.8–99.7), specificity was 100% (95%CI = 94.6–100), positive predictive value was 100% (95%CI = 100–100), and negative predictive value was 98.5% (95%CI = 91.2–99.8; positive likelihood ratio was not possible to calculate because there were no false positives). The AUC for cardiac PCD-CT with ECG-gating was 0.99 (95%CI = 0.97–1.00) and for cardiac PCD-CT without ECG-gating was 0.89 (95%CI = 0.71–1.00), but this difference was not statistically significant ($p = 0.266$).

PCD-CT and TEE disagreements

Among the three patients classified as false positive (cardiac PCD-CT with LAA thrombus, TEE without LAA thrombus): one patient had undergone intravenous thrombolysis and received anticoagulation before TEE, one patient had received anticoagulation before TEE, and the three patients received TEE 5 days after PCD-CT. Cardiac PCD-CT images of the three false positive cases are presented in Figure 2 and show filling defects fulfilling the defined criteria for LAA thrombus. Densities of the LAA thrombus in these three patients were 49, 79, and 95 HU (median densities in true positive cases = 79 HU, IQR = 68–88). Filling defect/AA HU ratios in these three patients were 0.09, 0.15, and 0.16 (median filling defect/AA HU ratios in true positive cases = 0.17, IQR = 0.14–0.19).

The patient classified as false negative (cardiac PCD-CT without LAA thrombus, TEE with LAA thrombus) did not undergo systemic thrombolysis and was not anticoagulated before he received TEE, which occurred 2 days after cardiac PCD-CT. Stroke etiology in this patient was interpreted to be related to patent foramen ovale and interatrial septal aneurysm, with contribution of a prothrombotic state because of an active systemic lupus erythematosus and past pulmonary embolism.

Discussion

The main finding of this study is that cardiac PCD-CT integrated in the emergent imaging diagnostic for patients with acute ischemic stroke and TIA has diagnostic accuracy to detect LAA thrombi of 96%, with a good sensitivity (90%), excellent specificity (97%), high negative predictive value (99%), and high positive likelihood

Table 1. Baseline characteristics of the study population according to the presence of LAA thrombus, as defined by consensus reading of cardiac photon-counting detector CT.

Baseline characteristics	No LAA thrombus (*n* = 89)	LAA thrombus (*n* = 12)	*p*
Female sex (*n*, %)	37 (41.6)	5 (41.7)	1.000
Age, years (median, IQR)	58 (50–67)	74 (65–81)	<0.001
Body mass index (kg/m^2)	26.3 (23.9–29.3)	26.8 (25.3–29.7)	0.344
Comorbidities			
Arterial hypertension (*n*, %)	62 (69.7)	11 (91.7)	0.171
Diabetes mellitus (*n*, %)	18 (20.2)	3 (25.0)	0.710
Dyslipidemia (*n*, %)	61 (68.5)	5 (41.7)	0.103
Active smoking (*n*, %)	28 (31.5)	1 (8.3)	0.171
Coronary heart disease (*n*, %)	11 (12.4)	4 (33.3)	0.076
Atrial fibrillation			<0.001
Known before stroke (*n*, %)	14 (15.7)	6 (50.0)	
Detected after stroke (*n*, %)	7 (7.9)	4 (33.3)	
Previous stroke (*n*, %)	5 (5.6)	2 (16.7)	0.194
Oral anticoagulation (*n*, %)	14 (15.7)	6 (50.0)	0.012
Final diagnosis			0.671
Transient ischemic attack (*n*, %)	12 (13.5)	2 (16.7)	
Acute ischemic stroke (*n*, %)	77 (86.5)	10 (83.3)	
Baseline NIHSS (median, IQR)	4 (1–8)	5 (1–11)	0.882
Large vessel occlusion[a] (*n*, %)	32 (36.0)	2 (16.7)	0.329
Intravenous thrombolysis (*n*, %)	24 (27.0)	3 (25.0)	1.000
Mechanical thrombectomy (*n*, %)	26 (29.2)	2 (16.7)	0.502
Cardioembolic etiology (*n*, %)	26 (29.2)	12 (100)	<0.001
Door-to-CT time, minutes (median, IQR)	23 (16–46)	18 (12–23)	0.068
CT-to-TEE time, days (median, IQR)	2 (1–4)	2 (1–5)	0.682
Cardiac CT image quality parameters			
Signal-to-noise ratio	21.0 (14.1–28.2)	22.4 (16.2–29.2)	0.571
Contrast-to-noise ratio	22.5 (15.1–30.8)	22.8 (15.9–32.8)	0.652
TEE findings[b]			
LA width,[c] mm (median, IQR)	38 (32–43)	44 (40–54)	0.002
LA length,[d] mm (median, IQR)	40 (33–45)	44 (37–50)	0.073

(Continued)

Table 1. (Continued)

Baseline characteristics	No LAA thrombus ($n = 89$)	LAA thrombus ($n = 12$)	p
LAA orifice diameter, mm (median IQR)			
Measured at 45°–60°	14 (11–17)	18 (15–22)	0.006
Measured at 80°–100°	14 (11–16)	17 (14–19)	0.022
Measured at 120°–135°	14 (12–16)	19 (15–21)	<0.001
LAA depth, mm (median, IQR)			
Measured at 45°–60°	27 (23–33)	34 (31–38)	0.002
Measured at 80°–100°	26 (22–30)	31 (29–34)	0.003
Measured at 120°–135°	25 (20–27)	29 (27–35)	0.001
LAA flow velocity, cm/s (median IQR)	55 (43–67)	24 (19–28)	<0.001

[a]Defined as occlusion of the internal carotid artery, first or second segments of the middle cerebral artery (M1 or M2), basilar artery.
[b]Statistical threshold for analyses set at an alpha value of 0.006 (Bonferroni correction).
[c]Measured at 0° from midpoint of the mitral valve annulus to the farthest measurable left atrial point.
[d]Measured at 0° from the intraatrial septum to the lateral LA wall.
CT, computed tomography; IQR, interquartile range; LA, left atrium; LAA, left atrial appendage; NIHSS, National Institutes of Health Stroke Scale; TEE, transesophageal echocardiography.

Table 2. Two-by-two contingency table with classification of cases by TEE (gold standard) and cardiac PCD-CT.

Method		TEE	
		No LAA thrombus	LAA thrombus
Cardiac PCD-CT	No LAA thrombus	88	1
	LAA thrombus	3	9

LAA, left atrial appendage; PCD-CT, photon-counting detector computed tomography; TEE, transesophageal echocardiography.

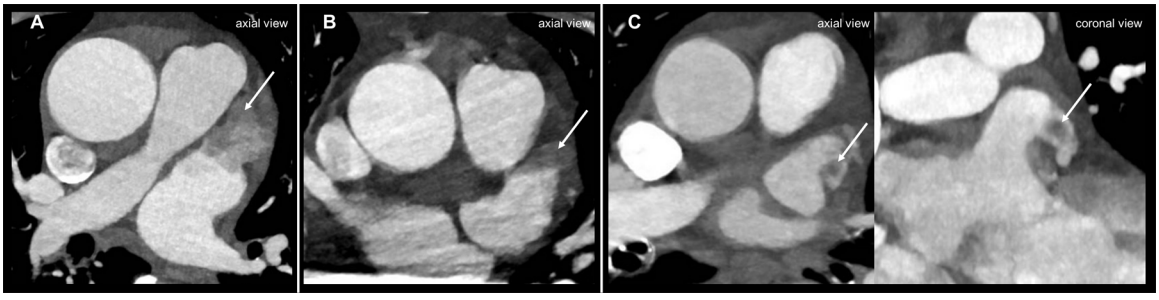


Figure 2. Cardiac PCD-CT imaging of the three false positive cases (a–c). Left atrial appendage thrombi were found in PCD-CT imaging (arrows) but not in transesophageal echocardiography.
PCD-CT, photon-counting detector computed tomography.

ratio (27.3). Although several recent studies using cardiac CT integrated in the acute imaging protocol for assessment of acute ischemic stroke patients demonstrated benefits in the detection of cardioaortic sources of embolism,[13] diagnostic accuracy of this strategy for detection of LAA thrombus has remained unknown.

Integrating emergent cardiac imaging in the etiological investigation of stroke patients allows early detection of major embolic causes such as intracardiac thrombi and implementation of early personalized effective secondary prevention strategies (such as anticoagulation). In the study by Rinkel et al.,[7] 6.4% of all patients otherwise classified with embolic stroke of undetermined source (ESUS) had a high-risk cardioembolic source identified by cardiac CT.[7] Another study found intracardiac thrombi in 8.3% of patients with ESUS, which would have been otherwise missed.[26] This demonstrates that cardiac CT can have a relevant impact on the treatment of a subgroup of stroke patients. Despite this, the impact of cardiac CT in this setting on the management of stroke patients may be limited, because the majority of patients in whom a LAA thrombus is found will have AF known before stroke or detected during hospital stay and will receive early anticoagulation according to the current recommendations.[27,28] This is in keeping with the results of the DAYLIGHT trial, which did not show that patients randomized to extended CT angiogram had higher frequency of findings which resulted in a de novo therapy.[8] Importantly, cardiac CT should not be used as a replacement for echocardiography in the diagnostic workup of stroke patients, because important stroke causes such as severe reductions of the ejection fraction, apical akinesia/aneurysm, patent foramen ovale, significant mitral valve stenosis, and endocarditic vegetations will likely be missed.

The high negative predictive value we found in our study suggests that cardiac CT may reliably exclude LAA thrombus, and this could be clinically useful to inform strategies for the selection of patients who are more likely to benefit from the performance of TEE. Although TEE is considered the gold standard for detection of LAA thrombus in the current literature,[29] it has several limitations. TEE is semi-invasive, time-consuming, tolerated by many patients only under sedation and it is not readily available or routinely performed in the majority of stroke units worldwide.[30] Likewise, interpretation of TEE may be more observer-dependent, as suggested by the lower interobserver agreement in comparison to cardiac PCD-CT. In comparison to cardiac MRI, our strategy of performing cardiac CT has the advantages of being more readily available, not having contraindications related to metallic implants, that the acquisition time is very short, that no specific preparation and little patient cooperation is needed, and that it is an opportunistic exam performed in the context of the emergent stroke imaging that these patients undergo, without need of additional contrast agent administration.

This is, to our knowledge, the first study analyzing the diagnostic accuracy of cardiac imaging using PCD for the detection of LAA thrombus. In comparison to conventional energy-integrating detectors, PCD reduces radiation exposure,[31] delivers higher spatial resolution, has a better CNR, and reduced electronic noise.[32] These characteristics may possibly be associated with a better diagnostic performance of cardiac PCD-CT to detect LAA thrombus. A lower sensitivity and specificity for emergent non-ECG gated cardiac CT in acute ischemic stroke patients using a conventional energy-integrating detector was found in a previous study.[10] However, the superiority of PCD to detect LAA thrombi in this setting remains unknown and to be tested in head-to-head comparison studies.

We found a sensitivity of 90% for emergent cardiac PCD-CT in the setting of an acute ischemic stroke, which is lower than what was found in previous meta-analyses (95%–98%).[9,29] This may be related to the different technical specifications and protocol of cardiac CT. Most of the studies included in the meta-analyses performed dedicated cardiac CT outside an emergency setting and included cooperative patients, and many studies used arm positioning and breath-hold, which may induce better overall image quality for evaluation of LAA thrombus.[33] The fact that ECG-gating was achieved in only 60% of cases and because we chose an early-phase fixed delay scan time (in order not to delay emergent revascularization treatments) may have influenced the results.[34] Our sensitivity analysis points to non-significant slightly better diagnostic accuracy of cardiac PCD-CT with ECG-gating in comparison

to absent ECG-gating, but our study is underpowered to demonstrate such effect. Cardiac PCD-CT imaging of the false positive cases in our study convincingly demonstrates the presence of LAA thrombus (Figure 2), which may have dissolved during the 5-day period between PCD-CT and TEE, or may have been missed in TEE. Taking this into consideration, accuracy and specificity could be, in reality, higher than what we found. Indeed, by limiting the analysis to patients with a time interval between cardiac PCD-CT and TEE of $\leqslant$3 days, we found an increased accuracy, increased specificity, and increased positive predictive value. Although TEE is considered the gold standard for detection of LAA thrombus, 2D TEE can miss LAA side lobes difficult to visualize as well as small thrombi in the LAA apex. Advanced imaging techniques such as 3D TEE or the use of ultrasound enhancing agent, which were not routinely used, are recommended for visualization of the whole LAA and for differentiation between LAA thrombi and artifacts.[35,36] We would also like to point out that the high negative predictive value suggests that cardiac PCD-CT can reliably exclude LAA thrombi and this could help clinicians to prioritize subgroups of patients for undergoing TEE.

Our finding that patients with LAA thrombus in PCD-CT had larger LAA orifice diameters in TEE is in line with previous results showing an increased risk of stroke in AF patients with larger LAA orifice.[37,38] Reduced blood flow velocity in LAA was also associated with increased risk of stroke in patients with AF,[39,40] however, lower LAA blood flow velocity in patients with LAA thrombus in our study may be secondary to the presence of thrombus.

Despite not having any missing data for the included patients, our study is limited by its retrospective nature. Another limitation is that we do not perform cardiac PCD-CT or TEE in all consecutive patients with acute ischemic stroke or TIA admitted to our center. From a total of 2830 patients, we included only 101 patients in the final study population, which is a reflection of local protocols for stroke patient care, but represents a high risk of selection bias. Only about 15% of all patients with acute ischemic stroke or TIA underwent TEE during the index admission, and these patients are typically younger or have specific clinical indications for TEE, both of which could influence the prevalence of LAA thrombus in our study population (selection and verification bias). This increases pre-test probability of the presence of LAA thrombus, and may falsely increase the diagnostic performance measures we used in this study, therefore, our results must be interpreted with caution. There was no patient-related or physician-related selection bias for the performance of cardiac PCD-CT, because its availability is strictly related to hospital admission time. The small sample size and the fact that only 12 patients were found to have LAA thrombus in cardiac CT also represent a relevant limitation, which decreases the statistical robustness of the findings and weakens the strength of the conclusions. However, the sample size was calculated using a valid statistical method aiming to demonstrate an expected sensitivity. The technical specifications and conditions we chose to perform cardiac CT may be associated with a suboptimal image quality in comparison to elective dedicated cardiac CT. The fact that ECG-triggering was possible in only 60% of the cohort reflects the difficulty in applying this specific protocol in the acute stroke setting, in which patients are frequently uncooperative, thus reducing its generalizability. Additional limitations included that no ultrasound-enhancing agents for optimal detection of intracardiac thrombi were routinely used, and that intravenous thrombolysis and early anticoagulation in patients who initially had a LAA thrombus in cardiac-PCD-CT could have contributed to dissolving the thrombus, therefore increasing false positive cases. Among the strengths of this study, we emphasize the use of a photon-counting detector, the independent image assessment by two pairs of experienced observers blinded to clinical information, and the short time between cardiac CT and TEE.

Conclusion

Cardiac PCD-CT integrated as a part of the emergent imaging protocol for patients with acute ischemic stroke or TIA is a promising diagnostic tool that may reliably exclude LAA thrombi and may help to improve the etiological investigation of stroke. Further studies to understand its impact on therapeutic decisions and on outcomes are needed.

Declarations

Ethics approval and consent to participate

The current study was approved by the ethics committee of the University Hospital RWTH

Aachen (approval reference EK 24-304, date of approval August 30, 2024; an extension of the study period up to December 31, 2025 was also approved by the same ethics committee). Due to the retrospective nature of the study, patient informed consent was waived by the ethics committee of the University Hospital RWTH Aachen.

Consent for publication

Not applicable, as per journal's guidelines.

Author contributions

Annemarie Kirschfink: Data curation; Investigation; Visualization; Writing – original draft.

Mohamed Elhalal: Data curation; Investigation; Visualization; Writing – original draft.

Stefan Seidel: Investigation; Writing – review & editing.

Stefanie Kammer: Investigation; Writing – review & editing.

Dimah Hasan: Data curation; Writing – review & editing.

Michael Frick: Data curation; Writing – review & editing.

Nikolaus Marx: Resources; Writing – review & editing.

Jörg B. Schulz: Resources; Writing – review & editing.

Martin Wiesmann: Resources; Writing – review & editing.

Ertunc Altiok: Methodology; Supervision; Writing – review & editing.

Hani Ridwan: Methodology; Supervision; Writing – review & editing.

Arno Reich: Conceptualization; Formal analysis; Methodology; Project administration; Supervision; Writing – review & editing.

João Pinho: Conceptualization; Formal analysis; Methodology; Project administration; Supervision; Writing – review & editing.

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Competing interests

The authors declare that there is no conflict of interest.

Availability of data and materials

Anonymized data will be made available for research purposes upon reasonable request to the corresponding author and according to local legal and ethical requirements.*

ORCID iD

João Pinho https://orcid.org/0000-0002-3977-7146

Supplemental material

Supplemental material for this article is available online.

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