

Usefulness of Spectral Cardiac Computed Tomography for the Evaluation of Thrombotic Complications in Patients with Ischemic Stroke

Utilidad de la TC espectral cardíaca para la evaluación de complicaciones tromboticas en pacientes con ataque cerebrovascular isquémico

GASTÓN A. RODRÍGUEZ-GRANILLO^{1,2}, JUAN CIRIO³, CELINA CIARDI³, MARCOS CERON^{1,5}, BIBIANA RUBILAR⁴, CARLOS BLEISE⁶, CARLOS INGINO⁵, PEDRO LYLK⁶

ABSTRACT

Objective: The aim of this study was to evaluate the usefulness of spectral cardiac computed tomography (CT) angiography in patients with ischemic stroke.

Methods: In the setting of COVID-19 pandemic, we incorporated the use of spectral cardiac CT in patients with ischemic stroke to rule out the presence of cardioembolic sources, thrombotic complications or myocardial damage in a single session. Since July 2020, delayed phase cases acquisition were incorporated to cardiac CT scans in the context of ischemic stroke. We describe four and two with ischemic representative of the usefulness of the method and the cardiovascular findings.

Results: We present four cases recorded in a period of 40 days: two patients with cardioembolic source (aorta and left atrial appendage) and with ischemic stroke of undetermined source with evidence of cardiomyopathy (ischemic and non-ischemic).

Conclusions: In the setting of ischemic stroke, spectral cardiac CT with delayed acquisition could be useful to rule out the presence of cardioembolic sources and identify the underlying etiology.

Key words: Computed Tomography Angiography - Stroke - Thrombosis - Multidetector Computed Tomography

RESUMEN

Objetivo: Evaluar la utilidad de la angiotomografía computada (TC) espectral cardíaca en pacientes con ataque cerebrovascular isquémico (ACVi).

Materiales y métodos: En el contexto de pandemia de COVID-19 incorporamos la utilización de la TC espectral cardíaca en pacientes con ACVi para descartar en una única sesión, tanto fuentes cardioembólicas (FCE) como la presencia de complicaciones tromboticas o daño miocárdico. A partir de julio de 2020 incorporamos una adquisición tardía a las TC cardíacas en contexto de ACVi. Se presentan cuatro casos representativos sobre su utilidad y hallazgos cardiovasculares.

Resultados: Se presentan cuatro casos registrados en un lapso de 40 días. Dos pacientes con FCE (aorta y orejuela izquierda) y dos con ACVi de origen indeterminado donde se evidenció miocardiopatía (isquémica y no isquémica).

Conclusiones: En el contexto del ACVi, la TC espectral cardíaca, que incluya una adquisición tardía, permitiría, eventualmente, descartar la presencia de FCE e identificar la etiología subyacente.

Palabras clave: Angiografía por Tomografía Computarizada - Accidente Cerebrovascular - Trombosis - Tomografía Computarizada Multidetector

INTRODUCTION

Cardiac computed tomography (CT) has many applications besides the assessment of coronary artery anatomy, as the evaluation of myocardial perfusion and characterization of cardiomyopathies. (1) In addition, the accuracy of cardiac CT scan to rule out

cardioembolic sources (CES) is equivalent to that of transesophageal echocardiography (TEE). (2) Considering that up to 40% of acute ischemic strokes are due to cardioembolism, many of these patients need specific evaluation of CES. Although TEE is the reference standard, its availability is limited to the presence of

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Address for reprints: Instituto Médico ENERI, Clínica La Sagrada Familia - Avda. Libertador 6647 (C1428ARJ) Buenos Aires, Argentina - e-mail: grodriguezgranillo@gmail.com

¹ Department of Cardiovascular Imaging, Instituto Médico ENERI, Clínica La Sagrada Familia

² National Scientific and Technical Research Council (CONICET), Argentina

³ Stroke Unit, Instituto Médico ENERI, Clínica La Sagrada Familia

⁴ Department of Interventional Cardiology, Instituto Médico ENERI, Clínica La Sagrada Familia

⁵ Department of Cardiology, Instituto Médico ENERI, Clínica La Sagrada Familia

⁶ Department of Interventional Neuroradiology, Instituto Médico ENERI, Clínica La Sagrada Familia

experienced operators, it is associated with higher risk of aspiration in patients with sensory impairment and presents some contraindications, including esophageal disorders, gastrointestinal bleeding and coagulopathies. (3)

On the other hand, cardiac CT scan allows a better evaluation of left atrial appendage morphology, a factor associated with higher risk of ischemic stroke, and identification of CES in less prevalent sites as the left ventricular apex and some segments of the aorta which are difficult to evaluate with TEE. (4, 5)

Several studies have demonstrated the ability of cardiac CT scan for the assessment of myocardial late iodine enhancement (LIE). (6, 7) The recent incorporation of dual-layer spectral detector CT improves discrimination between tissues with similar density that cannot be detected by conventional CT.

In cardioembolic stroke, delayed-phase images can detect LIE, and discriminate between thrombi (typically "black" in delayed-phase images, with iodine content close to zero), viable myocardium/aorta (intermediate density with mild iodine content), and areas with focal increase of extracellular volume (ECV) corresponding to fibrosis, necrosis, or infiltrative processes (increased iodine content). (8) The quantification of the ECV using cardiac magnetic resonance imaging with T1 mapping has gained particular interest over the past years. (9, 10)

Several studies have demonstrated that cardiac spectral cardiac CT improves the evaluation of myocardial perfusion, LIE, and intracavitary thrombi. (11-13)

We have recently incorporated delayed-phase images to cardiac CT for the evaluation of ischemic stroke. We describe four cases representative of the usefulness of the method and the cardiovascular findings.

METHODS

To yield an accuracy comparable to TEE for ruling out cardioembolic sources, cardiac CT requires late acquisition 3 minutes after the administration of the contrast agent. Since July 2020 we have adopted the use of a low-dose (prospective ECG-gating) acquisition 5 minutes after contrast administration to simultaneously evaluate the presence of CES, cardiomyopathies, LIE, and coronary arteries in a single session, without delaying the indicated treatment of the ischemic stroke. We have introduced this strategy in the context of the pandemic, where the availability of personal protective equipment and TEE operators is limited and attempts have been made to limit their use because of the risk of transmission. This strategy was also promoted based on the publication of reports identifying myocardial damage in up to 40% of COVID-19 patients. (14)

Images were acquired with a Philips IQon dual-layer spectral detector CT scanner (Philips Healthcare, Best, Netherlands). This type of technology allows simultaneous acquisition of images using two energy levels as well as conventional CT images, enabling the discrimination between the different mechanisms by which X-rays interact with matter related with the attenuation coefficients of the materials: Compton scattering and the photoelectric effect. In

this way, it is possible to obtain multi-parametric information about density, reconstructions of virtual monochromatic images (VMI) and atomic number, among other parameters, which facilitate the discrimination between tissues with similar density in images obtained with a single-energy CT scan.

After intravenous administration of 60 to 70 mL of iodinated contrast (Ioversol, 350 mg/mL), images were obtained using prospectively gated CT scanning during the arterial phase, from the aortic arch to the diaphragm, if the patient presented sinus rhythm and could collaborate. Five minutes later, a prospectively ECG-gated scan was performed to obtain the images of the heart. The images were analyzed with a dedicated software (IntelliSpace Portal 11, Philips Healthcare, Best, Netherlands) using VMI at 40-50 keV and iodine mapping. The ECV was calculated at the level of the septum, using the hematocrit measured in the same day, with the equation $ECV = (1 - \text{hematocrit}) \times (\text{iodine concentration in the myocardium} / \text{iodine concentration in the ventricular chamber})$.

Ethical considerations

Written informed consent for the use of data was obtained in all cases, and all procedures were in accordance with the ethical standards of the Helsinki declaration.

RESULTS

Case #1

The first patient was a 73-year-old woman who was a current smoker and had a history of chronic obstructive pulmonary disease. She was admitted with aphasia (NIHSS: 6) of undetermined onset. The brain MRI showed hyperacute ischemic lesions at the cortico-subcortical frontotemporal and left periventricular levels. The CT angiography showed a addle-like thrombus in the bifurcation of the left middle cerebral artery. Mechanical thrombectomy with stent retriever and aspiration was performed, and a final grade 2b reperfusion on the modified TICI scale was achieved.

The patient evolved with favorable outcome without complications. Seven days later, the patient underwent a cardiac CT scan to rule out CES. A 7 x 21 mm thrombus was detected in the tubular segment of the aorta without iodine uptake (Figure 1, A and B), with no thrombi in the left atrial appendage or left ventricle. Myocardial ECV fraction was 29% (Figure 1 C), within normal limits.

Case #2

A 57-year-old male patient, with a history of type 2 diabetes and hypertension was admitted with diplopia and headache upon awakening, and unstable gait of undetermined onset (NIHSS: 0). Blood pressure on admission was 170/100 mm Hg and troponin values were normal. The brain MRI angiography demonstrated acute ischemia of the posterior cranial fossa without occlusion of the vessels explored. The patient had a favorable outcome with symptom relief. A spectral cardiac CT scan performed (Figure 2) to evaluate the etiology of the ischemic stroke detected asym-

Fig. 1. Conventional CT image (A) simultaneously obtained with spectral detector CT. The dual layer spectral detector allows identification of a thrombus (arrow) at the level of the tubular segment of the ascending aorta, settled on diffuse aortic atheromatosis. Iodine maps (B) are used to calculate iodine concentration of 0.15 mg/mL, suggestive of a thrombus. The myocardial extracellular volume fraction calculated is 29% (C) for a hematocrit of 38%.

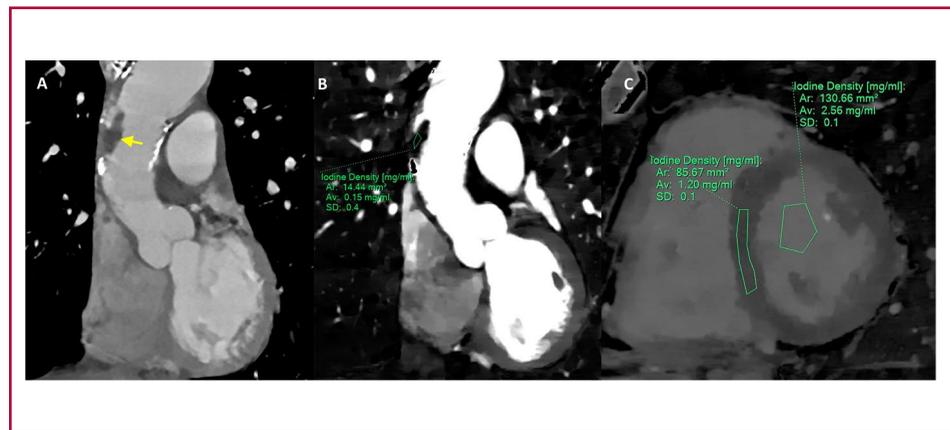
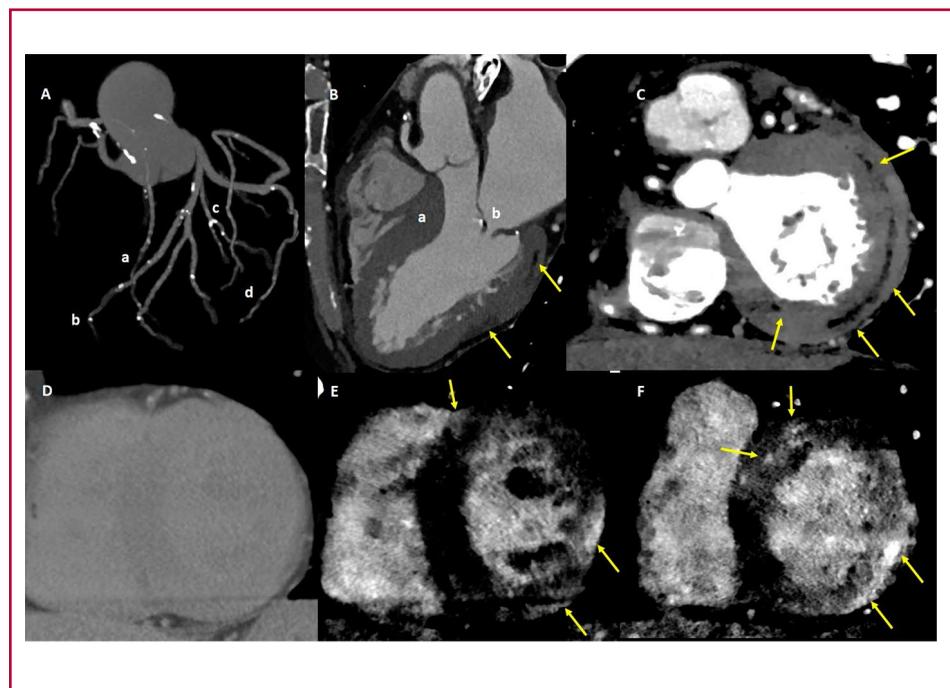


Fig. 2. Computed tomography coronary angiography (A) Multiple focal and severe lesions are observed in the distal third of the right coronary artery (a), left anterior descending coronary artery (b), diagonal and left marginal arteries (d). Three-chamber view (B) showing septal hypertrophy (a), thickened mitral valve (b), and intramyocardial fatty infiltration with patchy distribution in the lateral wall (arrows). Basal short-axis view (C) demonstrating fatty infiltration. The conventional CT scan with delayed phase images (D) does not identify delayed enhancement. After using reconstruction of virtual monochromatic images at low energy levels (E and F) a patchy pattern of delayed enhancement is observed in the myocardium and subepicardium.



metric septal hypertrophy, with areas of linear shaped intramyocardial fatty infiltration in the basal inferior and lateral walls. Intramyocardial LIE was observed in the mid inferior and lateral wall with a patchy distribution in the basal anterolateral wall, and with preserved left ventricular function. Several foci of atherosclerosis were present in the small vessels and heart valve thickness was unexpectedly increased for the patient's age. The ECV fraction at the level of the septum was 40% and 70% at the level of the lateral area with maximum enhancement. These findings were interpreted as non-ischemic-necrotic cardiomyopathy, which could correspond to a left-dominant arrhythmogenic cardiomyopathy with hypertrophy component. However, and although systolic function

was preserved, we could not rule out chemotherapy-induced cardiotoxicity due to the presence of lesions in the coronary arteries, heart valves and myocardium in a relatively young patient with a history of chemotherapy.

Case #3

A 74-year-old female patient with a history of permanent pacemaker and ischemic stroke five years earlier was admitted with left hemiparesis and dizziness (NIHSS: 6) within 5 hours of symptom onset. The cerebral CT angiography of the intracranial and extracranial vessels and the perfusion scan showed occlusion of the right posterior cerebral artery and hypoperfusion in the territory of the ipsilateral pos-

terior cerebral artery. The CT scan of the chest revealed bilateral peripheral ground-glass opacities (undetermined pattern for COVID-19). The cerebral angiography confirmed the occlusion of the P1 segment of the right posterior cerebral artery. The patient underwent thrombectomy with stent retriever, achieving a final grade 3 reperfusion on the modified TIC1 scale. The patient evolved with hypertensive acute pulmonary edema (210/100 mm Hg) with pro-BNP level of 6700 pg/mL and normal troponin levels requiring mechanical ventilation for 24 hours. The transthoracic echocardiogram reported an ejection fraction of 55%, absence of wall motion abnormalities and a moderately dilated left atrium. There were no significant lesions on the carotid ultrasound. The electrocardiogram showed atrial fibrillation and pacemaker activity with appropriate sensing and ventricular capture. The PCR test was negative for SARS-CoV-2. On postoperative day four, a spectral cardiac CT scan (Figure 3) to rule out CES revealed a thrombus in the left atrial appendage and anticoagulation was started. There was no LIE and the ECV fraction was 35%.

Case #4

The last patient was a 68-year-old man with a history of diabetes and smoking habits who was admitted with left hemiparesis of 6-hours since onset. The patient had no fever, blood pressure was 184/112 mm Hg and heart rate was 105 bpm. The brain MRI showed a recent right-sided ischemic lesion in the cerebellum and lenticulocapsular region and atheromatous infiltration of the basilar trunk, with moderate stenosis, and non-significant diffuse atheromatosis in the other territories. The patient underwent cerebral CT angiography which demonstrated the presence of diffuse atheromatosis and mild to moderate stenosis of the basilar artery. Medical therapy was started. The electrocardiogram showed complete right bundle branch

block and left anterior hemiblock with unspecific repolarization abnormalities. The transthoracic echocardiogram did not show wall motion abnormalities. As the laboratory tests revealed rise and fall in cardiac enzymes, the patient underwent coronary angiography evidencing coronary artery diffuse atheromatosis with multiple severe thrombotic lesions in the secondary branches. A stent was implanted in the distal right coronary artery. A cardiac CT scan performed to rule out CES (Figure 4) demonstrated diffuse atheromatosis of the coronary arteries with occlusions of the posterior descending, left marginal and diagonal coronary artery branches. There was an aneurysm in the mid right coronary artery with an eccentric non-occlusive intramural thrombus. The spectral analysis identified a severe perfusion defect in the inferior wall with transmural LIE and evidence of microvascular obstruction (no-reflow phenomenon, Figure 4 F-G). The ECV fraction at the level of the septum was 38% and 68% at the level of the lateral area with maximum enhancement.

DISCUSSION

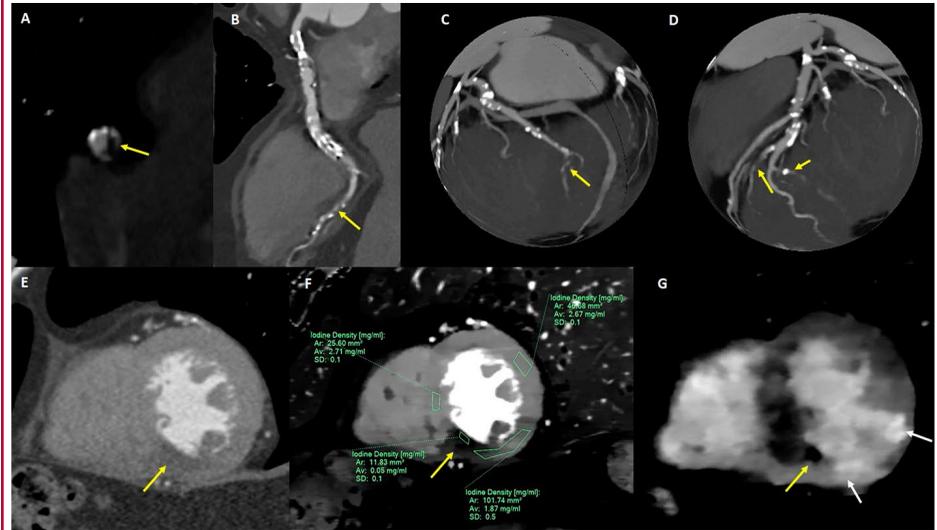
This case series represents a possible novel application of spectral cardiac CT in the context of ischemic stroke to rule out the presence of CES and identify the underlying etiology.

Spectral detector CT would allow detecting the presence of thrombi (iodine content <1.3 mg/mL) by facilitating the quantification of iodine content in a given tissue without the need for delayed phase images, which are usually necessary with single-energy CT. (15) As with this type of strategy images are acquired 5 minutes after the injection of the contrast agent instead of 3 minutes later, the discrimination of thrombi is facilitated by increasing the gradient between enhanced (ventricular chamber and myocardium) and non-enhanced (thrombus tissues), and the presence of LIE is simultaneously identified. In



Fig. 3. Thrombus (arrows) in the left atrial appendage identified with conventional CT scan (A and B) and diffuse calcification of the mitral valve. Virtual monoenergetic images at 40 keV, with absence of myocardial LIE (C). (C). The use of iodine maps (D-F) highlights the difference with the left atrium and the low concentration of iodine in the thrombus (0.26 mg/mL). Delayed phase images (E-F) allow better discrimination of the thrombus (E) and calculation of myocardial ECV of 35% (F) for a hematocrit of 36%. The presence of pacemaker and motion artifacts does not hinder thrombus detection

Fig. 4. Right coronary artery aneurysm (A and B) with extensive non-occlusive intramural thrombus (arrow A). The posterior descending coronary artery presents occlusive lesion (arrow B). "Globe" reconstructions (C and D) showing diffuse atheromatosis of the coronary branch tree including occlusive lesions in the left marginal artery (C) and diagonal artery (D). The conventional CT scan (E) demonstrates a subtle myocardial hypodensity in the inferoseptal wall (arrow), while spectral images CT with iodine maps allow the detection of a severe inferoseptal perfusion defect (arrow F) with iodine concentration of only 0.05 mg/mL and a mild perfusion defect (1.87 mg/mL) in the inferior and inferolateral wall. (G) Delayed-phase images show transmural late iodine enhancement in the inferior and inferolateral wall (white arrows) and a black area (yellow arrow) suggestive of microvascular obstruction/no-reflow phenomenon.



the setting of ischemic stroke, where the relevance of embolic stroke of undetermined source (ESUS) is increasing, the hypotheses-generating findings of this type of strategy could possibly shed some light on the etiology. (16) Finally, spectral cardiac CT, which has already been validated against cardiac MRI, allows the quantification of ECV fraction, a novel surrogate marker of interstitial fibrosis and of subtle preclinical changes linked to cell damage or edema in different cardiomyopathies, without need for the acquisition of non-contrast images as with conventional CT. (10)

Patients with stroke usually have rhythm disorders with elevated heart rate, in addition to sensory impairment and apnea intolerance; therefore, they do not represent the ideal patients to obtain high-quality imaging tests as in other clinical situations.

CONCLUSIONS

In the setting of ischemic stroke, spectral cardiac CT scan with delayed-phase images could be useful to rule out the presence of CES and identify the underlying etiology.

Conflicts of interest

None declared.

(See authors' conflicts of interest forms on the website/ Supplementary material)

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