Editorial Commentary

Contrast agent volume in coronary computer tomography angiography—where are the limits?

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Coronary artery disease (CAD) is still a major public health problem, remaining the most common cause of death and disability globally and being associated with relevant costs for our health care system (1,2). It can present in chronic or stable forms, currently named chronic coronary syndromes but also in acute forms ranging from unstable angina to myocardial infarction with cardiogenic shock or sudden cardiac death. The work-up of patients with known or suspected CAD is complex and usually involves a stepwise approach that includes clinical and demographic data, non-invasive tests and if required invasive coronary angiography (3). Recent data have revealed a lower pre-test probability in patients with CAD than previously anticipated (4). In parallel, a paradigm shift occurred in the evaluation of patients with suspected CAD, with the focus moving to non-invasive imaging techniques. Currently, the clinician can choose between imaging tests that aim at identifying myocardial ischemia such as stress-echocardiography, stress cardiac magnetic resonance imaging or myocardial scintigraphy and direct non-invasive anatomical imaging of the coronary tree using coronary computer tomography angiography (CCTA) (5). In the last decades, an abundance of studies was published, which cemented the central role of CCTA in the diagnostic approach of patients with known and suspected CAD. In this regard, CCTA was shown to provide (I) excellent negative predictive value and very good specificity for identifying relevant CAD, (II) in depth evaluation of the various stages and severity of the coronary atherosclerotic process, (III) functional information related to the hemodynamic significance of the coronary stenosis using FFR_{CT} and, most importantly, (IV) definite improvement of clinical outcomes (6).

Clinicians need however, to be aware of two relevant risks associated with a CCTA examination, which are (I) radiation exposure and (II) complications related to the administration of iodine contrast agent. Regarding radiation exposure, technological advancements within the last decades allowed for a significant reduction of the radiation exposure for the patients. Thus, the radiation exposure normally seen with spiral acquisitions (9-22 mSv) can be significantly reduced using prospective step and shoot protocols (2-4 mSv) and further minimized to <1 mSv by employing high-pitch spiral protocols using modern dual source machines in selected patients (7-9). Studies have proven the diagnostic feasibility of the high-pitch spiral technology and, although this type of acquisition cannot be applied in all scenarios, it already entered the clinical routine (10). The exceptionally low radiation exposure opens the door for performing longitudinal CCTA studies and thus for providing important information related to the evolution of the atherosclerotic process and its response to specific lipid-lowering or anti-inflammatory therapies.

The administration of contrast agent, on the other hand, is related to possible allergic reactions, hyperthyroidism

and worsening of the renal function. Especially in the case of contrast induced nephropathy, a dose-dependent relationship between the volume of contrast agent administrated and the risk of worsening of the renal function is widely accepted. However, according to recent reports, the risk for kidney injury due to contrast agent injections might have been overstated in the past (11,12). It would therefore by desirable to use the lowest volume of contrast agent possible without sacrificing the image quality. Most of the current CCTA scan protocols employ between 60 and 80 mL of iodinated contrast. The volume of contrast used is dependent on numerous factors such as the patient's habitus, method for determining the appropriate time frame for the acquisition (i.e., bolus tracking or test bolus), speed of administration of the contrast agent and type of CCTA protocol (13). Previous studies have reported good results with volumes as low as 40 mL of contrast agent (14). In the current study, Jin *et al.* tested an even lower dose of contrast agent (15). Thus, they evaluated 53 patients who underwent CCTA using 30 mL contrast agent [iobitridol, 350 mg iodine (mgI)/mL] and compared the data regarding diagnostic image quality with a group of 50 patients who underwent a CCTA using a routine dose contrast agent (0.7 mL/Kg, ≈42 mL). In all patients step and shoot protocols were employed, and the optimal time of acquisition was determined using the bolus tracking method. As expected, the authors found lower opacification in the coronary arteries in terms of HU in the low dose contrast agent group. However, the diagnostic image quality was deemed similar between the two groups. The results are promising and especially noteworthy as the authors used a step and shoot protocol. Thus, it appears that a low volume of contrast agent can be used in patients with higher heart rates, where high pitch spiral protocols would not be feasible. However, the data must be interpreted with care. As the authors stated, the population studied had a low body mass index (BMI), which may not be representative of the general CAD population. Patients with higher BMI usually need higher volumes of contrast agent in comparison to standard protocols (16). Secondly, there was no reference for assessing the severity of the CAD. Although the readers agreed that the diagnostic image quality was good in both groups, it is difficult to infer that the evaluation of the severity of the coronary stenosis was accurate in both groups without having follow-up data or an invasive reference standard. Lastly, the authors do not provide any information related to the calcium burden of the coronary arteries. The accuracy of CCTA is diminished in patients with high calcium burden and based on the data provided it is difficult to assess the feasibility of administrating a low dose contrast agent in patients with high calcium scores (17).

Overall, the study provides an important milestone to the body of literature related to CCTA and supports to use of low volumes of contrast agent in selected populations who undergo a CCTA examination, thus making CCTA even safer in the daily routine and importantly without sacrificing the diagnostic accuracy of the method, which is essential for both diagnostic classification and risk stratification of our patients.

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