

## Coronary Computed Tomography Angiography (CCTA) in the Real Not-so-Developed World

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## Abstract

During the War in Croatia, from 1991-1995, the majority of patients with CAD were treated conservatively. Revascularization was performed only rarely for ACS patients. In the "Ere of stentomania, 1995-2005", which due to the limited resources "flamed" in Croatia in smaller intensity than possibly elsewhere, and before the COURAGE-Ere, I performed over 8000 diagnostically procedures and over 1200 PCI-procedures. The fundamental clinical problem with CAD is in its unpredictability. For that reason our primary professional interest in the last decade has been focused on its early and non-invasive detection, where nowadays we believe CCTA can prove very usable. To evaluate how CCTA altered the management of patients with suspected CAD we studied 792 patients. After CCTA, obstructive CAD was excluded in 666 patients. During 12-month follow-up, 98.6% of these patients were free of major adverse cardiac events. Also, indication for ICA was revoked in 77.2% of patients. It was also revoked in all patients with low pre-test risk, 80.7% with intermediate and 72.6% with high risk. Medical therapy was changed in 54.7% of patients. Based on our 6-year experience and published evidence-based data, we believe that CCTA can help not only in reliable detection of CAD, but also to choose the most appropriate management for the vast majority of patients. CCTA also can allow for faster, easier and simpler evaluation, and replace ICA in the majority of patients, together with its complications, but also direct and indirect costs it is coupled with.

**Keywords:** Coronary artery disease, Coronary computed tomography angiography, Invasive coronary angiography

Although Croatia is a Mediterranean country, according to the European Society of Cardiology (ESC) chart risk it belongs in the category of high Cardiovascular Disease (CVD) risk countries [1]. During the war-years in Croatia, 1991-1995, the majority of patients with Coronary Artery Disease (CAD) were treated conservatively, both for medical and non-medical reasons. Revascularization was performed only rarely for patients with Acute Coronary Syndrome (ACS). Following that, in the so-called "era of stent mania", in the period of 1995-2005 (which, due to limited resources, "flamed" in Croatia in somewhat smaller intensity than elsewhere) we performed over 8000 diagnostic Invasive Coronary Angiography (ICA) procedures, and over 1200 PCI-procedures alone.

As we realize today, the fundamental clinical problem with CAD was, and still remains, its unpredictability. The most appropriate management strategy is still not completely defined, especially in countries with limited resources and underdeveloped healthcare systems such as Croatia. For that reason, our primary professional interest over the last decade had been focused on its early detection. We now believe Coronary Computed Tomography Angiography (CCTA) can prove very usable.

CCTA is the fastest and only growing application for computed tomography in the United States, with approximately 500,000 Americans undergoing CCTA each [2]. As a result, this has stimulated professional and public concern about the appropriateness of its widespread use. The AHA/ACC Appropriate Use Criteria (AUC) for CCTA from 2006 defined 37 clinical situations where this method was considered appropriate, whereas in 2010 this number increased to 93, demonstrating obvious growth [3,4].

Although recommendations for CCTA still remain cautious, diagnostic ICA for stable patients is now recommended more or less only if the results of non-invasive testing suggest a high likelihood of significant 3-vessel disease, severe affliction of the left main, proximal LAD, or single remaining patent vessel, if there is a proven large area of ischemia (>10% LV), especially if accompanied with dyspnea/CHF, and probably most important, if there is persistent limiting angina or an angina equivalent despite optimal medical therapy [5,6]. Last but not least, the patient has to willingly accept the possibility of immediate revascularization. In general the AHA/ACC and ECS guidelines were less prescriptive than the earlier NICE ones, partly because they put less emphasis on the cost-effectiveness of its recommendations [5-7].

Although indications may vary among different professional societies, ICA and CCTA are now being commonly and widely used by clinicians to assess anatomic disease burden in patients with CAD. For example, according to Cleveland Clinic data, a pioneer institution in ICA and PCI, the number of CCTA performed in their institution in 2012 was very similar to that of diagnostic ICA, 7706 vs. 8730 [8]. Furthermore, one recent analysis has de facto called into question the rationale for many of the revascularization procedures performed until recently, at least in patients with stable CAD [9]. In the meta-analysis of more than 5000 patients, PCI seemed to be no better than medical therapy alone in patients with documented ischemia on stress testing or Fractional Flow Reserve (FFR). In line with that, the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial systematically showed that at least 2/3 of patients with stable angina fare as well with optimal medical therapy alone, as they do with angioplasty/stenting or by-pass [10].

As a curiosity in this respect, when George W. Bush was stented in August 2013, a fierce dispute arose whether this intervention was really necessary, or if he would have fared better off with medical therapy only. Also interestingly, the primary diagnostic work-up used in his case was CCTA, and not ICA.

In our own study of 792 patients, we tried to evaluate how CCTA influenced the management and treatment of patients with stable CAD [11]. Although we did not systematically compare CCTA with ICA, we conducted a 12-month clinical follow-up for the following clinical events: cardiac death; nonfatal myocardial infarction; unstable angina pectoris requiring hospitalization; coronary revascularization not indicated on CCTA; cardiologist's decision whether to proceed with conservative treatment only or to proceed to ICA, as based on an initial CCTA examination. Among other results, we showed that CCTA was able to replace diagnostic ICA in the majority (77.2%) of these patients, no matter the pre-test risk stratification, so that 98.6% of these patients were free of major adverse cardiac events during the follow-up period. Also, following CCTA, medical therapy was upgraded in 35.6% of patients to meet optimal medical therapy criteria

as defined according to the COURAGE-trial, demonstrating the importance of visualizing CAD burden in clinical decision making [10].

As there exists a significant number of patients with stable CAD who still require revascularization, and also because disease burden visualization can influence the aggressiveness of medical therapy, we believe that some kind of morphological imaging is still mandatory in these patients [12]. Having in mind everything said above, we believe this diagnostic work-up should be kept as non-invasive as possible. As CCTA can provide accurate replacement for ICA in the vast majority of patients, we believe that it can be reliably used for this purpose, if local expertise allows [13]. This especially since one recent study seems to indicate that CCTA can allow improved CAD risk evaluation as compared to present methodology, as it allows analysis of not only plaque presence and/or severity, but also of coronary plaque extent, which has been associated with an elevated risk of cardiovascular death or myocardial infarction [14]. The lesions in question here were the nonobstructive ones that are not only usually invisible on ICA, but also remain undetected by so-called functional imaging (Figure 1).



Figure 1: Coronary Computed Tomography Angiography and Invasive Coronary Angiography in the same patient with stable angina

On CCTA, diffuse atherosclerotic burden is clearly visible with moderate stenosis on distal RCA, while on ICA only this single lesion on distal RCA is visible.

In conclusion, based upon the presented data and our clinical experience, we believe that CCTA can provide reliable diagnostic and prognostic information for adequate clinical decision-making and treatment of the majority of patients with stable CAD, and function as a possible gatekeeper to ICA and other more invasive and costly methods [15]. Having in mind the financial benefits associated with the use of CCTA as compared to diagnostic algorithms based upon stress-perfusion tests, this might prove even more important, especially in "not-so-developed" countries with limited resources and often not-developed-enough larger-community networks for management of CAD [16]. We look forward to more insights from the still ongoing 8000-patient ISCHEMIA, and other trials [17].

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