Interpretable Automated Computational Support for Coronary Artery Disease Assessment

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1. Introduction

1.1 Anatomy of the Coronary Arteries

The heart is the central organ of the cardiovascular system and requires a continuous supply of oxygen and nutrients to function properly. This supply is provided by the coronary artery tree, a specialized vascular network that delivers blood directly to the heart muscle, known as the myocardium. The coronary arteries originate from the root of the aorta and spread over the surface of the heart in a crown-like arrangement, from which the term *coronary* is derived [2]. As illustrated in Figure 1, the coronary arterial system is mainly composed of two vessels: the right coronary artery (RCA) and the left coronary artery (LCA).

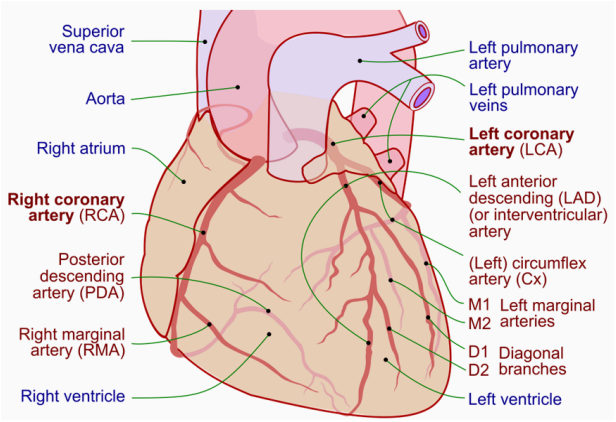

Figure 1. Representation of the anatomy of the coronary tree. Coronary arteries are labeled in red, and other anatomical structures are shown in blue. Adapted from Patrick J. Lynch [7].

The RCA primarily supplies the right atrium and right ventricle, while the LCA divides into two major branches: the left anterior descending artery (LAD) and the circumflex artery (Cx). These branches supply most of the left ventricle and the interventricular septum [2]. From these main arteries, smaller branches extend throughout the myocardium to ensure regional blood delivery to specific areas of the heart.

A key characteristic of the coronary circulation is its limited collateral connectivity. Unlike other vascular networks in the body, coronary arteries generally lack sufficient alternative pathways to redirect blood flow in the presence of an obstruction. As a result, a narrowing or blockage in a proximal arterial segment directly compromises blood flow to all downstream regions supplied by that vessel [3].

Coronary anatomy also exhibits inter-patient variability, including differences in vessel size, branching patterns, and coronary dominance. Dominance is defined by the artery that gives rise to the posterior descending artery (PDA) and can be classified as right-dominant, left-dominant, or codominant. Right-dominant circulation, in which the PDA originates from the RCA, is the most common configuration, followed by left dominance and codominance [4]. Understanding this anatomical organization is essential for interpreting the location and severity of coronary lesions and constitutes the anatomical basis for stenosis quantification, risk stratification, and clinical decision-making in CAD diagnosis.

1.2 Coronary Artery Disease and Clinical Motivation

Coronary artery disease (CAD) remains one of the leading causes of morbidity and mortality worldwide and is responsible for a significant proportion of cardiovascular events, including myocardial infarction and sudden cardiac death [1]. CAD is characterized by the progressive accumulation of atherosclerotic plaque within the

coronary arteries, which leads to a narrowing of the vessel lumen. This narrowing restricts blood flow to the myocardium and, if not detected and treated in time, can result in myocardial ischemia or infarction.

Figure 2 illustrates the pathological mechanism underlying CAD, highlighting the difference between a healthy coronary artery and one affected by plaque accumulation. While a normal artery allows unobstructed blood flow, plaque buildup reduces the effective lumen diameter, limiting oxygen delivery to the heart muscle and increasing the risk of adverse cardiac events.

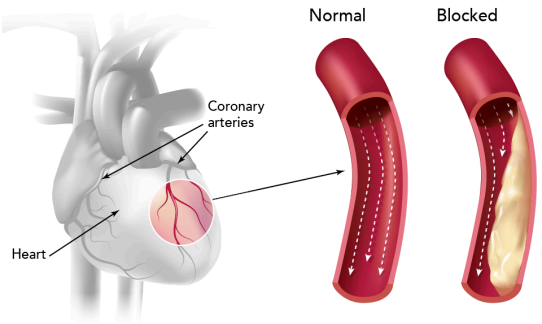

Figure 2. Schematic illustration of coronary artery disease, comparing a normal coronary artery with one affected by atherosclerotic plaque. Adapted from Kaiser Permanente [8].

For these reasons, early and accurate diagnosis of CAD is essential for appropriate patient management and risk stratification. Identifying coronary artery narrowing at an early stage allows clinicians to select the most suitable treatment, prevent disease progression, and reduce the likelihood of severe cardiac events. In current clinical practice, coronary computed tomography angiography (CCTA) is widely used as a standard, non-invasive imaging technique for the evaluation of coronary arteries, in accordance with international clinical guidelines [5].

CCTA provides detailed three-dimensional images of the coronary artery tree, enabling clinicians to directly visualize coronary anatomy. Through these images, it is possible to detect the presence of atherosclerotic plaques, analyze their location and extent, and estimate the degree of luminal narrowing. As a result, CCTA plays a key role in assessing disease severity and supporting clinical decision-making in patients with suspected or known CAD.

Despite advances in imaging technology, the diagnostic workflow for CAD remains time-consuming and highly dependent on expert visual assessment, particularly in low-to-moderate risk patients, which represent a large proportion of clinical cases [6]. At Hospital de la Santa Creu i Sant Pau, non-pathological or low-complexity cases may still require approximately 30 minutes of reporting time, while more complex cases can take up to one or two hours [6]. This high time cost motivates the development of automated and semi-automated tools that support clinicians in decision-making while preserving interpretability and clinical control.

1.3 Stenosis Quantification: A Key Indicator of CAD Severity

Among the different indicators used to assess coronary artery disease, coronary stenosis severity plays a central role in clinical diagnosis and risk stratification. Stenosis refers to the reduction of the vessel lumen caused by atherosclerotic plaque accumulation, and its severity has been shown to be strongly associated with the risk of myocardial ischemia and adverse cardiac events [9]. Consequently, the accurate quantification of stenosis is a key step in CAD evaluation and clinical reporting.

In clinical practice, stenosis severity is commonly expressed using geometric measurements derived from imaging data. The most widely used metrics include percentage diameter stenosis (%DS), minimal lumen diameter (MLD), and minimal lumen area (MLA). These measures quantify the degree of narrowing by

comparing the lumen at the most constricted point of a lesion with a reference diameter or area estimated from adjacent, relatively healthy vessel segments located proximal and distal to the lesion [10].

Although these definitions are conceptually simple, accurately quantifying stenosis in practice is challenging. Coronary arteries often have complex shapes, with curves and bends, and atherosclerosis can affect long vessel segments, making it difficult to identify truly healthy reference regions. In addition, limitations in image resolution, segmentation errors, and noise in CCTA-derived data can influence diameter and area measurements, leading to variability in stenosis estimates [11].

In routine clinical practice, stenosis assessment is often performed visually or using semi-automatic tools provided by proprietary software. Although these methods are widely used, they depend heavily on the clinician's interpretation and can vary between observers, which reduces consistency and reproducibility. In addition, manual or semi-automatic assessment increases reporting time, especially in patients with multiple lesions or complex coronary anatomy [6].

For these reasons, there is strong clinical and research interest in the development of robust, reproducible, and transparent stenosis quantification methods that can be integrated into automated or semi-automated clinical pipelines. Such methods have the potential to standardize measurements, reduce reporting time, and provide reliable quantitative inputs for downstream tasks such as CAD-RADS assignment, clinical decision support, and patient prioritization.

1.4 CAD-RADS and the Need for Decision Support

To improve standardization in coronary artery disease reporting and facilitate clinical communication, the Coronary Artery Disease–Reporting and Data System (CAD-RADS) was introduced as a structured framework for summarizing CAD severity, primarily based on stenosis measurements obtained from CCTA [10]. CAD-RADS assigns categorical scores ranging from 0 to 5, reflecting the severity of the most significant coronary lesion and providing recommendations that guide subsequent clinical management.

By offering a common reporting language, CAD-RADS improves consistency across clinicians and institutions. However, its assignment still relies largely on the manual interpretation of stenosis severity across multiple vessels and coronary segments. This process requires the integration of quantitative measurements with anatomical and clinical context, making it cognitively demanding, particularly in time-constrained clinical environments [6].

In practice, CAD-RADS scoring may be affected by inter-observer variability, especially in borderline cases or in patients presenting with multiple lesions of moderate severity. This variability can lead to conservative or inconsistent scoring and may impact downstream clinical decisions, such as further testing or patient prioritization [9].

For these reasons, there is growing interest in algorithmic and visual support for CAD-RADS assignment. Such support can be provided through rule-based mappings from quantitative stenosis measurements, as well as through exploratory machine learning approaches that leverage structured features derived from imaging data. Importantly, these tools are designed to assist clinicians by providing objective, reproducible suggestions, while preserving clinical judgment and final decision authority [10].

1.5 Automation Challenges in the Clinical Workflow

At Hospital de la Santa Creu i Sant Pau, the CAD diagnostic workflow involves several stages, including image acquisition, image analysis, reporting, and patient prioritization [6]. While advances in imaging technology have

significantly improved image quality and diagnostic capabilities, many steps in this workflow remain fragmented and largely manual.

In clinical practice, automated image analysis tools are often not fully adopted due to concerns about their robustness, interpretability, and reliability. As a result, stenosis quantification is commonly performed manually or with semi-automatic tools, requiring significant expert effort and increasing reporting time. In addition, patient prioritization usually depends on multiple information sources and clinical judgment, which can limit reproducibility and scalability [6].

These limitations are particularly relevant in high-volume clinical settings, where clinicians must balance accuracy with efficiency. The absence of integrated, quantitative, and interpretable tools increases cognitive workload and constraints the adoption of automated solutions in daily practice.

Figure 3 illustrates the current and proposed CAD diagnostic workflows at Hospital de la Santa Creu i Sant Pau, highlighting the potential role of automated stenosis quantification and structured outputs as intermediate components between image analysis and clinical decision-making.

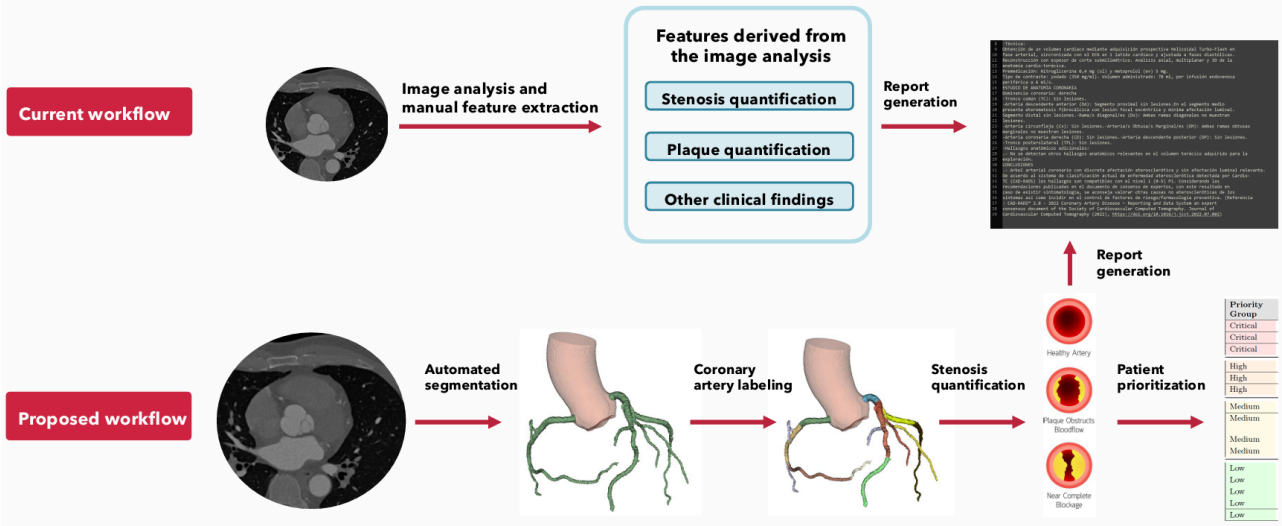

Figure 3. Current and proposed CAD diagnostic workflow at Hospital de la Santa Creu i Sant Pau, emphasizing the role of automated image analysis, structured stenosis quantification, and decision-support outputs. Adapted from the AI framework proposed by Acebes Pinilla [6].

These challenges motivate the development of modular, visually interpretable automation tools that can be progressively integrated into clinical workflows. Such components aim to support clinicians by reducing manual workload, standardizing quantitative assessments, and enabling reliable downstream tasks such as CAD-RADS assignment and patient prioritization.

1.6 Contextual Work and Project Positioning

This Final Degree Project is developed within an ongoing collaboration between Universitat Pompeu Fabra (UPF) and Hospital de la Santa Creu i Sant Pau, and builds upon previous and parallel research efforts aimed at improving the automation and efficiency of coronary artery disease assessment from CCTA data.

Within this collaborative framework, several related projects have addressed complementary aspects of the CAD diagnostic pipeline. In particular, the work by Maren Clapers focused on the automatic labeling of coronary artery segments from CCTA-derived segmentations, providing structured anatomical information that facilitates vessel-level and segment-level analysis. This contribution enables the association of quantitative measurements with specific coronary segments, which is essential for standardized reporting and clinical interpretation.

In parallel, the work by Eva Ferrer addressed patient prioritization and reporting for CAD diagnosis, proposing decision-support interfaces and structured outputs designed to assist clinicians in managing clinical workflows and patient prioritization. This work highlighted the importance of transforming quantitative imaging information into clinically actionable indicators that can be integrated into hospital-level prioritization systems.

Additionally, previous methodological work by Ela Burrull designed a stenosis quantification pipeline based on geometric formulations, serving as a technical reference for stenosis measurement from coronary artery geometries. This work demonstrated the feasibility of geometry-based stenosis quantification and provides a foundation upon which more robust, reproducible, and clinically integrated approaches can be built.

The present project positions itself as a bridge between these contributions, focusing on the robust quantification of coronary stenosis and on the transformation of geometric measurements into clinically meaningful indicators. In particular, this work aims to connect CCTA-derived geometric data with downstream tasks such as CAD-RADS support, visualization, and patient prioritization, contributing to a more integrated and interpretable CAD assessment pipeline.

Importantly, this project does not address coronary artery segmentation or labeling itself. Instead, it assumes that such inputs are available, either from previous work within the collaboration or through synthetic or proxy data generation when necessary. This assumption allows the project to concentrate on stenosis analysis, quantitative assessment, and clinical decision support, which constitute its core contributions.

1.7 Project Scope, Objectives, and Thesis Organization

The main objective of this Final Degree Project is to contribute to the automation and clinical support of coronary artery disease assessment through robust and interpretable stenosis quantification from CCTA-derived geometric data.

More specifically, the project aims to:

- Identify and obtain the geometric information required for stenosis quantification using open-source methodologies and reproducible workflows, or, when such data are unavailable, perform statistical analyses to generate representative synthetic data.

- Implement a stenosis quantification pipeline based on geometric formulations, with a focus on robustness and transparency.

- Analyze and aggregate stenosis measurements at point, segment, and vessel levels to produce clinically meaningful indicators.

- Support CAD-RADS assignment through quantitative measurements and exploratory machine learning approaches.

- Develop visualization tools that facilitate clinical interpretation and reduce decision-making time.

- Structure quantitative outputs to enable integration with patient prioritization systems used in clinical practice.

Machine Learning and Deep Learning techniques can be explored as supporting tools, particularly for stenosis quantification and CAD-RADS prediction. To address the limitations of black-box models, explainable artificial intelligence (XAI) methods can be applied to provide transparency at the patient level, helping clinicians understand how predictions or classifications are obtained. These explainability features can be integrated into

the visualization tool to enhance clinical interpretation and decision support. The emphasis of the project remains on supporting clinical decision-making rather than fully automating clinical judgment.

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