

# Enhanced Prioritization and Reporting for Coronary Artery Disease Diagnosis

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# Enhanced Prioritization and Reporting for Coronary Artery Disease Diagnosis

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*Better is possible. It does not take genius. It takes diligence.  
It takes moral clarity. It takes ingenuity.  
And above all, it takes a willingness to try.*

- Atul Gawande



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## Summary / Abstract

Coronary artery disease (CAD) remains a significant cause of mortality, particularly in industrialized nations, contributing to a significant portion of deaths worldwide. Timely diagnosis and treatment are critical for mitigating its high morbidity and mortality rates. However, current diagnostic protocols in hospitals often suffer from inefficiencies and lengthy processes.

This Bachelor's thesis aimed to optimize the CAD diagnosis workflow within the radiology department of Hospital de la Santa Creu i Sant Pau. The focus was on implementing methodologies for automatic case reporting and patient prioritization, specifically in the scheduling of coronary computed tomography angiography (CCTA) acquisitions and determining the order of CCTA reporting. This optimization was achieved in collaboration with clinical and technological experts from the institution. The implemented algorithms are rule-based, guided by clinical criteria from the literature and physicians. The prioritization of patients ensures that severe cases receive prompt attention, aiming to reduce diagnosis time. Additionally, the automatic generation of preliminary reports integrates clinical information and findings extracted from CCTA images through image analysis.

Implementing the optimized workflow for CAD diagnosis through simulation experiments demonstrated a potential reduction in diagnosis time for more severe cases and increased clinician satisfaction with the CAD diagnosis workflow and workload. This study highlights the transformative potential of automatic approaches in streamlining CAD diagnosis, offering promise for improved patient care outcomes in clinical practice.

## Keywords

Coronary Artery Disease (CAD), Coronary Computed Tomography Angiography (CCTA), Coronary Artery Disease Reporting and Data System (CAD-RADS), Automatic Reporting, Prioritization



## Preface or prologue

Cardiovascular diseases, including coronary artery disease (CAD), are a significant cause of mortality in industrialized nations, representing a substantial portion of deaths worldwide. Factors such as increased life expectancy, sedentary lifestyles, and poor dietary habits have contributed to CAD becoming one of the most prevalent diseases globally, with an approximate prevalence of 5% [1]. Additionally, CAD stands as the primary cause of death in industrialized nations, accounting for 30% of global mortality [2] [3]. Early diagnosis and treatment are crucial in mitigating the high morbidity and mortality associated with CAD [4]. However, the current diagnostic framework employed in hospitals is often lengthy and inefficient.

This Bachelor's thesis is part of a broader project aimed at optimizing processes within the radiology department of Hospital de la Santa Creu i Sant Pau in Barcelona (Spain) by implementing a comprehensive artificial intelligence (AI)-driven framework within the setting. This integrated system seeks to streamline the diagnostic process through automated image processing and analysis, patient prioritization, and reporting mechanisms. Specifically, this thesis focuses on the topics of patient prioritization and reporting to enhance CAD diagnosis via coronary computed tomography angiography (CCTA) images at Hospital de la Santa Creu i Sant Pau in collaboration with clinical and technological experts from the institution.

With an average of over 26 thousand patients for external cardiology consultations annually [5] and a waiting list currently comprising over 800 patients for cardiology consultations and over 480 for CT scans [6] [7], Hospital de la Santa Creu i Sant Pau could benefit from automating diagnostic processes, such as those for CAD. This approach could lighten clinicians' workload, allowing them to better allocate their efforts to assessing more severe and complex cases promptly.



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# 1 Introduction

## 1.1 Coronary artery disease diagnosis

### 1.1.1 Anatomy of the coronary arteries

The heart is the center of the cardiovascular system and is responsible for pumping blood through the entire body. Since the heart is a muscle, it also needs oxygen and nutrients. This supply is achieved through the heart's vascular system called the coronary tree. The coronary tree originates from the root of the aorta and consists mainly of two vessels; the right coronary artery (RCA) which supplies to the right atrium and ventricle, and the left coronary artery (LCA) which further divides into the left anterior descending artery (LAD) and the circumflex artery (Cx) which supply to the left atrium and ventricle [8].

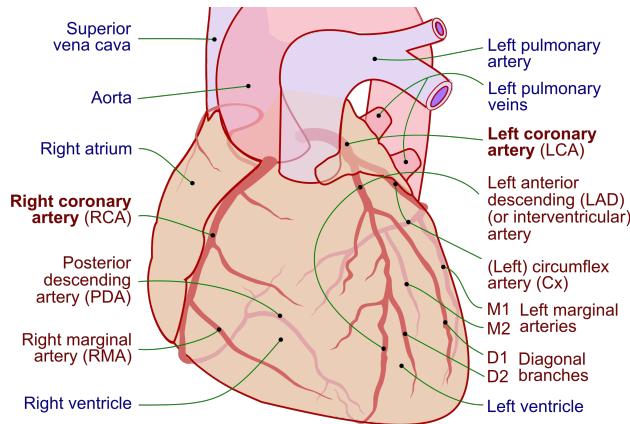


Figure 1: Representation of the anatomy of the coronary tree. Coronary arteries are labeled in red, and other structures in blue. From Patrick J. Lynch [9].

The anatomy of this network is divided into three dominances, determining the origin of arteries supplying the posterior and bottom parts of the heart, namely the posterior descending artery (PDA) and the descending posterolateral artery (PLA). Typically, the coronary tree's anatomy is characterized by right dominance (originating in the RCA), followed by left dominance (originating in the Cx), and codominance (originating in both the RCA and Cx).

However, the lack of interconnectivity in the coronary tree prevents the redirection of blood flow in the event of an obstruction. This reduced blood flow can induce myocardial ischemia, potentially resulting in myocardial infarction (MI) and subsequent tissue necrosis. Such arterial blockage characterizes Coronary Artery Disease (CAD).

### 1.1.2 Coronary artery disease

CAD is a complex condition influenced by genetic and environmental factors [10]. Risk increases with age and other aspects such as physical inactivity, obesity, unhealthy diet, smoking, diabetes, high low-density lipoprotein (LDL)-cholesterol, hypertension, and family history of cardiovascular issues [11]. In industrialized nations, CAD affects about 5% of the population [1] and is a leading cause of death, responsible for 30% of global deaths [2] [3]. CAD involves atherosclerotic plaque accumulation in coronary vessels,

leading to vessel narrowing, ischemia, and potentially severe complications like acute coronary syndrome (ACS) and MI. Calcium deposition in plaque serves as an early CAD indicator.

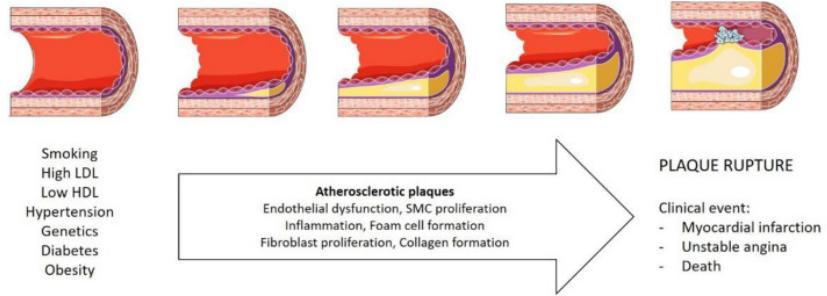


Figure 2: Coronary artery disease progression. LDL: low-density lipoproteins. HDL: high-density lipoproteins. SMC: smooth muscle cells. From G. Conceição, 2020 [12].

Some techniques for CAD diagnosis include invasive coronary angiography (ICA), X-ray imaging and contrast injection to visualize coronary lumen narrowing, intravascular ultrasound (IVUS), and optical coherence tomography (OCT) to assess the evolution of the coronary atherosclerotic plaque [13]. However, due to the notable invasiveness and associated risks of these techniques, an increasingly accepted non-invasive alternative for first-line CAD diagnosis is Coronary Computed Tomography Angiography (CCTA), employing contrasted CT (Computed Tomography) imaging to evaluate coronary arteries, measure vessel narrowing, and assess plaque composition and morphology. In line with advancing diagnostic practices, reference organizations such as the American College of Cardiology (ACC) and the American Heart Association (AHA) provide clinical guidelines for CAD diagnosis [14] (Figure 3). Moreover, there are standardized methods to facilitate the systematic reporting of CAD findings, such as the coronary artery calcium (CAC) scoring proposed by Agatston et al., 1990 [15], correlating the total coronary calcium with MI risk (Table 1), and CAD-RADS 2.0 (CAD Reporting and Data System) [16], stratifying patients based on the degree of luminal stenosis (Table 2). Enhanced versions of CAD-RADS may incorporate additional parameters like plaque burden, ischemia, and the presence of stents or grafts, thus allowing for a more comprehensive diagnosis.

Table 1: Degree of coronary artery calcification depending on absolute CAC scores and consequent clinical interpretations. CAC: coronary artery calcium. Adaptation from Neves et al., 2017 [18].

Absolute CAC score (Agatston method)	Degree of coronary artery calcification	Clinical interpretation
0	Absent	Very low risk of future coronary events.
1-100	Discrete	Low risk of future coronary events; low probability of myocardial ischemia.
101-400	Moderate	Increased risk of future coronary events (aggravating factor); consider reclassifying the individual as high risk.
>400	Accentuated	Increased probability of myocardial ischemia.

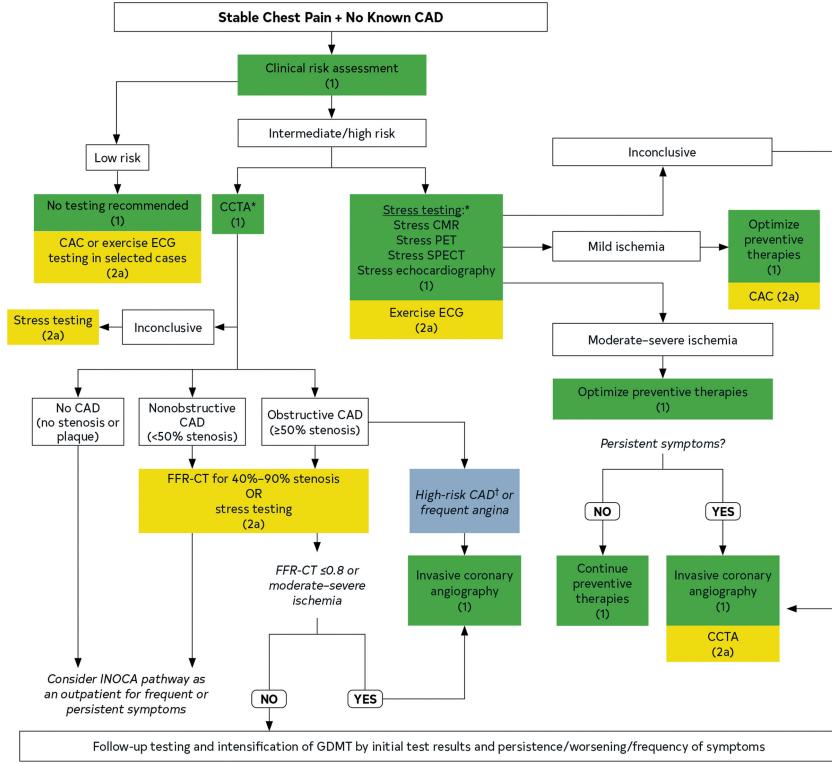


Figure 3: Pipeline for evaluating patients with stable chest pain and unknown CAD. CAD: coronary artery disease. CAC: coronary artery calcium. CT: computed tomography. FFR-CT: fractional flow reserve CT. ECG: electrocardiogram. CCTA: coronary CT angiography. ICA: invasive coronary angiography. GDMT: guideline-directed medical therapy. CMR: cardiovascular magnetic resonance imaging. INOCA: ischemia and no obstructive coronary artery disease. PET: positron emission tomography. SPECT: single-photon emission CT. From Gulati et al., 2021 [17].

## 1.2 Current radiology workflow for CAD

The methodology for acquiring CCTA patient images varies based on clinical cases and hospital protocols. Hospital de la Santa Creu i Sant Pau follows standard guidelines with minor differences, managed by a specialized unit for cardiac imaging named Unitat d’Imatge i Funció Cardiaca (UIFC). Images are stored in the hospital’s PACS (Picture Archiving and Communication System) for subsequent processing and evaluation by Cardiac Imaging Experts. However, this process, alongside the high volume of images, creates a bottleneck in diagnosing CAD and detecting severe cases due to its manual and lengthy nature.

Various methods are employed to prioritize patient evaluation, yet these approaches lack standardization and demonstrate variability among clinicians. The assignment of priority does not consistently favor more severe cases. Additionally, around 65% of cases exhibit CAD-RADS levels indicating no significant stenosis (0 or 1), resulting in reduced urgency in reporting<sup>1</sup>. In contrast, timely diagnosis and reporting are critical for cases with high CAD-RADS levels indicating severe conditions. This distribution highlights that Cardiac Imaging Experts allocate considerable resources to evaluating non-severe cases rather than prioritizing more critical scenarios.

<sup>1</sup>Data from UFC statistics at Hospital de la Santa Creu i Sant Pau from 2013 to 2022.

Table 2: CAD Reporting and Data System. CAD: coronary artery disease. CAD-RADS: CAD reporting and data system. LCA: left coronary artery. Adaptation from Canan et al., 2020 [19].

CAD-RADS Category	Interpretation	Degree of Maximal Coronary Stenosis
0	Absence of CAD	0%, neither plaque nor stenosis
1	Minimal CAD	1%-24%, minimal stenosis or plaque without stenosis
2	Mild CAD	25%-49%
3	Moderate stenosis	50%-69%
4A	Severe stenosis	One or two vessels, 70%-99%
4B	Severe stenosis	LCA >50% or three vessels $\geq 70\%$
5	Total occlusion	100%
N	Obstructive CAD cannot be excluded	Nondiagnostic

### 1.3 AI in healthcare

#### 1.3.1 Importance of AI in radiology departments

Artificial intelligence (AI) has the potential to revolutionize several fields, including medicine, by automating labor-intensive and time-consuming processes like CAD diagnosis. Although it is unlikely that AI will replace healthcare professionals, it can represent a substantial enhancement and aid in healthcare efficiency and diagnosis. For example, in the cardiac imaging workflow, several algorithms have been developed in different applications, such as classification, automatic quantification, informing, diagnosis, and risk prediction [20]. Specific examples of the implementation of AI in cardiac imaging under a clinical environment are found in Figure 4.

In literature, work has been done regarding patient stratification and prioritization, such as Rowan et al., 2007 [21], which proposed using Artificial Neural Networks (ANNs) to predict the risk of experiencing morbidities and consequently having an extended stay in the intensive care unit of postoperative cardiac patients. Yan et al., 2017 [22] proposed using k-means clustering for stratifying heart failure patients according to their risk of readmission to the hospital due to comorbidities. Moreover, there is also research on further steps of the cardiac imaging workflow, such as in case reporting. As part of the MAIRA research project from Microsoft Health Futures, Liu et al., 2023 [23] evaluated the capability of large language models (LLMs), specifically GPT-4, for generating radiology reports, comparing favorably with other models in the literature. Additionally, Bannur et al., 2024 [24] employed the large multimodal model MAIRA-2, integrating an LLM with a visual encoder, to generate reports based on extracted findings from X-ray images. Although there is work investigating the optimization of CAD diagnosis (Gabriel et al., 2023 [25]), there is no known study focused on the optimization of CAD diagnosis through patient management in every step of the pipeline.

On the other hand, the integration of AI in clinical settings presents challenges [26]. Generalizing models to diverse populations can pose problems, adequate data labeling

and re-training are continually needed to ensure accuracy, user-friendly interfaces are key for clinical adoption, and secure data handling and logistic constraints, such as data storage, limit AI implementation. To summarize, the successful use of AI to improve patient care requires addressing several technological, logistical, and human concerns.

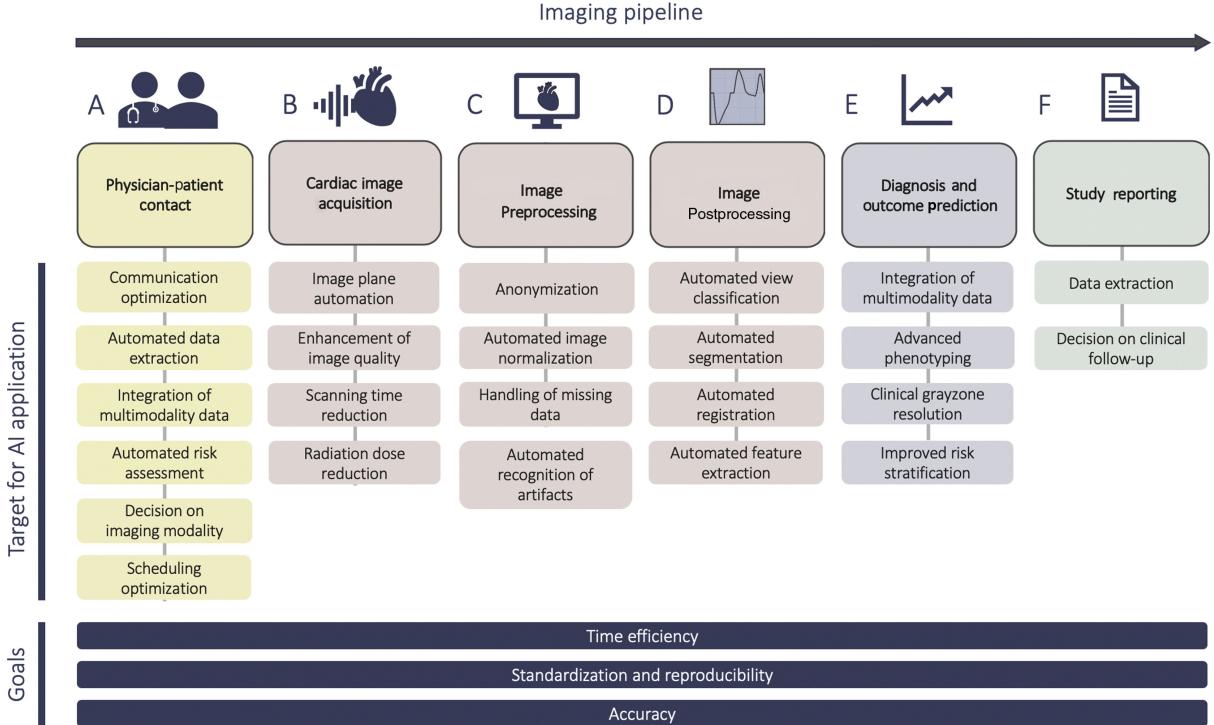


Figure 4: The pipeline shows several steps of the cardiac imaging workflow and specific areas for AI implementation. AI: artificial intelligence. From Loncaric et al., 2021 [20].

### 1.3.2 State of the Art: Implementation of AI for CAD diagnosis

For those reasons, a breakthrough in this field would be the implementation of a comprehensive AI-driven workflow that could automate and standardize the CAD diagnosing process, as well as improve its efficiency and accuracy. With this goal, Acebes, 2023 [27] proposed a series of objectives to enhance this process from CCTA images. For this, the workflow that he proposed encompasses automated image processing (such as segmentation, post-processing, and quantification), patient prioritization, and reporting mechanisms.

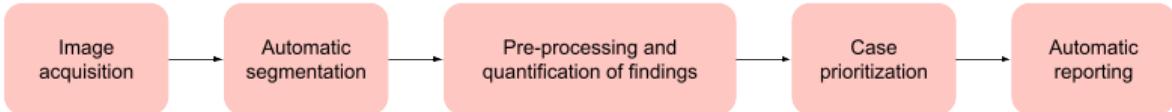


Figure 5: AI-driven pipeline to be implemented in the UIFC of a hospital in the specific case of diagnosing CAD from CCTA images. AI: artificial intelligence. UIFC: Unitat d'Imatge i Funció Cardiaca. CAD: coronary artery disease. CCTA: coronary computed tomography angiography. Adaptation from Acebes, 2023. [27]

Tasks such as coronary automatic segmentation have been studied in the context of undergraduate and master theses between Universitat Pompeu Fabra and Hospital del Santa Creu i Sant Pau through the use of nn-UNet (Acebes, 2021 [28]), UNETR (Sanchez, 2022 [29]), and the MONAI platform (Treserres, 2023 [30]). Furthermore, El Emrani, 2023 [31] proposed a methodology to create a clinically validated database that combined the patients' demographic and clinical data with the images of their studies. However, the automated segmentations obtained by these means until now are not sufficient. So far, only lumen segmentations have been obtained, but to properly assess CAD, vessel wall, plaque, and labeling should also be correctly identified. Moreover, results from previous works presented problems segmenting smaller vessels, which could also hinder subsequent analysis steps. Despite all these advances regarding CCTA automatic finding extraction, there has been no work yet exploring further steps such as case prioritization and automatic reporting.

Apart from this context, automatic coronary artery segmentation and analysis have been implemented in commercial software tools aimed at aiding clinicians in diagnosing CAD. Examples include syngo.via [32] used at Hospital de la Santa Creu i Sant Pau, Cleerly® ISCHEMIA™ [33] for evaluating CCTA findings to determine the risk of coronary artery ischemia, and Artrya Salix [34] for helping clinicians identify and analyze the extent and type of arterial plaque from CCTA images. However, despite their utility, these commercial solutions often operate as black-box AI software, which can pose challenges in transparency and explainability and may not seamlessly integrate with existing hospital infrastructure.

## 1.4 Objectives

In this regard, the primary objective of this project is to propose a theoretical workflow to aid clinicians in optimizing the CAD assessment process. This thesis aims to automatically prioritize patients, ensuring that severe cases are addressed first, thus enabling clinicians to allocate their efforts efficiently for timely patient care. Additionally, the project seeks to generate structured automatic preliminary case reports based on the patient's clinical data and findings derived from CCTA images. This approach aims to reduce clinicians' workload by eliminating manual annotation, requiring only the validation of preliminary reports generated against CCTA images.

To achieve this, specific intermediate objectives include understanding and characterizing the CAD diagnosis workflow at Hospital de la Santa Creu i Sant Pau, and the design and implementation of an initial version of a visualization platform that integrates this optimized solution, to be presented to clinicians for their feedback and validation.

The effectiveness of the main objective will be assessed by measuring the potential reduction in diagnosis time for severe cases and the improvement in clinician workload. It should be noted that the project will focus exclusively on prioritization and reporting tasks within the workflow, assuming that the results from preceding steps, such as image analysis, have already been obtained.

## 2 Methods

To achieve the main goal of optimizing the CAD diagnosing workflow, the PDCA (Plan-Do-Check-Act) cycle was used as a framework [35]. This methodology aims for the continual improvement of processes by breaking them down into pieces and iteratively improving each one. The PDCA cycle consists of 4 steps: analyzing the problem and planning a solution for it (Plan), implementing the said solution (Do), studying its effectiveness (Check), and taking the necessary actions based on the findings obtained (Act).

### 2.1 Plan

#### 2.1.1 Investigation of the problem

As previously mentioned, the CAD diagnosing workflow at Hospital de la Santa Creu i Sant Pau is complex. It does not follow a specific standard, making it difficult to study the process's problems since it is subject to inter- and intra-user variability. However, through a thorough field investigation, the current workflow was defined, as seen in Figure 6.

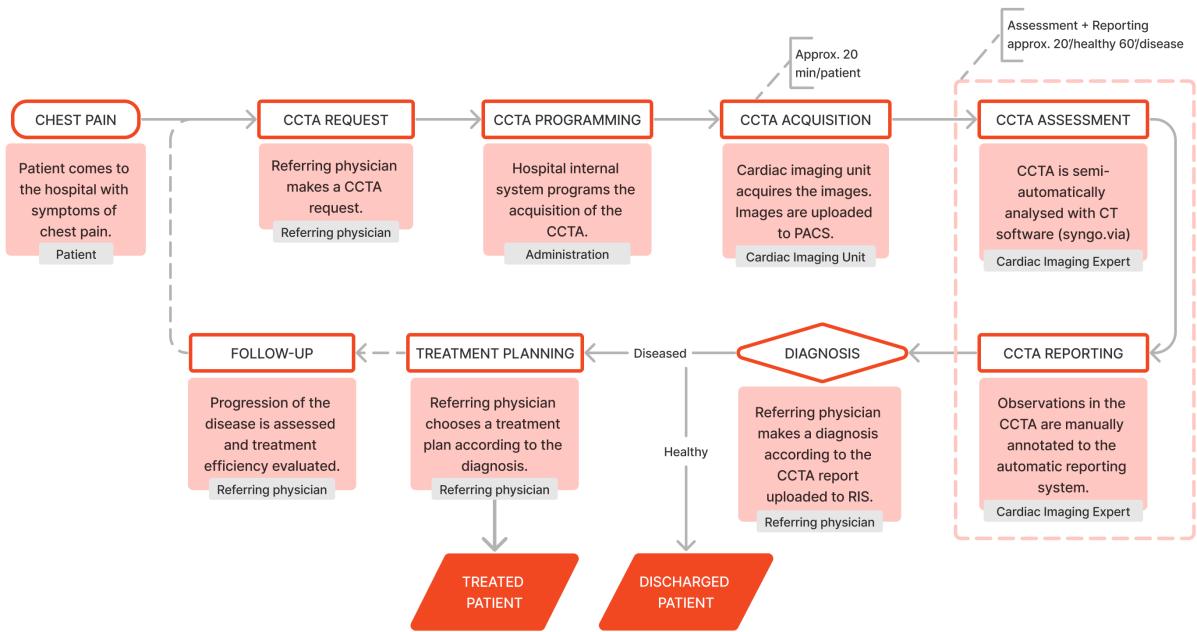


Figure 6: Representation of the current CAD diagnosing workflow in Hospital de la Santa Creu i Sant Pau. CAD: coronary artery disease. CT: computed tomography. CCTA: coronary CT angiography. PACS: picture archiving and communication system. RIS: radiology information system. Diagram following the ANSI/ISO standards [36].

Patient consultations originate from various sources. Direct referrals come from general practitioners when patients exhibit symptoms or from Emergency Rooms (ER) in cases of acute symptoms. Patients may also attend follow-up appointments, typically if they have a history of heart disease. Additionally, referrals can come from other specialties or for pre-surgery tests. When a patient is directed to the cardiology department with symptoms of chest pain or suspicion of heart disease, the cardiologist requests a CCTA study through the hospital's management system. The scheduling of the acquisition is managed by the administration of the UIFC, aiming to schedule it as soon as

possible, while also considering the availability of infrastructure and personnel. If there is no obvious reason to prioritize a case (for example, if the patient exhibits acute chest pain), the acquisition of images is scheduled without a specific order.

For patients suspected of having CAD, image acquisition occurs on a scheduled basis twice a week in the early morning. Additionally, urgent cases from the emergency department are accommodated without prior scheduling. Each session, lasting around 2 hours, allows for image acquisition from around 5 patients. An imaging technician, supervised by a Cardiac Imaging Expert, conducts this process for which, currently, the SOMATOM Force by Siemens Healthineers [37], equipped with 384 (2x192) slices, is utilized.

The specific tests performed may vary based on the patient's condition and medical requirements but typically involve a contrast-enhanced CT examination of the coronary arteries to assess vessel anatomy. On average, the acquisition process takes about 24 minutes per patient, depending on the types and quantity of tests conducted. After acquisition, the images are stored in the hospital's PACS, and acquisition details are manually introduced by the technicians into the Cardiac Imaging database, which already contains the patient's clinical and demographic information.

Upon viewing the images during acquisition, the Cardiac Imaging Expert prioritizes reporting on cases that initially appear more complex. The semi-automated reporting of CCTA involves image analysis using the commercial software tool syngo.via [32], which simplifies the diagnostic process by incorporating advanced tools and algorithms. While CCTA studies primarily focus on coronary vessels, the Cardiac Imaging Expert evaluates all visible structures with the software's assistance. The evaluation begins with extracardiac findings, followed by an examination of cardiac structures such as the aorta, cardiac valves, and coronary vessels. The software tool aids in analyzing coronary vessels, facilitating the visual inspection of narrowings and calcifications, and generating segmentations and curved multiplanar reformations (cMPR) to assess vessel stenosis. This information is manually entered into the Cardiac Imaging database, which automatically generates the corresponding report using a template. The report is then uploaded into the Radiology Information System (RIS). Image analysis is time-consuming, taking a minimum of 20 minutes for a healthy patient and up to an hour for those with more severe findings, such as stenosed vessels, plaque accumulation, calcium deposits, and other significant anomalies.

Once the case report is completed, the referring clinician promptly schedules an appointment with the patient as necessary, based on the report's findings. Using the information from the images, the clinician determines the next steps, including whether additional tests are required or if specific treatment is necessary. Depending on the report's results, the clinician decides whether the patient needs further follow-up, which may involve regular check-ups, periodic CCTA acquisitions and analysis, and/or additional tests.

The CAD diagnosing workflow presents a complex and time-consuming process, exemplified by the operational challenges faced at Hospital de la Santa Creu i Sant Pau. Annually, the hospital handles a substantial load of over 26 thousand external cardiology consultations [6]. This influx significantly burdens the cardiology department, leading to

a waiting list of over 800 patients awaiting consultations, with an average wait period of over 120 days [5]. Furthermore, the demand for CT acquisitions is similarly strained, with over 480 patients queued and an average wait time of 39 days [7]. Therefore, to address the inefficiencies of this workflow, the *5 Whys* technique was used, an iterative approach to uncovering root causes through cause-and-effect analysis [38]. From this analysis (Figure 7), the root cause was the lack of prioritization for image acquisition, assessment, and case reporting.

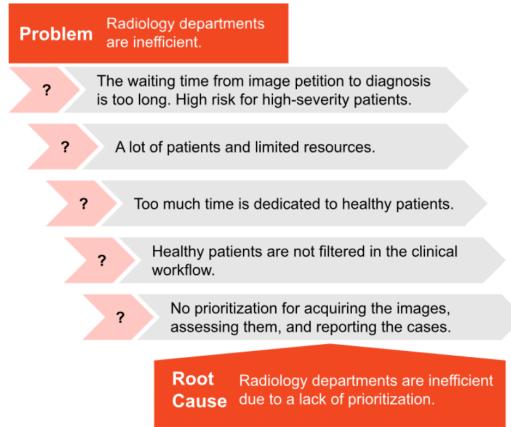


Figure 7: *5 Whys* analysis of the inefficiencies problems of the Coronary artery disease diagnosis workflow. The analysis starts with the inefficiencies of radiology departments and reaches the lack of prioritization as the root cause.

### 2.1.2 Planning of a solution

To solve the aforementioned problem, the following solution plan was generated:

- Prioritize patients before image acquisition so the more severe cases are acquired first.
- Filter unsuitable patients to undergo coronary automatic segmentation and analysis because they have some procedure such as stents or bypasses, or because the image quality is deficient, and therefore, have to be manually assessed.
- Automatically generate preliminary case reports from the clinical information of the patient and the one obtained from the image analysis and prioritize the more urgent cases so their reports can be assessed first by a clinician.

## 2.2 Do

To achieve an optimized process, the proposed solution plan was tested theoretically within the framework of the global CAD diagnosis workflow, as shown in Figure 8. The steps outlined in the solution plan are represented in purple and are further explained below. All these processes were coded using the programming language Python version 3.11.5 [39]. All the code for the implementation described can be found in this Repository ([https://github.com/01ferrereva/BT-23\\_24](https://github.com/01ferrereva/BT-23_24)).

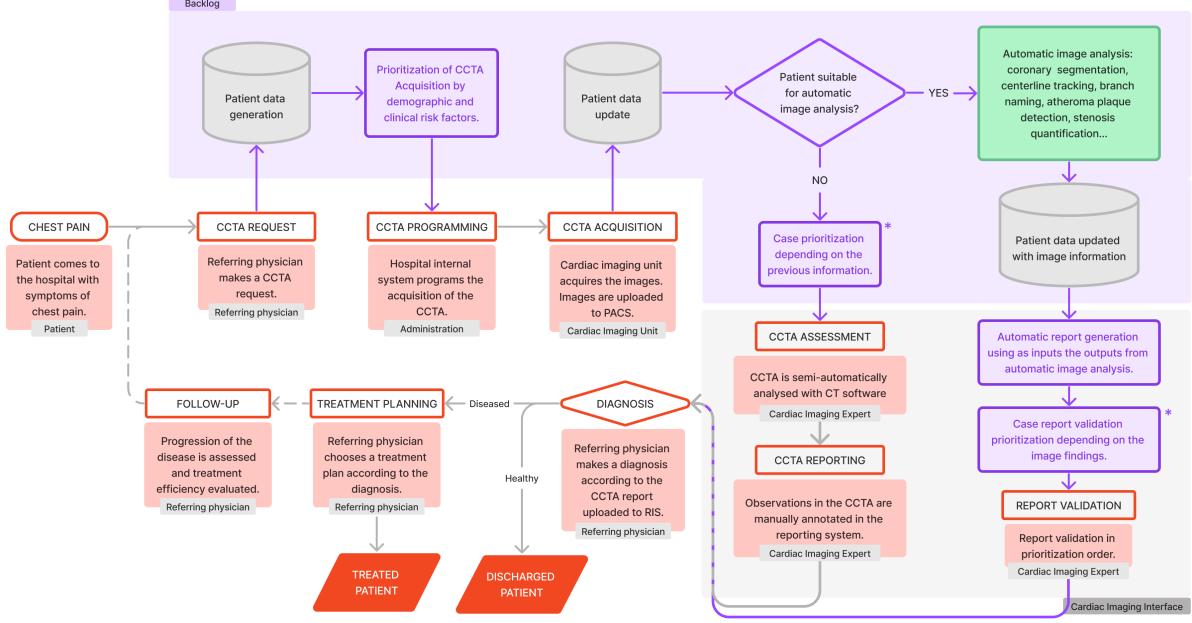


Figure 8: Representation of the proposed solution plan theoretically tested in synthetic data within the framework of the current Coronary Artery Disease (CAD) diagnosis workflow at Hospital de la Santa Creu i Sant Pau. Red boxes represent the existing CAD diagnosis workflow steps, gray cylinders represent patient databases, purple boxes indicate the proposed steps for optimizing the current workflow to be implemented in this project, and the green box represents the automatic image analysis algorithm, which is part of the proposed optimization but is outside the scope of this project. The light purple panel shows the processes running in the background, while the light gray panel indicates the processes to be integrated into the interface described in Section 2.2.5. (\*) Methodologies corresponding to the prioritization of report validation or generation. The diagram follows ANSI/ISO standards [36].

### 2.2.1 Database generation

A synthetic patient database was established to systematically test subsequent workflow steps, encompassing all necessary information to execute the generated algorithms (Table 3). This database started with fundamental clinical and demographic patient data provided in the original workflow by the referring physician through the hospital’s management system. Additionally, it included a unique identifier, typically generated automatically by the hospital’s system, and the scheduled order for CCTA acquisition and reporting, typically managed by UIFC administration. After the CCTA acquisition, the synthetic database was updated with technique details recorded in the original workflow by the CT acquisition technicians. Following image analysis (Section 2.2.4), image findings were incorporated into the database. These findings are currently annotated by reporting physicians as detailed in Section 2.1.1. All synthetic data generated adhered to medical standards and aligned with incidence rates derived from the Cardiac Imaging database, accurately reflecting the hospital’s patient population.

### 2.2.2 Prioritization of image acquisition

The patients from the created database requiring a CCTA acquisition were prioritized based on a higher probability of having CAD. The first method used to achieve this was the Framingham Risk Score (FRS), which is an empirical algorithm that calculates

the percentage of the 10-year cardiovascular risk of a person. The FRS is based on the Framingham Heart Study [40], which is an ongoing long-term cardiovascular study, and it was validated in the US. Because the study was performed in the US mainly in European Americans and African Americans, the FRS could over/underestimate risk in other populations or ethnicities. The algorithm implemented for the image acquisition prioritization corresponds to the version created in 2008, which rules can be found online [41]. Because of the biased results of this algorithm toward US populations, the prioritization method was changed to REGICOR [42], which consists of the FRS-calibrated equation to adapt to the Spanish population (explained in Annex 2). However, based on clinical recommendations, the methodology was changed to the Pre-test Probability of CAD [43]. This method determines the likelihood of a patient having CAD based on chest pain symptoms before any diagnostic tests are performed (further detailed in Annex 2). Subsequently, patients were ordered for image acquisition based on the descending probability of CAD.

Table 3: Information from the generated synthetic database along the different steps of the workflow. CCTA: coronary computed tomography angiography. CAC: coronary artery calcium.

Initial information at the moment of consultation	Patient identification	Unique 6-digit patient identifier (following the format used in the Hospital de la Santa Creu i Sant Pau)
	Scheduled order	Random initial order for CCTA acquisition and reporting (nº between 1 and n, where n is the total number of patients)
	Demographic information	<ul style="list-style-type: none"> <li>- Sex</li> <li>- Age</li> <li>- Whether the patient smokes</li> <li>- Clinical data</li> <li>- Motive of consultation</li> <li>- Type of chest pain (typical/atypical/non-specific)</li> <li>- Diabetes</li> <li>- Hypertension</li> <li>- Dyslipidemia</li> <li>- Whether the study was marked as urgent</li> <li>- Whether the patient has undergone previous medical procedures such as stents, grafts, ...</li> </ul>
Information after CCTA acquisition	Technique information	<ul style="list-style-type: none"> <li>- Image quality (good, adequate, or deficient)</li> <li>- Acquisition limitations such as artifacts</li> </ul>
	Image analysis information	<ul style="list-style-type: none"> <li>- Coronary tree dominance (right, left, or codominant)</li> <li>- Stenosis degree range by segment</li> <li>- CAC score</li> </ul>

### 2.2.3 Filtering for suitability for image analysis

The image analysis workflow may encounter limitations in cases with poor image quality, the presence of structures such as stents or grafts, or movement artifacts, which can render the results unreliable. Consequently, cases in the synthetic database identified as unsuitable for image analysis based on prior information were categorized as non-evaluable, requiring manual evaluation instead. Therefore, patients were filtered based on information obtained both before and after CCTA acquisition, including details regarding

previous procedures, image quality, and acquisition limitations. Information regarding previous procedures, sourced from electronic health records (EHRs), and details about image quality and artifacts, are recorded in the Cardiac Imaging database. However, for testing purposes, the aforementioned synthetic database (Section 2.2.1) was utilized to evaluate this methodology.

#### 2.2.4 Information obtained by image analysis

Information derived from the CCTA images was synthetically generated, and details are summarized in Table 3, encompassing the degree of vessel stenosis and the presence of calcium deposits. This image-derived information, in the ideal pipeline, should be automatically extracted, for instance, through an AI-based algorithm, which is not yet developed and falls outside the scope of this Bachelor's Thesis.

#### 2.2.5 Automatic preliminary case report generation

Following the theoretical extraction of CCTA findings from suitable patients, this image information, along with clinical patient data, was utilized to generate a preliminary case report. The report generated included information such as the dominance of the coronary tree, the stenosis degree ranges for each coronary segment, the CAD-RADS, and the CAC score range, along with other clinical data. For unsuitable patients unable to undergo automatic image analysis, the report included only clinical information. This combined clinical and image data was presented to clinicians in a written report, automatically inserting all corresponding information into the reporting template currently employed at Hospital de la Santa Creu i Sant Pau (refer to Annex 3).

#### 2.2.6 Prioritization of report assessment

Clinical data and simulated information from CCTA images (limited to suitable patients) were also used to prioritize preliminary case reports for assessment by the Cardiac Imaging Expert. Various methodologies were tested to achieve this prioritization, with scoring systems generated to stratify patients as effectively as possible based on the evaluated characteristics (Table 4).

Table 4: Progression and iterations of the prioritization methodologies for preliminary case report validation. Max.: maximum. CAD-RADS: coronary artery disease reporting and data system. CACs: coronary artery calcium score.

	Method 1 (0/1)	Method 2 (0-5)	Method 3 (0-5)	Method 4 (0-7)
Max. stenosis >50%	+1			
CAD-RADS ≥3		+3	+3	+CAD-RADS value
Non-evaluable vessel		+1		
Non-evaluable critical vessel		+1		
Accuracy of stenosis result <30%			+1	
CACs >100			+1	+1
Critical vessels with stenosis >50%				+1

The first prioritization method proposed involved classifying the patients based on whether they had a maximum stenosis degree of more than 50% following clinical instructions. Patients above this threshold were classified as urgent for validation, while

the remaining patients were classified as non-urgent.

The second method assumed the image analysis algorithm could extract maximum stenosis degrees for each vessel to calculate CAD-RADS. It also accounted for the possibility of the algorithm failing to produce results due to inaccurate segmentation or analysis outcomes. Prioritization was based on a scoring system ranging from 0 to 5, where 0 indicates non-urgent and 5 denotes the most urgent cases, following clinical guidelines. This scoring allocated 3 points to patients with CAD-RADS 3 and higher. An additional point was given to patients with non-evaluable vessels, and another point was added if these vessels included critical arteries (LCA, LAD, Cx, and RCA). This method was enhanced by incorporating the algorithm's capability to extract coronary tree dominance.

Unlike the second method, the third method assumed the image analysis could provide a stenosis degree for all vessels, alongside the accuracy of those results, and directly extract the CAC score from CCTA. In this approach, prioritization included adding a point for patients with a CAC score over 100 and an additional point for those with a critical vessel having a stenosis accuracy under 30%.

In contrast, the fourth method assumed the automatic image analysis could estimate stenosis degrees for each vessel within ranges to account for result uncertainty rather than providing precise accuracy. Here, patients were scored on a scale from 0 to 7 based on their CAD-RADS value (CAD-RADS over 2 scored accordingly, and 0 if lower). Additional points were given for a CAC score over 100 and critical vessels with a stenosis degree over or equal to 70%.

### Final prioritization methodology

Finally, following clinical recommendations, patients were prioritized based on specific criteria (Table 5). Initially, patients were classified into four priority groups.

- Critical priority was assigned to patients with stenosis  $\geq 70\%$  in critical coronary segments (p-RCA: proximal RCA, m-RCA: medial RCA, p-Cx: proximal Cx, p-LAD: proximal LAD, m-LAD: medial LAD, and LCA).
- High-priority cases were subdivided into two: patients with pre-existing coronary disease who had a stent or a bypass, and patients with a CAD-RADS over 3.
- Medium-priority cases were subdivided into two groups: patients theoretically processed through the automatic image analysis workflow with CAD-RADS of 3, and patients unsuitable for the automatic image analysis workflow.
- Low priority was assigned to patients with CAD-RADS values of 0, 1, or 2.

Additional parameters, such as CAC score, pre-test probability of CAD, the severity of the consultation's motive, and whether the request was urgent, were used for further prioritization if necessary. This method effectively segmented patient groups for optimal prioritization. Additionally, the methodology aimed to alert clinicians based on prioritization criteria, prompting immediate actions such as requesting a CCTA reacquisition for studies with suboptimal image quality.

Table 5: Final prioritization methodology. Example of the classification of 15 synthetic patients into 4 groups: Critical priority, High priority, Medium priority, and Low priority. Further division of patients sequentially by CAD-RADS value, CACs, pre-test probability of CAD, severity of consultation motive, and urgency of the study request. Gray cells indicate patients who have not yet been fully subclassified. CAD-RADS: coronary artery disease reporting and data system. CACs: coronary artery calcium score. ACS: acute coronary syndrome. CAD: coronary artery disease. ECG: electrocardiogram.

Priority Group	1.Stenosis $\geq 70\%$	2.CAD-RADS	3.Prev. proc.	4.CACs	5.Pre-test (%)	6.Consultation Motive	7.Urgent	Output Order
Critical	YES	4B	-	349	31	Suspected ACS	NO	1
Critical	YES	4B	-	101	40	No information	NO	2
Critical	YES	4A	-	79	37	Chest pain	YES	3
High	NO	-	Stent	-	28	Revascularized CAD	NO	4
High	NO	5	-	403	45	Chest pain	NO	5
High	NO	4A	-	254	67	Chest pain	YES	6
Medium	NO	3	-	121	59	CAD screening	NO	7
Medium	NO	-	-	Excessive calcium	41	Coronary calcification study	NO	8
Medium	NO	-	-	-	68	CAD screening	NO	9
Medium	NO	-	-	-	46	Chest pain	YES	10
Low	NO	2	-	8	21	CAD screening	NO	11
Low	NO	1	-	12	31	Coronary vein study	NO	12
Low	NO	0	-	0	0	ECG alteration	NO	13
Low	NO	0	-	0	0	Coronary vein study	YES	14
Low	NO	0	-	0	0	Coronary vein study	NO	15

### 2.2.7 Interface mockup

When creating medical software tools meant to interact with clinicians, it is crucial to create an intuitive user interface, even if the software mostly runs in the background. It makes the interpretation of the software results easier and allows for intuitive report validation by clinicians. It also simplifies interaction, encourages adoption, and cultivates efficient communication between physicians and the software, ultimately improving patient care and clinical results.

This interface mockup was designed using Figma [44] and developed through the PyQt library in Python [45] (details in Annex 4). The interface addresses various processes within the CAD diagnosis workflow. Firstly, it allows referring physicians to log into their sessions and search for or enter patient information. It also facilitates UFC administration by enabling visualization of the proposed order for CCTA acquisition and understanding the rationale behind it, aiding in the scheduling of acquisitions. Lastly, it streamlines the workflow for Cardiac Imaging Experts by allowing them to log into their session, view the prioritization order of patients, and understand the reasoning behind it. Cardiac Imaging Experts can then select patients from their work list to validate preliminary case reports generated by the automatic image analysis workflow or create case reports for patients unsuitable for automatic analysis. This mockup resembles the currently used Cardiac Imaging database, which presents the reporting physician with demographic and clinical information (non-modifiable), and, if applicable, the information theoretically extracted from the automatic image analysis. The stenosis degree for each segment is what the Cardiac Imaging Expert must correct or complete. To evaluate

this, a prototype visual support window was designed to aid the Cardiac Imaging Expert in reporting findings. As a mockup, it pretends to demonstrate viability with limitations, using data from pre- and post-processed images from the public ASOCA database [46] and the hospital’s database. It displays the CCTA image with options to overlay the coronary arteries segmentation, a 3D reconstruction of the coronary tree, and the vessels’ cMPRs from a preset group of images.

## 2.3 Check

### 2.3.1 Clinical assessment: prioritization and reporting methodologies

To assess the clinical effectiveness of the prioritization strategy, clinical feedback was collected using a template based on the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Case Reports [47]. This template evaluates the implementation of the optimization algorithm qualitatively and semi-quantitatively (refer to Annex 5). On the other hand, validating preliminary case reports by radiologists is crucial for two primary reasons: ensuring accurate diagnosis and providing feedback to enhance the performance of automatic algorithms. Thus, the interface described in Section 2.2.5, through which radiologists review and correct preliminary case reports, was evaluated by clinicians via a feedback form outlined in Annex 5. Both evaluations were conducted by two Cardiac Imaging Experts from Hospital de la Santa Creu i Sant Pau.

### 2.3.2 Effectiveness appraisal

To demonstrate the achievement of the goal of optimizing the CAD diagnosis workflow, two key indicators were assessed: the potential reduction in diagnosis time for severe cases and the impact on clinician workload. Severe cases were defined as those with a CAD-RADS  $\geq 3$ . The first indicator was evaluated by comparing the time from consultation to image acquisition and from image acquisition to diagnosis for severe cases in the current diagnosis method versus a potentially optimized workflow. The second indicator measured clinician satisfaction with workload under the optimized workflow compared to the current process. Results were obtained from the optimization assessment template and by surveying clinicians about their satisfaction. Further details on this validation process can be found in Annex 6.

## 2.4 Act

### 2.4.1 Testing of the optimization workflow with synthetic and hospital data

The steps outlined in Section 2.2 were tested using synthetic and hospital data. Initially, a synthetic cohort of 15 patients was created and prioritized for CCTA acquisition based on their higher probability of CAD. For patients suitable for automatic image analysis, image findings were generated, which were used together with clinical information to rank all patients by severity for evaluation by the Cardiac Imaging Expert. This clinical and image information was presented in an automatically generated report.

For testing with hospital data, patient information from the hospital’s database was used. Two groups of patients scheduled for CCTA acquisition and reporting on different

days (5 patients per day) were included. In this case, only the ordering of CCTA acquisition and reporting was tested.

#### 2.4.2 Implementation of workflow into the hospital's infrastructure

The feasibility of implementing the proposed workflow for CAD diagnosis should be theoretically evaluated in a large-scale scenario, specifically at Hospital de la Santa Creu i Sant Pau. This evaluation should consider limitations regarding infrastructure, regulations (refer to Annex 1), and other factors critical to the successful integration of the workflow into the hospital environment.

Firstly, the integration of this solution should be evaluated against the current hospital infrastructure. According to ongoing work (as of June 2024) by Tomàs [48], a student at UPF, concerning the hospital's infrastructure, the clinical practice workflow follows the diagram in Figure 9, where patient data may originate from clinical or radiological sources and are stored in a results center database or the hospital's PACS, respectively. This data, along with RIS (Radiology Information System) information, is typically required for assistive software such as the one proposed in this Bachelor Thesis.

As there is no existing infrastructure dedicated to these software solutions, Tomàs proposes a new infrastructure ('Computational Server') to integrate these algorithms and data, generating outputs that can be stored similarly in other hospital databases. This approach could facilitate the implementation of the optimization pipeline within the hospital's existing infrastructure.

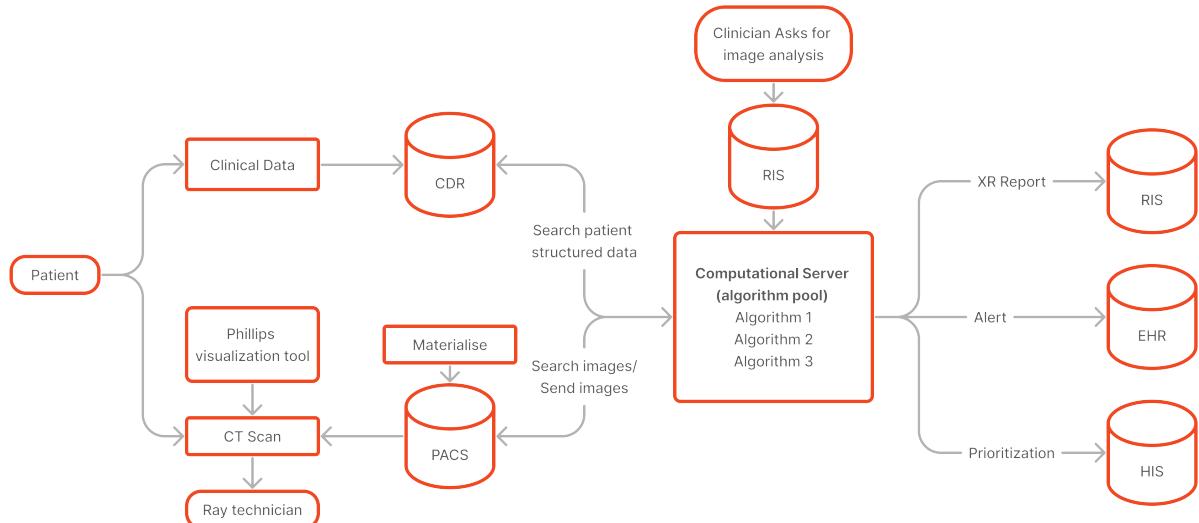


Figure 9: Adaptation of Tomàs diagrams representing the workflow of the clinical practice in the hospital and the infrastructure involved. CDR: clinical data repository. HIS: hospital information system. CT: computed tomography. PACS: picture archiving and communication system. RIS: radiology information system. EHR: electronic health record.

## 3 Results

### 3.1 Final optimized CAD diagnosis workflow implementation

The primary outcome of this project is the design and evaluation of an optimized workflow for diagnosing CAD. This final implementation orders the acquisition of CCTA images for a group of initial patients and establishes criteria to identify cases unsuitable for automatic image analysis due to unfavorable characteristics. Patients meeting suitability criteria (Section 2.2.3) undergo image analysis, which, along with clinical data, fills the automatic case report system. Conversely, patients not qualifying for the automatic image analysis have the case report system filled only with clinical information, with image-related data manually entered by the reporting clinician. From both clinical and image data, a prioritized list of patients is generated to guide clinicians in assessing the more severe cases first.

In summary, this project produced an algorithm that takes the clinical information of a pool of patients as input and produces a prioritization list for CCTA image acquisition (Figure 10).

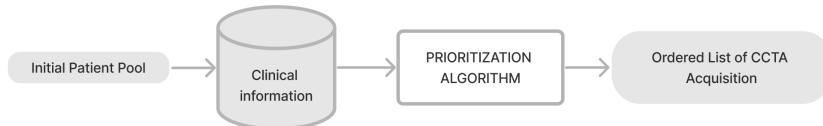


Figure 10: Diagram of the resulting implementation for generating an ordered list by priority of CCTA image acquisition from a group of patients and their clinical information. CCTA: coronary computed tomography angiography.

Additionally, it established a process for automatically generating preliminary case reports and ordered reporting worklists from synthetic patient clinical data and CCTA images (Figure 11).

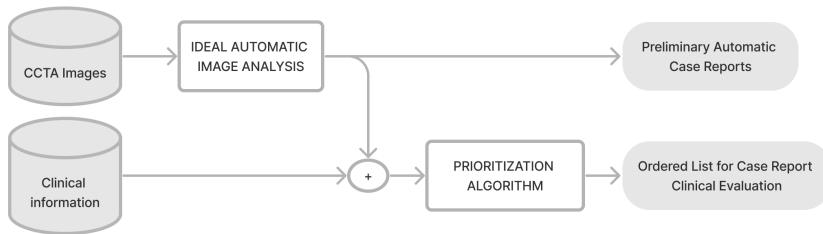


Figure 11: Diagram of the resulting implementation for automatically generating preliminary case reports for each patient and an ordered list of the cases to be assessed by the reporting clinician from patients' clinical and image-derived data. CCTA: coronary computed tomography angiography.

As described in Section 2.4.1, these algorithms were tested using both the synthetic database mentioned in Section 2.2.1 and real hospital data from patients scheduled for CCTA acquisition and assessment on two different days.

### 3.1.1 Results from prioritization of CCTA acquisition

#### Results from synthetic data

The results from the synthetic database show that the algorithm effectively orders patients by descending probability of CAD (Figure 12). These changes in patient order compared to the previous schedule (shown in brackets in the ‘Order’ column) demonstrate a substantial reordering that prioritizes clinical urgency and optimizes the workflow. For example, patient 449244 has moved up 11 positions, representing a decrease in position number of 91.67%, while patient 449233 has moved down 10 positions, representing an increase in position number of 333.33% (Table 6).

CCTA Acquisition Order											
Order	ID	Age	Sex	Chest pain	Diabetes	Hypertension	Dyslipidaemia	Smoking	CACs	Model	%risk
1 (before: 12)	449244	73	Female	Typical	Yes	Yes	No	No	-	Clinical	68.95
2 (before: 1)	449239	69	Male	Typical	Yes	No	No	No	-	Clinical	62.13
3 (before: 2)	449236	80	Female	Atypical	Yes	No	Yes	No	-	Clinical	58.73
4 (before: 5)	449246	65	Male	Atypical	Yes	Yes	No	Yes	-	Clinical	52.07
5 (before: 9)	449247	77	Male	Atypical	No	Yes	No	No	-	Clinical	38.65
6 (before: 4)	449240	55	Male	Typical	No	No	No	No	-	Clinical	31.02
7 (before: 6)	449234	73	Male	Non-specific	No	No	Yes	No	-	Clinical	22.11
8 (before: 11)	449238	58	Male	Non-specific	No	Yes	No	No	-	Clinical	9.34
9 (before: 13)	449243	71	Female	Non-specific	No	Yes	Yes	No	-	Clinical	8.49
10 (before: 10)	449245	45	Female	Typical	No	Yes	No	No	-	Clinical	8.22
11 (before: 15)	449235	58	Male	Non-specific	No	No	No	No	-	Clinical	6.84
12 (before: 7)	449237	68	Female	Atypical	No	No	No	No	-	Clinical	6.36
13 (before: 3)	449233	42	Female	Typical	No	No	No	No	-	Clinical	5.04
14 (before: 14)	449242	60	Female	Atypical	No	No	No	No	-	Clinical	3.97
15 (before: 8)	449241	53	Female	Non-specific	No	No	No	No	-	Clinical	1.4

Figure 12: Snapshot of the interface integrating the developed algorithm for CCTA acquisition prioritization, showing UIFC administrators the optimized order for scheduling patients based on CAD risk. The first column displays the optimized order, with the previous order in brackets. The second column lists patient IDs, and subsequent columns indicate factors used to calculate the optimized order, such as age, sex, type of chest pain, diabetes, hypertension, dyslipidemia, smoking, and known CACs. The second last row shows the model type used to calculate the CAD probability in the last column. Purple panels indicate the session in which a group of patients will have the CCTA acquired. CAD: coronary artery disease. CCTA: coronary computed tomography angiography. CACs: coronary artery calcium score. UIFC: Unitat d’Imatge i Funció Cardiaca.

Considering that each session can accommodate the acquisition and reporting of CCTAs for around five patients and that only two sessions are scheduled per week, this optimized scheduling order ensures that high-risk cases are assessed up to a week earlier than programmed. For example, patient 449244, originally in the 12th position and scheduled for the 3rd session (1st session of the 2nd week), has been prioritized to the 1st position, allowing this patient to be assessed in the 1st session (1st session of the 1st week).

Table 6: Representation of the original and optimized orders for CCTA acquisition with their position and percentage changes. CCTA: coronary computed tomography angiography.

Original Position	Optimized Position	Position Change	Percentage Change
12	1	-11	-91.67%
1	2	1	100.00%
2	3	1	50.00%
5	4	-1	-20.00%
9	5	-4	-44.44%
4	6	2	50.00%
6	7	1	16.67%
11	8	-3	-27.27%
13	9	-4	-30.77%
10	10	0	0.00%
15	11	-4	-26.67%
7	12	5	71.43%
3	13	10	333.33%
14	14	0	0.00%
8	15	7	87.50%

## Results from hospital data

Patients scheduled for CCTA acquisition on October 30, 2023 (day 1) and November 8, 2023 (day 2), underwent prioritization using the CCTA acquisition algorithm. Each day had five scheduled patients (patients from 1 to 5 and from 6 to 10 on days 1 and 2, respectively). Patients 2, 4, 7, and 9 were identified as severe cases with CAD-RADS values of 5, 4B, 3, and 3, respectively. These high-risk cases were prioritized for CCTA acquisition. Compared to the original order, patients 2 and 7 moved up by one position, and patients 4 and 9 moved up by two positions. Conversely, non-severe patients 1, 3, and 5 were rescheduled from 1st, 3rd and 5th position to positions 4, 3, and 5, respectively, on day 1, and patients 6, 8, and 10 were rescheduled from positions 1, 3, and 5 to positions 5, 3, and 4, respectively, on day 2 (see Table 7).

### 3.1.2 Results from prioritization of CCTA reporting

#### Results from synthetic data

This algorithm offers clinicians a visual framework for organizing case reporting systematically, prioritizing urgent cases first (Figure 13). Unlike the previous algorithm, patient order is rearranged based on image findings' criticality, ensuring timely attention. For example, the first patient, which is being reported in the 1st session, would have been reported in the 2nd since it was initially in the 8th place on the list.

Moreover, this algorithm generates a visual interface (Figure 14) that combines clinical and demographic patient data alongside CCTA findings (assuming automated image processing-based data is available)<sup>2</sup>. This includes details like coronary tree dominance, stenosis degree and plaque type per segment, global calcium score, and CAD-RADS modifiers. Cardiac Imaging Experts can refine this information by accessing visual support through the 'OPEN VISUAL SUPPORT' button, which offers the original CCTA im-

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<sup>2</sup>Information and graphical support regarding the generated interface can be found in Annex 4. A demo of the functioning of the interface can be found in the Repository mentioned in Section 2.2.

ages, the option to overlay the coronary arteries' segmentation, 3D reconstructions of the coronary tree, and cMPRs for each vessel. After verifying the inputted data, experts can validate the case report, triggering the generation of an RIS report.

Working List									
	Urgent study	Order	Patient	Priority	CAD-RADS	Clinical info	Notes	Explainability	
1st session (1st session of 1st week)	True	1 (before: 8)	Amado Quevedo	CRITICAL	4A*	Other		+ Validate	
	False	2 (before: 2)	Salvador Quintana	HIGH	-	Assessment of revascularized coronary artery disease	Suboptimal, Stent/ACTP	+ Report	
	True	3 (before: 5)	Fatima Lasa	HIGH	-	Other	Stent/ACTP	+ Report	
	True	4 (before: 7)	Alfonso Báez	HIGH	-	No information	Coronary bypass	+ Report	
	False	5 (before: 9)	Maria Teresa Becerra	HIGH	4A	Screening for coronary artery disease in cardiomyopathy		+ Validate	
2nd session (2nd session of 1st week)	False	6 (before: 3)	Cosme Soler	MEDIUM	3	Chest pain/atypical symptoms in patient without known CAD		+ Validate	
	True	7 (before: 10)	Anibal Guardia	MEDIUM	3	Checkup, patient without cardiologic symptomatology or known coronary arter		+ Validate	
	False	8 (before: 1)	Ruben Valera	MEDIUM	3	Other		+ Validate	
	False	9 (before: 14)	Flor Calvet	MEDIUM	3	Other		+ Validate	
3rd session (1st session of 2nd week)	False	10 (before: 6)	Eloida Vallejo	MEDIUM	3	Other		+ Validate	
	False	11 (before: 13)	Emiliano Lledó	MEDIUM	3	Chest pain/atypical symptoms in patient without known CAD		+ Validate	
	True	12 (before: 12)	Flavia Arteaga	MEDIUM	-	Assessment of revascularized coronary artery disease	Suboptimal	+ Report	
	False	13 (before: 11)	Azucena Fortuny	LOW	2	Chest pain/atypical symptoms in patient without known CAD		+ Validate	
	False	14 (before: 4)	Maria José Barrera	LOW	2	Other		+ Validate	
	False	15 (before: 15)	Osvaldo Anguita	LOW	2	No information		+ Validate	

Figure 13: Snapshot of the interface displaying the integrated algorithm for prioritizing clinical assessments. This interface provides Cardiac Imaging Experts with the recommended order for reporting a pool of patients based on image findings and other risk factors. The columns include; an indication of urgent studies from the Emergency Room, the order of reporting (with original scheduled order in brackets), randomly generated patient names, priority level, CAD-RADS value (if available), reason for consultation, alerts for patients with stents or bypasses (indicating potential complexity) or for cases needing repeated studies due to suboptimal quality. Additionally, there's an explanation column regarding the order and a validation option for cases with acquired image findings or for reporting cases without findings. CAD: coronary artery disease. CAD-RADS: CAD reporting and data system. ACTP: Percutaneous transluminal coronary angioplasty.

## Results from hospital data

The hospital patients also underwent the CCTA reporting prioritization algorithm. High-risk cases (patients 2, 4, 7, and 9) were prioritized first for CCTA reporting. Compared to the original order, patient 4 was moved up by two positions, while both patients 7 and 9 were moved up by one position. Conversely, non-severe cases 1, 3, and 5 were rescheduled for CCTA reporting from positions 1, 4, and 5 to positions 4, 3, and 5, respectively, on day 1, and cases 6, 8, and 10 were rescheduled from positions 4, 1, and 5 to positions 5, 3, and 4, respectively, on day 2 (see Table 7).

### 3.2 Clinical assessment

As presented in Section 2.3, the proposed workflow was evaluated by physicians at Hospital de la Santa Creu i Sant Pau, who rated both solutions favorably. The optimization solution received a score of 6/6, while the interface received 3.5/4. It's important to note that the difference in scale is due to the evaluation templates used for each solution: the

optimization solution was assessed with a template containing 6 questions, whereas the interface template contained 4 questions. Each favorably-answered question contributed one point towards the total score.

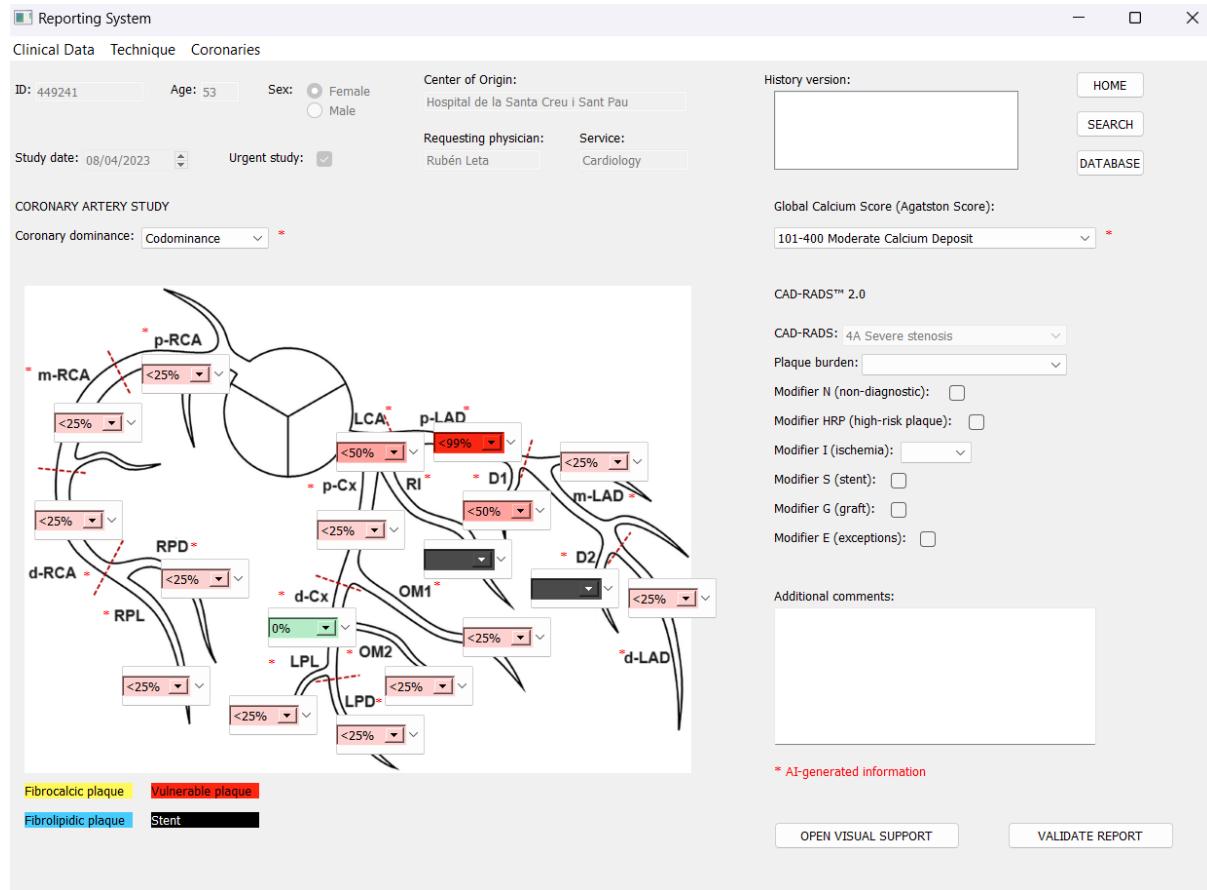


Figure 14: Snapshot of the interface displaying the integrated algorithm for generating preliminary case reports. This interface presents Cardiac Imaging Experts with the patient’s clinical information alongside data automatically extracted from the CCTA image. CCTA: coronary computed tomography angiography. CAD-RADS: coronary artery disease reporting and data system. AI: artificial intelligence. RCA: right coronary artery. RPD: right posterior descending artery. RPL: right posterolateral artery. LCA: left coronary artery. LAD: left anterior descending artery. Cx: circumflex artery. D1: first diagonal. D2: second diagonal. OM1: first obtuse marginal. OM2: second obtuse marginal. RI: ramus intermedius. LPL: left posterolateral artery. LPD: left posterior descending artery. p-: proximal segment. m-: medial segment. d-: distal segment.

Clinicians highlighted issues with the current workflow, including lack of prioritization, especially for studies of suboptimal quality, lack of automation in the clinicians’ working list and structured reporting, and workflow fragmentation across different systems. Both clinicians agreed that these problems could be addressed by the proposed solution. Furthermore, they believed that the optimized workflow could enhance the current one by reducing analysis time, allowing to assess more patients. Regarding the interface, they recommended incorporating a graphical diagram of the coronary tree to input the stenosis degree of each segment, a modification that was implemented in the final version. Detailed results of the assessment can be found in Annex 5.

### 3.3 Effectiveness Results

The number of days between patient consultation and CCTA acquisition, and between CCTA acquisition and diagnosis were extracted from the hospital’s management system for every case, as shown in Table 7. These days were ordered increasingly in the ‘Optimized wait time’ column to demonstrate that the first prioritized patient would be diagnosed in the minimum possible time, and so forth. By prioritizing the most urgent cases (patients 2, 4, 7, and 9), the average diagnosis times for severe cases were reduced to 32 days for day 1 and 48 days for day 2. This represents a substantial improvement compared to the original workflow, where severe cases took an average of 85 days (over 62% more time) and 188 days (over 74% more time) for days 1 and 2, respectively.

Table 7: Table documenting the original and optimized order of patients scheduled for CCTA acquisition and assessment (1st to 5th), alongside the duration between consultation with the cardiologist and CCTA acquisition (in days) and between CCTA acquisition and diagnosis by the referring physician (in days). It also calculates the total duration from consultation to diagnosis and the variance introduced by the optimized workflow in percentage. Patients with severe CAD (CAD-RADS  $\geq 3$ ) are highlighted in red. The results from the optimized workflow for CCTA acquisition and reporting prioritization are highlighted in grey. CAD: coronary artery disease. CAD-RADS: CAD reporting and data system. CCTA: coronary computed tomography angiography. PT: patient. Orig. ord.: original order. Orig. wait: original wait time. Opt. ord.: optimized order. Opt. wait: optimized wait time. Orig. workflow: original workflow. Opt. workflow: optimized workflow.

Days	Patients	CCTA acquisition				CCTA reporting				Total Diagnosis Time		
		Orig. ord.	Orig. wait (days)	Opt. ord.	Opt. wait (days)	Orig. ord.	Orig. wait (days)	Opt. ord.	Opt. wait (days)	Orig. workflow (days)	Opt. workflow (days)	Time variance
DAY 1	PT 1	1st	19	4th	210	1st	23	4th	51	42	261	521%
	PT 2	2nd	26	1st	19	2nd	18	2nd	18	44	37	-16%
	PT 3	3rd	210	3rd	75	4th	91	3rd	23	301	98	-67%
	PT 4	4th	75	2nd	26	3rd	51	1st	1	126	27	-79%
	PT 5	5th	230	5th	230	5th	1	5th	91	231	321	39%
DAY 2	PT 6	1st	120	5th	321	4th	6	5th	70	126	391	210%
	PT 7	2nd	15	1st	15	2nd	5	1st	5	20	20	0%
	PT 8	3rd	173	3rd	120	1st	7	3rd	7	180	127	-29%
	PT 9	4th	321	2nd	70	3rd	34	2nd	6	355	76	-79%
	PT 10	5th	70	4th	173	5th	70	4th	34	140	207	48%

## 4 Discussion

### 4.1 Analysis of results

#### 4.1.1 CCTA acquisition prioritization

As presented in Section 3.1.1, the prioritized ordering of CCTA acquisition can lead to a time variance of up to one week, enabling prompt diagnosis of high-risk patients. The constrained capacity (5 patients per session) and fewer sessions (2 per week) create a bottleneck in the assessment and diagnosis of CAD patients. Prioritizing CCTA scheduling has the potential to substantially accelerate the evaluation of severe cases.

As of April 2024, Hospital de la Santa Creu i Sant Pau has 883 patients on the cardiology consultation waiting list. If, for instance, 5% of these patients (the incidence rate of CAD [1]) required CAD assessments, completing the necessary CCTAs would take more than 4 months. In this case, prioritizing severe cases becomes crucial in ensuring timely detection and assessment, thereby preventing prolonged delays for high-risk patients.

#### 4.1.2 CCTA reporting prioritization

Prioritizing CCTA reporting not only ensures prompt diagnosis of severe cases but also aids clinicians in making faster, more informed decisions. The prioritization strategy (Figure 13) includes various alarms to assist clinicians, such as alarms for critical cases with over 70% stenosis in a main vessel (4th column), urgent requests from the ER (1st column), patients with existing stents or coronary bypasses, and studies of suboptimal quality (7th column). These alarms help clinicians prioritize their workload efficiently.

For instance, critical cases can be evaluated promptly, allowing urgent treatment or hospital admission before the patient is discharged. For urgent ER requests, clinicians can decide whether to prioritize these cases based on their severity. For example, the first patient in Figure 13 was an ER request with severe findings, which is already prioritized. However, the 7th case on the list, which is also an ER request, may not be prioritized over more severe patients even though being an urgent request. If the alarm indicates a patient has a stent or coronary bypass, it notifies the clinician of a confirmed CAD case, which may be more complex and time-consuming to report. Finally, alarms for suboptimal quality studies save clinicians time by identifying unreliable images quickly, allowing for prompt arrangements to repeat the CCTA acquisition as soon as possible.

Besides the alarm system, ordering patients by severity helps clinicians manage their workload better. Addressing complex and severe cases first, rather than at the end of the day when fatigue sets in, ensures thorough assessment and appropriate treatment. This prioritization improves efficiency and patient care.

#### 4.1.3 Interface and preliminary case report validation

The generated interface (Figure 14) helps streamline data and algorithms involved in CAD diagnosis. It manages patient databases, visually reports relevant information, explains decisions from prioritization algorithms, and allows clinicians to interact with and

modify data for accurate patient case reporting.

A mockup of the interface was created as a proof of concept, demonstrating that an initial pool of patients can be ordered for CCTA acquisition and that preliminary case reports can be generated automatically from clinical information and CCTA images, jointly with a list indicating the order in which patients should be reported ordered by severity. From the results, it can be considered that the goal was successfully achieved. Currently, the hospital's reporting system does not integrate with other systems containing clinical information (hospital's management system), CCTA images (PACS), and the radiology reporting system (RIS). However, the proposed interface could integrate these databases and algorithms using the infrastructure described in Section 2.4.2.

Additionally, the interface allows clinicians to test and evaluate the proposed solution, demonstrating the process for validating preliminary case reports. The preliminary report, presented in a graphical and comprehensible format, includes all coronary-related findings from the CCTA image and relevant clinical information. Clinicians could easily correct necessary information and validate the final report for RIS entry. Clinical assessments indicate that the interface was well received by cardiologists, suggesting that with further refinement, it could be fully integrated into the hospital's workflow and the routine of Cardiac Imaging Experts.

#### 4.1.4 Effectiveness of the solution

From the clinical assessment in Section 3.2, it can be concluded that clinicians were very satisfied with the optimization workflow presented. The results suggest that automating tasks, such as manual entry of clinical information and image findings into the reporting system, could lighten clinicians' workloads. Additionally, patient management would be optimized, allowing clinicians to focus on severe cases rather than spending time and resources on healthy cases. Clinicians endorsed these outcomes, believing that this methodology could speed up the analysis and diagnosis process, enabling more patients to be treated. They also indicated that the proposed solution addressed some issues of the current workflow, improving their satisfaction and workload with respect to the original process.

As demonstrated in Section 3.3, prioritizing patients can potentially reduce the overall time dedicated to diagnosing severe CAD patients. For example, on day 1, severe cases 2 and 4 originally took 44 and 126 days from consultation to diagnosis, respectively. Case 2, with a CAD-RADS of 5, posed a high risk of MI due to a completely occluded coronary artery, while case 4, with a CAD-RADS of 4B, also faced severe risks. The implementation of the proposed algorithms reduced diagnosis times to 37 (16%) and 27 (79%) days, respectively, highlighting the importance of early diagnosis and treatment in improving patient outcomes [4].

Similarly, on day 2, cases 7 and 9 originally took 20 and 355 days to diagnose, respectively. Although case 7 was diagnosed quickly, case 9, despite having a less severe CAD-RADS, faced nearly a year-long delay, risking disease progression. The optimized workflow reduced the diagnosis time for patient 9 to 76 days (79%), a more acceptable

timeframe. This methodology thus improves prognosis by ensuring timely diagnosis and treatment for severe CAD cases. In contrast, non-severe cases sometimes experienced longer diagnosis times, which, while not harmful, could be mitigated by notifying patients that their low-risk cases might be delayed due to their lower priority.

## 4.2 Limitations of the project

While the proposed workflow for prioritizing CCTA acquisition and reporting shows promise in an ideal scenario, several real-world factors must be considered that could impact its effectiveness.

### 4.2.1 Limitations of the proposed workflow algorithms

The proposed workflow algorithms have several limitations that need to be addressed for practical implementation. The most critical issue is the current absence of an automatic image analysis algorithm, necessitating manual reporting by clinicians, which hinders potential workflow optimization. This automatic image analysis algorithm, apart from vessel lumen segmentation, should quantify and classify plaque and label segmented vessels to identify lesion locations accurately since lesion location is critical for patient prognosis. Furthermore, the current algorithms depend on specific input formats and cannot handle missing or varied data, necessitating the development of more robust algorithms for real-world hospital environments. Another noteworthy limitation is the small number of real patients (only 10) in which these algorithms have been tested, which is not sufficient to obtain significant results.

Addressing these limitations is essential for successfully applying the proposed workflow improvements in clinical settings. To overcome some of these challenges, for instance, increasing the size of the testing dataset to include 300-500 patients, dimensions commonly used in related literature [21] [25], could yield more significant results. Additionally, these limitations could be addressed by continually refining automatic algorithms for image feature extraction, such as identifying atherosclerotic plaque and labeling coronary vessels. This refinement process would involve manually extracting ground truths for coronary plaque segmentation and manual vessel labeling.

### 4.2.2 Coordination among multiple parties

The workflow assumes that patient diagnosis and treatment schedules depend solely on one doctor. In reality, the coordination among multiple cardiologists, technicians, and other medical staff is crucial. The proposed workflow does not account for the variability and complexity of scheduling among different healthcare professionals, including referring physicians for initial and follow-up consultations, technicians for CT scans, and reporting physicians.

Additionally, it does not consider patients' schedules and their availability to attend appointments consistently. Assuming that patients will attend their medical appointments without fail can lead to missed appointments which can disrupt the workflow and

delay diagnosis and treatment, necessitating a more flexible and adaptive scheduling system.

#### 4.2.3 Resource availability

The workflow assumes unlimited access to infrastructure resources such as CT scanners. However, in practice, their availability can be limited, and scheduling these resources can be challenging. The workflow should account for potential delays and conflicts in resource allocation.

#### 4.2.4 Prioritization based on non-clinical factors

While prioritizing based on severity is essential, other factors may also influence prioritization, such as patient interest or pressure from other medical peers. These factors can affect the impartiality and efficiency of the proposed system.

#### 4.2.5 Neglecting non-severe cases

Focusing primarily on severe cases might result in neglecting non-severe ones. It is important to ensure that patients do not remain on the waiting list indefinitely, even if they are deemed low-risk.

#### 4.2.6 Limited focus on CAD

While the primary focus of the current workflow is on extracting information from coronary arteries for CAD diagnosis, Cardiac Imaging Experts routinely examine CCTA images for abnormalities in other anatomical structures. These findings, although not directly impacting patient prioritization, serve as crucial alerts for clinicians. For example, patients presenting with chest pain but without CAD may have underlying conditions such as valve disease [49], aortic stenosis [50], or non-cardiac issues affecting the thoracic cavity like lung nodules that could be cancerous [51]. These anatomical structures could be taken into account by adapting the automatic image analysis algorithm to segment and analyze other structures to extract additional information. Therefore, when developing automatic image analysis algorithms, it is essential to consider these broader aspects of image interpretation to ensure comprehensive health assessment and timely clinical intervention.

#### 4.2.7 Balanced workload

Prioritizing severe cases might not always be the most efficient strategy considering human factors. If a relevant portion of the cases (e.g., 5 out of 15) are severe and complex, it might be counterproductive to handle all these complex cases in one day. This approach could lead to clinician burnout and decreased decision accuracy by the end of the day. Therefore, balancing the workload by mixing complex cases with less demanding ones

throughout the day might be more beneficial, except in life-or-death situations.

### 4.3 Future work

#### 4.3.1 Use of real data

The data utilized in this project is primarily synthetic, excluding the data from the patients tested in Sections 3.1.1 and 3.1.2, which was, in its majority, extracted from the hospital. This reliance on synthetic data is partly for convenience, enabling a relatively rapid proof-of-concept of the proposed workflow. Additionally, it stems from the challenges associated with obtaining clinical data from the hospital. While some data can be retrieved from the structured Cardiac Imaging database, most of the clinical data necessary for the algorithms resides in the hospital’s management system, an unstructured database with stringent data protection constraints, complicating data extraction efforts. To address the issue of unstructured information, natural language processing (NLP) tools could be employed to extract structured data from the unstructured EHRs of patients. This type of methodology has been used before with successful results, where BuHamra et al., 2022 [52] generated an NLP system to extract, in a timely manner, causes of death from EHRs during the pandemic.

Additionally, there are other relevant metrics, like the CAC score, that are not currently measured. The CAC score, typically obtained through non-contrast CT, would require another separate CT acquisition apart from the necessary contrast-enhanced CCTA acquisition. This second CT is not acquired to avoid over-irradiating patients. However, studies in the literature, such as the one of Wang et al., 2022 [53], suggest that the Agatston CAC score can be reliably extrapolated from CCTA, providing comparable results to those obtained through the non-contrast CT.

#### 4.3.2 Combining anatomical and functional information

Another improvement on the workflow would be the integration of findings from CCTA images, which are typically used to assess the anatomy of the coronary arteries, with functional information such as perfusion to the heart, which, when combined with anatomical data from CCTA, can lead to more accurate and comprehensive diagnoses. Incorporating both anatomical and functional information would enhance diagnostic accuracy and patient outcomes [54].

#### 4.3.3 Other diagnostic tests before CCTA

The current workflow for diagnosing CAD in Hospital de la Santa Creu i Sant Pau prioritizes the direct use of CCTA to look directly into the anatomy of the coronary arteries instead of requesting other related tests. However, patients presenting with chest pain before having a CCTA acquired may often undergo an array of diagnostic tests, primarily electrocardiograms (ECGs), supplemented by additional tests like blood tests and exercise stress tests, although these are less commonly employed [55]. These tests might

provide valuable inputs for patient prioritization. Although the hospital currently prioritizes direct CCTA to assess coronary anatomy, incorporating data from prior diagnostic tests could enhance the prioritization process. This integration would require developing methods to seamlessly incorporate data from various diagnostic tests into the prioritization algorithms.

#### 4.3.4 Automatic image quality evaluation

Currently, the assessment of image quality and artifacts is conducted manually by technicians during image acquisition, with results annotated in the Cardiac Imaging database. To optimize the workflow and reduce the workload on healthcare professionals, this process could be automated using AI-driven image analysis algorithms. This methodology has already been implemented in some studies in the literature. For instance, Chun et al., 2022 [56] reported a patient-specific CT image quality evaluation method that reliably generated a quantitative image quality evaluation. Similarly, Su et al., 2024 [57] developed an automatic deep learning (DL)-based algorithm to reliably assess the image quality of chest CTs. Therefore, developing robust algorithms to evaluate image quality automatically would streamline the workflow and ensure consistent quality assessment.

#### 4.3.5 Generation of a more visual and intuitive interface

While the interface of this project was primarily developed as a proof-of-concept for implementing the proposed workflow, enhancing it for future real-world integration into hospital infrastructure is essential. Utilizing graphical user interface (GUI) tools like Flet<sup>3</sup> for example, could enable the creation of a more intuitive, user-friendly, and visually appealing interface. A well-designed interface would streamline navigation and system utilization, thereby enhancing overall efficiency and user satisfaction.

#### 4.3.6 Validation of results with other clinicians and healthcare centers

The current workflow might be biased due to its reliance on the methodology preferred by the UIFC, which emphasizes diagnosing CAD primarily through CCTA images. This preference introduces bias, assuming this approach is universally applicable across other hospitals or departments. However, other radiology departments and hospitals may have different protocols and practices.

This workflow was presented to the physicians of Rigshospitalet [58], a specialized medical center in Denmark. Although they found the idea interesting, they commented that it would not be useful in their hospital since the prioritization of patients is done before arrival. They only treat patients deemed severe, so the idea could be more useful for other hospitals that refer patients to Rigshospitalet. Therefore, the importance of adapting the workflow to suit different hospitals and departments is highlighted. Validating the workflow with clinicians from various settings ensures its broader applicability and benefits. Multicenter studies and feedback from diverse clinical settings are essential

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<sup>3</sup><https://flet.dev/>

to generalize and refine the workflow.

#### 4.3.7 Extrapolation to other areas

Although this project is focused on the UIFC and CAD diagnosis, the workflow could be extended to other cardiac-related areas with a clear and repetitive methodology, such as Left Atrial Appendage (LAA) occluder assessment, TAVI (Transcatheter Aortic Valve Implantation) and preoperative planning. In contrast to the CAD diagnosis process, where physicians' working lists comprise only around 5 patients for CCTA reporting, other cardiac diagnosis areas often have long waiting lists for CT reporting. Therefore, these areas could benefit significantly from prioritization algorithms to detect urgent cases.

Furthermore, this workflow could be applicable in other radiology areas beyond cardiology. Although the basis of the optimized workflow would be maintained, implementing the workflow in other radiology departments would require some adaptations. For instance, the prioritization algorithms would need to be adjusted to consider different risk factors and urgency indicators relevant to other specialties. Additionally, image analysis algorithms would need to be customized to analyze other anatomical structures, and preliminary case reports would require modification to include pertinent information for different contexts.

#### 4.3.8 Clinicians' adaptation to new workflows

Lastly, integrating new diagnostic tools into radiology-based diagnosis can be challenging due to resistance to change from established practices and skepticism towards new technologies. To facilitate the adoption of these methodologies, comprehensive training and education for clinicians are essential. Open communication and collaboration among healthcare professionals, engineers, and IT specialists will also be crucial. Demonstrating the tangible benefits of the new processes, including how they simplify complex tasks, customizing them for seamless integration into current workflows, and implementing changes gradually will help mitigate resistance and ensure successful adoption.

## 5 Conclusions

The project has successfully achieved its primary objective of proposing a theoretical workflow to aid clinicians in optimizing the CAD assessment process. Automatic prioritization of patients ensured prompt scheduling of CCTA acquisition and reporting for severe cases, effectively utilizing clinicians' time and streamlining the assessment order based on case severity. Additionally, the workflow generated automatic preliminary case reports from CCTA images and clinical data, alleviating the manual annotation burden on Cardiac Imaging Experts, requiring only their validation of the automatically generated reports. Furthermore, specific objectives were achieved by thoroughly studying and understanding the current workflow for CAD diagnosis, and the described algorithms were implemented in a visual interface, allowing clinicians to test and validate the solution.

The initial indicators set out in the project, such as reduced diagnosis time for severe CAD cases ( $CAD-RADS \geq 3$ ) and enhanced clinician satisfaction with the workflow, have shown positive outcomes. Theoretical reductions in diagnosis time were demonstrated in Section 3.3, while Section 3.2 revealed high clinician satisfaction with the new workflow.

However, despite these successes, the proposed workflow faces challenges in real-world implementation. Factors such as resource constraints, scheduling complexities, patient compliance, and the need for a holistic patient care approach beyond CAD pose significant limitations. Balancing workload and considering human factors are crucial to maintaining clinician efficiency and accuracy.

Future iterations of the workflow should address these challenges comprehensively to enhance practicality and effectiveness in clinical settings. Integrating automatic tools into radiology-based diagnosis remains essential to improving efficiency within traditional radiology departments. Careful planning and execution of proposed future work can further enhance CAD diagnosis optimization, leading to improved patient care and outcomes.

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# Additional Information

Enhanced Prioritization and Reporting for  
Coronary Artery Disease Diagnosis

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Bachelor's Thesis UPF 2023/2024

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**SANT PAU**  
Dimension Lab

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## 1 Annex 1: Regulatory impact

Integrating the proposed tool necessitates adherence to regulatory standards to ensure legal compliance, patient safety, product quality, and healthcare professional confidence. This section outlines the definition of a software medical device (MDSW) and discusses the regulatory and legal requirements that the CAD diagnosis optimization solution must meet for market introduction.

The intended deployment of the product in Hospital de la Santa Creu i Sant Pau, located in Spain, necessitates compliance with both national and international regulations. Specifically, the product would be subject to Spanish Royal Decree 192/2023 (herein, RD 192/2023) [1], regulating medical devices in Spain, and European Regulation (EU) 2017/745 (herein, EU MDR) [2], which governs medical devices within the European Union. Additionally, any potential deployment of the product in countries outside the European Union requires thorough investigation to ensure regulatory compliance.

For classification as a Medical Device Software (MDSW), adherence to the medical device definition outlined in Article 2 of the Regulation EU MDR is imperative. The proposed solution, aimed at facilitating CAD diagnosis through automatic interpretation of CCTA images and influencing clinical decision-making, falls within the scope of Class IIa medical devices, as per Rule 11 of Chapter III of Annex VIII of EU MDR. Given the significant health implications of CAD diagnosis and its direct impact on patient management, adherence to the aforementioned regulatory requirements is essential. Uncertainties regarding classification can be addressed through consultation with regulatory authorities such as the Agencia Española del Medicamento y del Producto Sanitario (AEMPS).

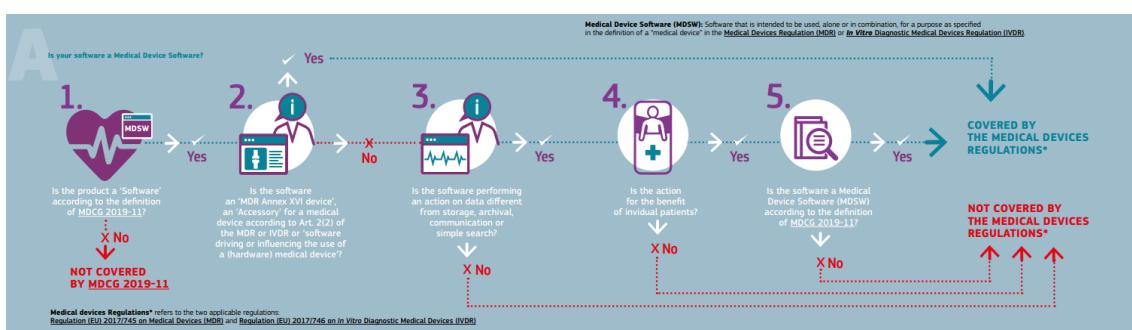


Figure 1: Scheme to assist the qualification of software as a Medical Device Software by the European Commission, based on the MDCG 2019-11 guiding the qualification and classification of software in Regulation (EU) 2017/745 - MDR and (EU) 2017/746 - IVDR. MDCG: medical device coordination group document. MDR: medical device regulation. IVDR: in vitro diagnostic regulation. MDSW: medical device software. Retrieved from [3].

The device, if primarily utilized within EU healthcare institutions, may qualify for exemption from EU MDR requirements under specific conditions (outlined in Clause 5 of Article 5). However, adherence to relevant safety and performance standards outlined in Annex I of the EU MDR remains mandatory. Alternatively,

compliance with Article 10 of the EU MDR is necessary for market introduction, alongside other stipulated requirements. Moreover, compliance with RD 192/2023 can be largely attained by adhering to the EU MDR. Additional requirements from this royal decree may include communication with the Spanish competent regulatory authority (AEMPS), the language of compliance documentation, often Spanish, and other specific details stipulated in the regulatory framework.

## 2 Annex 2: CCTA acquisition algorithms rules

### 2.1 REGICOR Equation

The REGICOR equation is based on the probability calculation of an event in the Cox proportional hazards regression model:

$$P_{X_{i(t)}} = 1 - S_{x_{i(t)}} = 1 - e^{-[H_{0(t)}e^{(\sum(\beta_i x_i) - \sum(\beta_i x_m))}]} = \\ = 1 - e^{-[-\ln(S_{0(t)}e^{(\sum(\beta_i x_i) - \sum(\beta_i x_m))})]} = 1 - S_{0(t)}e^{(\sum(\beta_i x_i) - \sum(\beta_i x_m))}$$

Where  $P_{X_{i(t)}}$  is the probability of a coronary event happening in a time t (which for the evaluated case will be 10 years),  $x_{i(t)}$  is the set of risk factors of a patient,  $S_{x_{i(t)}}$  is the probability of no coronary event happening for this patient,  $H_{0(t)}$  is the cumulative basal rate of coronary events,  $S_{0(t)}$  is the basal probability of being free of coronary events,  $\sum(\beta_i x_i)$  is a linear function of average risk for every risk factor  $x_i$  of an individual,  $\sum(\beta_i x_m)$  is a linear function of average risk for every risk factor  $x_m$  in the studied population, and  $\beta_i$  are the coefficients of the Cox proportional hazards regression model. These coefficients can be found in the following table of Figure 2.

From this table, it can be extracted that the  $S_{0(t)}$  for men is 0.951 and for women is 0.978, by subtracting the 10-year incidence in Girona of ischemic cardiopathy (100% - 4.9% = 95.1% for men, and 100% - 2.2% = 97.8% for women). Moreover, by calculating the addition of the multiplied Cox coefficients with the prevalence in Girona of each risk factor we obtain that the  $\sum(\beta_i x_m)$  is 3.49 for men and 10.24 for women. Therefore, to calculate the risk for an individual we would only have to calculate the  $\sum(\beta_i x_i)$  by multiplying the Cox coefficients with the corresponding results for each factor of the specific patient. The resulting 10-year risk should be approximate to the one presented in the tables of Figure 3 and Figure 4.

- Equation for men:

$$1 - 0.951e^{(\sum(\beta_i x_i) - 3.49)}$$

- Equation for women:

$$1 - 0.978e^{(\sum(\beta_i x_i) - 10.24)}$$

### 2.2 Pre-Test Probability of CAD Models

The study conducted by Genders et al. [5] developed updated models that integrate variables including age, sex, symptoms, and cardiovascular risk factors. These models allow for precise estimation of CAD probability in low-prevalence populations. Additionally, the inclusion of coronary calcium scores in these prediction models improves the accuracy of these estimates.

The study proposed three models: a basic model including age, sex, chest pain, and setting; a clinical model incorporating age, sex, chest pain, setting, and risk factors such as diabetes, hypertension, dyslipidemia, and smoking; and an expanded model encompassing all clinical variables along with the coronary calcium score.

These models are based on the following equation:  $\text{logit}(P_{CAD}) = \alpha_{new} + BX + \text{offset}(lp)$ , where  $\text{logit}$  is the natural log odds of the probability;  $P_{CAD}$  is the probability of obstructive coronary artery disease;  $\alpha_{new}$  is the intercept of logistic regression model;  $lp$  is the linear predictor of the clinical model and, for the basic model,  $B = (\beta_{age}, \beta_{sex}, \beta_{atypical}, \beta_{typical})$  is a vector of regression coefficients, and  $X = (x_{age}, x_{sex}, x_{atypical}, x_{typical})$  is a vector with subject variables where  $x_{age}$  takes the value of the individual's age in years,  $x_{sex}$  takes value 1 if the individual is male and 0 if the individual is female, and  $x_{atypical}$  and  $x_{typical}$  take value 1 if true and 0 if false.

In this study, typical chest pain is considered when all the following criteria are met: (1) substernal chest pain or discomfort that is (2) provoked by exertion or emotional stress and (3) relieved by rest or nitroglycerine (or both). On the contrary, atypical chest pain was considered with two of these criteria, and if only one or none of the criteria was met, the patient's symptoms were considered non-specific.

To calculate the probability of CAD, which is the objective of these models, we first need to isolate  $P_{CAD}$  in the following way:

$$\begin{aligned}
\text{logit}(P_{CAD}) &= \log(\text{odds}) = \ln\left(\frac{P_{CAD}}{1 - P_{CAD}}\right) = a + bx \implies \\
\implies \frac{P_{CAD}}{1 - P_{CAD}} &= e^{a+bx} \implies P_{CAD} = (1 - P_{CAD})e^{a+bx} \implies \\
\implies P_{CAD} &= e^{a+bx} - P_{CAD}e^{a+bx} \implies P_{CAD} + P_{CAD}e^{a+bx} = e^{a+bx} \implies \\
\implies P_{CAD}(1 + e^{a+bx}) &= e^{a+bx} \implies P_{CAD} = \frac{e^{a+bx}}{1 + e^{a+bx}}
\end{aligned}$$

Therefore, the probability of CAD in the basic model can be calculated in the following way:

$$\begin{aligned}
\text{logit}(P_{CAD}) &= \alpha_{new} + \beta_{age}x_{age} + \beta_{sex}x_{sex} + \beta_{atypical}x_{atypical} + \beta_{typical}x_{typical} + \text{offset}(lp) \implies \\
\implies P_{CAD} &= \frac{e^{\alpha_{new} + \beta_{age}x_{age} + \beta_{sex}x_{sex} + \beta_{atypical}x_{atypical} + \beta_{typical}x_{typical} + \text{offset}(lp)}}{1 + e^{\alpha_{new} + \beta_{age}x_{age} + \beta_{sex}x_{sex} + \beta_{atypical}x_{atypical} + \beta_{typical}x_{typical} + \text{offset}(lp)}}
\end{aligned}$$

By adding the risk factors to the equation, we obtain the clinical model where  $P_{CAD}$  is calculated in this manner:

$$\text{logit}(P_{CAD}) = \alpha_{new} + \beta_{age}x_{age} + \beta_{sex}x_{sex} + \beta_{atypical}x_{atypical} + \beta_{typical}x_{typical} + \beta_{diabetes}x_{diabetes} +$$

$$\begin{aligned}
 & + \beta_{HTA}x_{HTA} + \beta_{dyslipidemia}x_{dyslipidemia} + \beta_{smoking}x_{smoking} + offset(lp) \implies \\
 \implies P_{CAD} = & \frac{e^{\alpha_{new} + \beta_{age}x_{age} + \beta_{sex}x_{sex} + \dots + \beta_{smoking}x_{smoking} + offset(lp)}}{1 + e^{\alpha_{new} + \beta_{age}x_{age} + \beta_{sex}x_{sex} + \dots + \beta_{smoking}x_{smoking} + offset(lp)}}
 \end{aligned}$$

Finally, for the expanded model, we just need to add the variable of CACs in the equation:

$$\begin{aligned}
 logit(P_{CAD}) = & \alpha_{new} + \beta_{age}x_{age} + \beta_{sex}x_{sex} + \beta_{atypical}x_{atypical} + \beta_{typical}x_{typical} + \beta_{diabetes}x_{diabetes} + \\
 & + \beta_{HTA}x_{HTA} + \beta_{dyslipidemia}x_{dyslipidemia} + \beta_{smoking}x_{smoking} + \beta_{CCS}ln(x_{CCS}+1) + offset(lp) \implies \\
 \implies P_{CAD} = & \frac{e^{\alpha_{new} + \beta_{age}x_{age} + \beta_{sex}x_{sex} + \dots + \beta_{smoking}x_{smoking} + offset(lp)}}{1 + e^{\alpha_{new} + \beta_{age}x_{age} + \beta_{sex}x_{sex} + \dots + \beta_{CCS}ln(x_{CCS}+1) + offset(lp)}}
 \end{aligned}$$

The coefficient values for each of these models are given in the provided chart of Figure 5.

		Male			Female		
		Cox model coefficients	Framingham prevalence	Prevalence in Girona	Cox model coefficients	Framingham prevalence	Prevalence in Girona
Age (average in years)		0.0483	48.3	54.6	0.3377	49.6	54.2
Age squared					-0.0027	2604.5	3054.9
	<160	-0.6505	7.5%	5.9%	-0.2614	7.9%	4.9%
	160-199	0	31.3%	20.7%	0	30.3%	11.8%
Total cholesterol (mg/dL)	200-239	0.1769	39.0%	34.8%	0.2077	32.7%	35.3%
	240-279	0.5054	16.5%	28.1%	0.2439	20.0%	24.6%
	≥280	0.8571	5.7%	10.5%	0.5351	9.1%	13.4%
	<35	0.4974	19.2%	17.0%	0.8431	4.3%	3.8%
	35-44	0.2431	35.7%	31.9%	0.3780	14.9%	17.0%
cHDL (mg/dL)	45-49	0	15.5%	12.7%	0.1979	12.4%	12.3%
	50-59	-0.0511	19.0%	20.9%	0	27.7%	26.0%
	>60	-0.4866	10.6%	17.5%	-0.4295	40.7%	40.9%
	Optimal (SBP<120)/(DBP<80)	0.0023	20.2%	18.1%	-0.5336	34.8%	27.5%
	Normal (SBP 120-129)/(DBP 80-84)	0	24.3%	19.3%	0	48.6%	16.5%
Blood pressure (mmHg)	Normal high (SBP 130-139)/(DBP 85-89)	0.2832	20.2%	20.1%	-0.0877	15.0%	16.2%
	Stage I (SBP 140-159)/(DBP 90-99)	0.5217	22.5%	28.4%	0.2629	18.6%	28.6%
	Stage II-III (SBP≥160)/(DBP≥100)	0.6186	12.8%	14.1%	0.4657	10.0%	11.5%
Diabetes		0.4284	5.0%	9.3%	0.5963	3.8%	6.7%
Smoking		0.5234	40.3%	42.3%	0.2925	37.8%	12.0%
10-year incidence	Of ischemic cardiopathy *		10.0%	4.9% <sup>b</sup>		3.8%	2.2% <sup>b</sup>

Figure 2: Coefficients of the Cox proportional hazards regression model of the Framingham Risk Score function for the incidence of all types of coronary events in 10 years and prevalence of each risk factor in Framingham (US) and Girona (Spain). (a) Fatal or non-fatal myocardial infarction, with or without angina symptoms. (b) Estimated from real data of incidence of symptomatic myocardial infarction (mortal or not), and the rate of angina and silent myocardial infarction in Framingham. SBP: Systolic Blood Pressure. DBP: Diastolic Blood Pressure. cHDL: high-density lipoprotein cholesterol. Table extracted from [4]

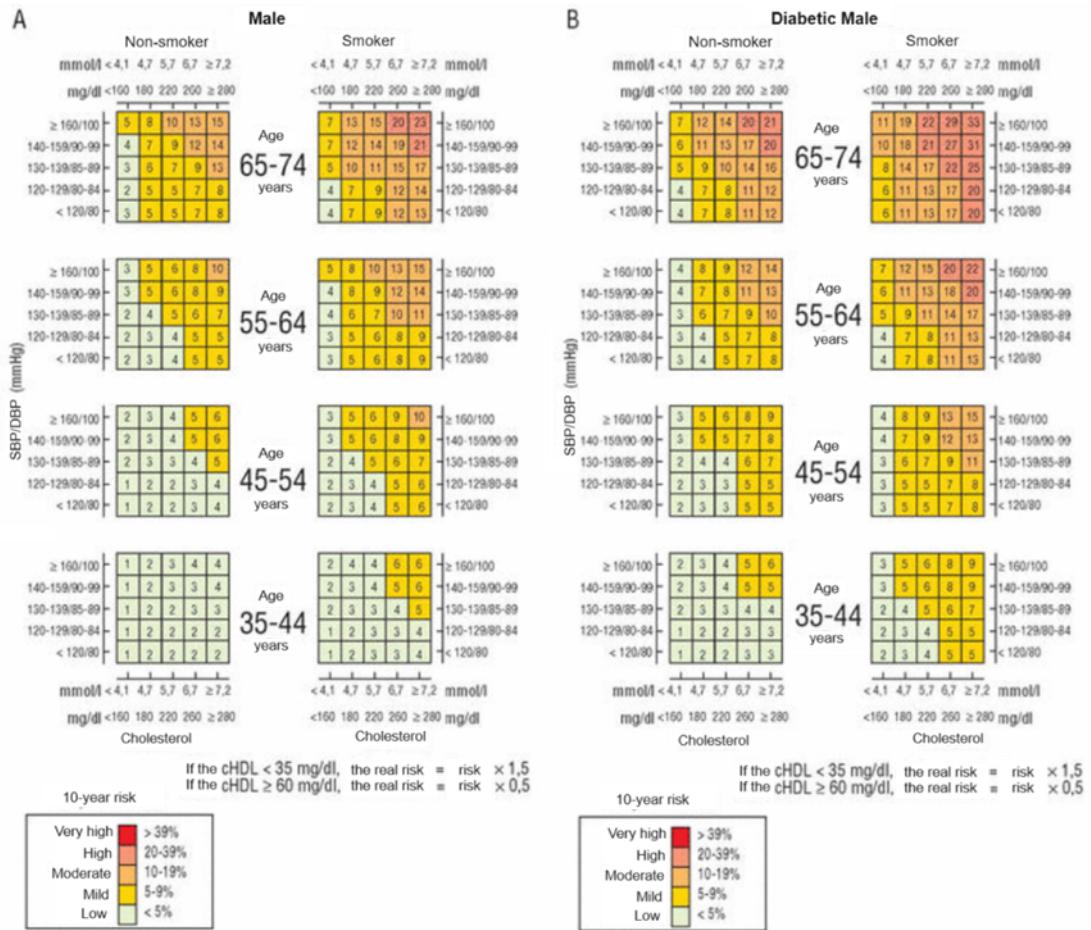


Figure 3: REGICOR 10-year cardiovascular risk results in males depending on the combination of risk factors such as diabetes, age, blood pressure, cholesterol, smoking, and cHDL. cHDL: high-density lipoprotein cholesterol. Table extracted from [4]

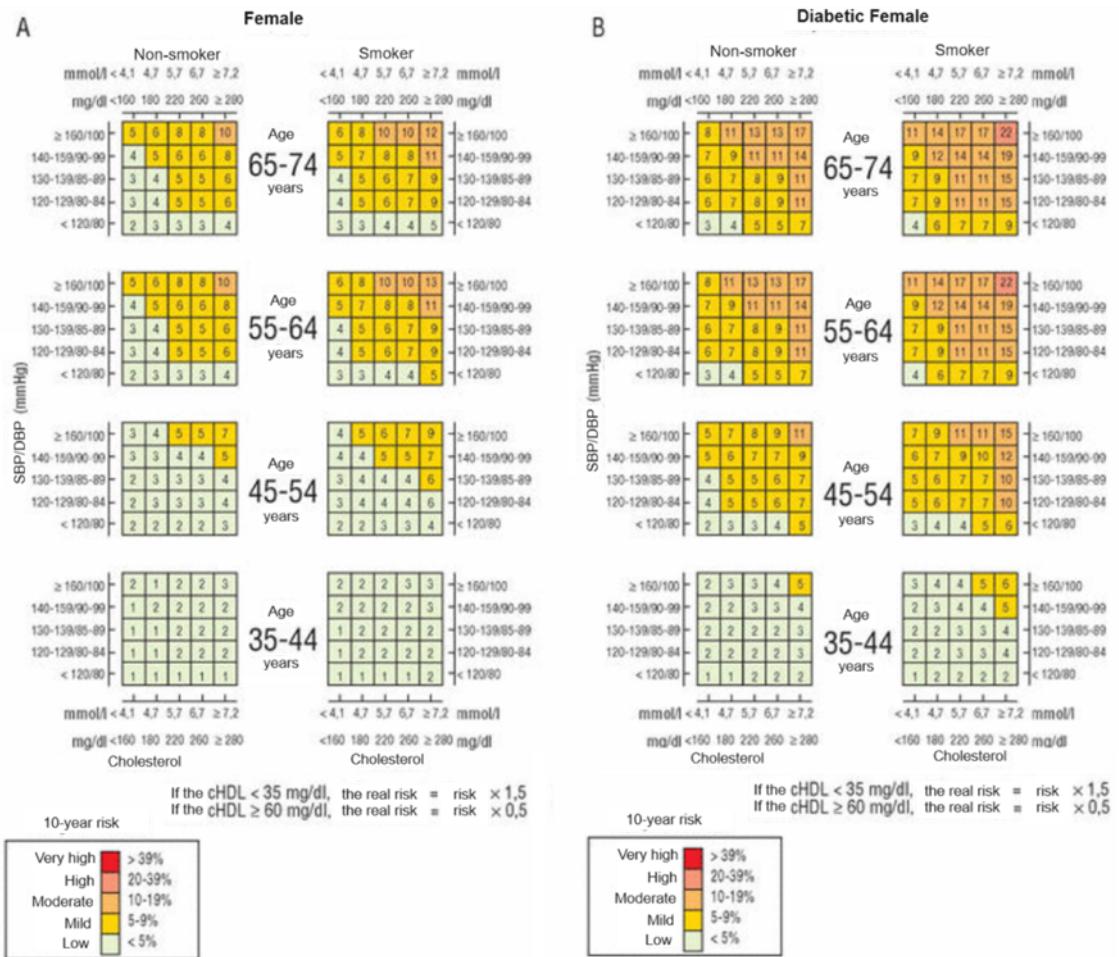


Figure 4: REGICOR 10-year cardiovascular risk results in females depending on the combination of risk factors such as diabetes, age, blood pressure, cholesterol, smoking, and cHDL. cHDL: high-density lipoprotein cholesterol. Table extracted from [4]

	Basic			Clinical			Clinical + CCS		
	Coef.	OR	95% CI	Coef.	OR	95% CI	Coef.	OR	95% CI
Intercept	-6.917	-	-	-7.539	-	-	-5.975	-	-
Age	0.063	<b>1.07</b>	1.06-1.07	0.062	<b>1.06</b>	1.06-1.07	0.011	1.01	1.00-1.02
Male sex	1.358	<b>3.89</b>	3.24-4.66	1.332	<b>3.79</b>	3.13-4.58	0.786	<b>2.19</b>	1.75-2.75
Atypical chest pain*	0.658	<b>1.93</b>	1.48-2.52	0.633	<b>1.88</b>	1.44-2.46	0.718	<b>2.05</b>	1.50-2.80
Typical chest pain*	1.975	<b>7.21</b>	5.64-9.22	1.998	<b>7.37</b>	5.64-9.63	2.024	<b>7.57</b>	5.56-10.3
Diabetes				0.828	<b>2.29</b>	1.73-3.04	0.658	<b>1.93</b>	1.41-2.64
Hypertension				0.338	<b>1.40</b>	1.18-1.67	0.235	<b>1.26</b>	1.04-1.54
Dyslipidaemia				0.422	<b>1.53</b>	1.25-1.86	0.185	1.20	0.95-1.53
Smoking				0.461	<b>1.59</b>	1.30-1.94	0.207	1.23	0.97-1.55
Log transformed CCS †							0.577	<b>1.78</b>	1.64-1.93
Setting ‡	1.065	<b>2.90</b>	1.69-4.99	1.049	<b>2.85</b>	1.60-5.10	1.566	<b>4.79</b>	2.19-10.5
Setting x log transformed CCS							-0.157	<b>0.86</b>	0.77-0.95
Diabetes x typical chest pain				-0.402	<b>0.67</b>	0.42-1.06	-0.780	<b>0.46</b>	0.27-0.77

Bold odds ratios indicate significant association (p-value < 0.05).

Coef. = beta-coefficient; OR = odds ratio; SE = standard error; CCS = coronary calcium score

\* Reference category is 'Non specific chest pain'

† Natural logarithm of CCS+1.

‡ High-prevalence vs. low-prevalence (reference)

Figure 5: Table of coefficients for each of the three models of the Pre-test score to predict the probability of CAD. Table extracted from [5]

### 3 Annex 3: Template for coronary case reporting used in Hospital de la Santa Creu i Sant Pau

#### CORONARY ANATOMY STUDY

**Coronary dominance:** [right / left / codominance].

-**Left main coronary artery (LCA):** [No lesions / level of stenosis].

-**Left anterior descending artery (LAD):** [No lesions / level of stenosis and in which segment].

-**Diagonal branch/es (Dx):** [No lesions / level of stenosis and in which artery].

-**Circumflex artery (Cx):** [No lesions / level of stenosis and in which segment].

-**Obtuse marginal artery/ies (OM):** [No lesions / level of stenosis and in which artery].

-**Left posterior descending artery (LPD)<sup>4</sup>:** [No lesions / level of stenosis].

-**Left posterolateral branch (LPL)<sup>4</sup>:** [No lesions / level of stenosis].

-**Ramus intermedius (RI):** [No lesions / level of stenosis].

-**Right coronary artery (RCA):** [No lesions / level of stenosis and in which segment].

-**Right posterior descending artery (RPD) <sup>5</sup>:** [No lesions / level of stenosis].

-**Right posterolateral trunk (RPL)<sup>5</sup>:** [No lesions / level of stenosis].

-Additional anatomical findings: [ ]

#### CONCLUSIONS

Epicardial coronary artery tree [without / with] parietal calcification and [no / ] stenotic atherosclerotic lesions.

According to the current classification system of atherosclerotic disease detected by Cardio-CT (CAD-RADS) the findings are compatible with the level [ ] (0-5).

Considering the recommendations published in the expert consensus document, with this result, no additional explorations are required for the study of coronary artery atherosclerotic disease.

(Reference: CAD-RADS™ 2.0 - 2022 Coronary Artery Disease - Reporting and Data System an expert consensus document of the Society of Cardiovascular Computed Tomography. Journal of Cardiovascular Computed Tomography (2022), <https://doi.org/10.1016/j.jcct.2022.07.002>)

<sup>4</sup>Artery reported only for cases with left dominance or codominance.

<sup>5</sup>Artery reported only for cases with right dominance or codominance.

## 4 Annex 4: Design and Mockup of the Interface

### 4.1 Interface Design

#### 4.1.1 Interface for Referring physician

First of all, the referring physician logs in their working session by introducing their ID, and their password and pressing enter or clicking on the arrow. Afterward, the physician must select one of the two options depending on whether they want to register a new patient (for which a new ID will be generated) or want to search an existing patient in the database.



Figure 6: Referring physician's Login (left). Selection window for new patient registration or for searching existing patients (right).

Then, the clinician must enter the necessary information for the patient and check the checkbox 'Petition for CCTA acquisition' if the patient needs a CCTA (Figure 7).

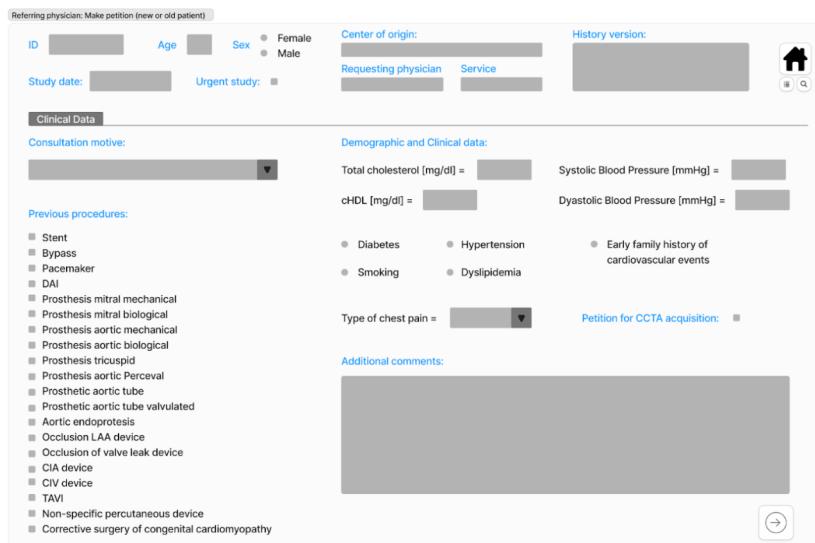
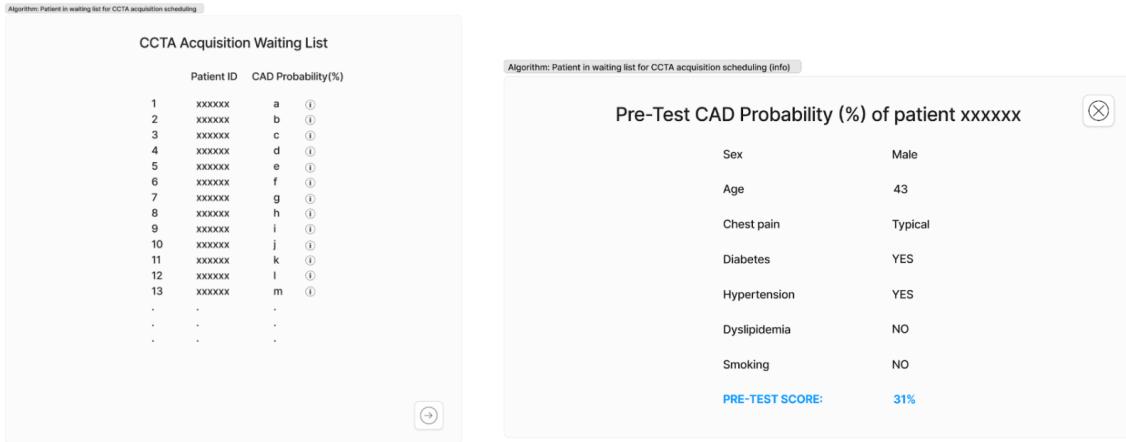


Figure 7: System to report clinical and demographic patient information. DAI: Implantable cardioverter-defibrillators. LAA: left atrial appendage. CIA: atrial septal defect. CIV: ventricular septal defect. TAVI: transcatheter aortic valve implantation. cHDL: high-density lipoprotein cholesterol. CCTA: coronary computed tomography angiography.

#### 4.1.2 Interface for UIFC administration

From the information inputted by the referring physician, patients needing a CCTA will be ordered by priority for acquisition. This order will be shown to the UIFC administrator in charge of scheduling CCTA acquisitions with the corresponding explainability of the results by clicking on the information button at the right of the patient (Figure 8).



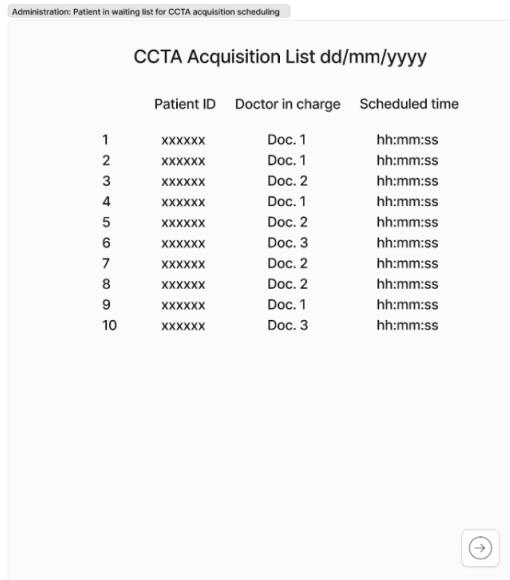
Patient ID	CAD Probability(%)
1	a (i)
2	b (i)
3	c (i)
4	d (i)
5	e (i)
6	f (i)
7	g (i)
8	h (i)
9	i (i)
10	j (i)
11	k (i)
12	l (i)
13	m (i)
.	.
.	.
.	.

Pre-Test CAD Probability (%) of patient xxxxx	
Sex	Male
Age	43
Chest pain	Typical
Diabetes	YES
Hypertension	YES
Dyslipidemia	NO
Smoking	NO
<b>PRE-TEST SCORE:</b>	<b>31%</b>

Figure 8: Optimal CCTA acquisition order (left) and Explainability of order (right). CAD: coronary artery disease. CCTA: coronary computed tomography angiography.

From this CCTA acquisition optimal order, the UIFC administrator will schedule the CCTA acquisitions linked to the corresponding day and Cardiac Imaging Expert (Figure 9).

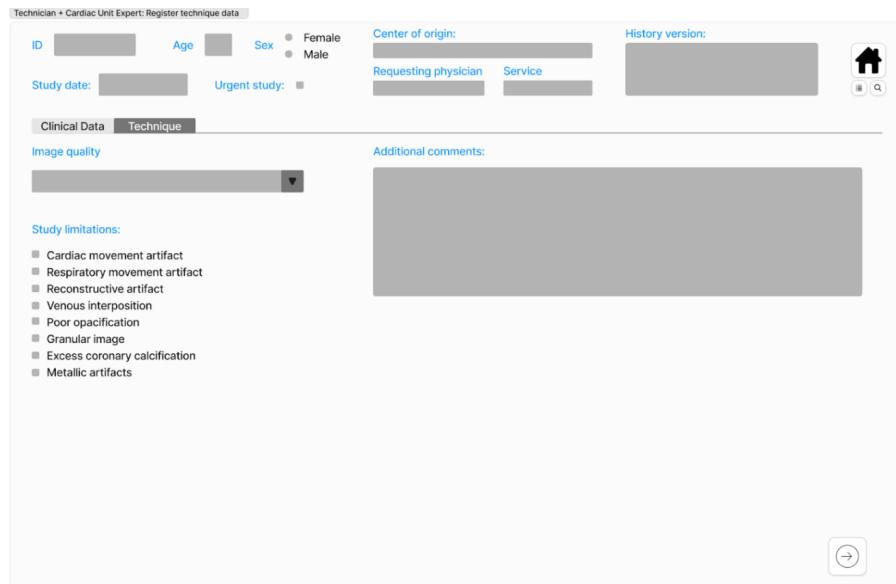


Patient ID	Doctor in charge	Scheduled time
1	xxxxxx	Doc. 1 hh:mm:ss
2	xxxxxx	Doc. 1 hh:mm:ss
3	xxxxxx	Doc. 2 hh:mm:ss
4	xxxxxx	Doc. 1 hh:mm:ss
5	xxxxxx	Doc. 2 hh:mm:ss
6	xxxxxx	Doc. 3 hh:mm:ss
7	xxxxxx	Doc. 2 hh:mm:ss
8	xxxxxx	Doc. 2 hh:mm:ss
9	xxxxxx	Doc. 1 hh:mm:ss
10	xxxxxx	Doc. 3 hh:mm:ss

Figure 9: CCTA acquisition scheduled order. CCTA: coronary computed tomography angiography.

#### 4.1.3 Interface for CCTA technician

After image acquisition, the technician will input the technique information into the database (Figure 10).

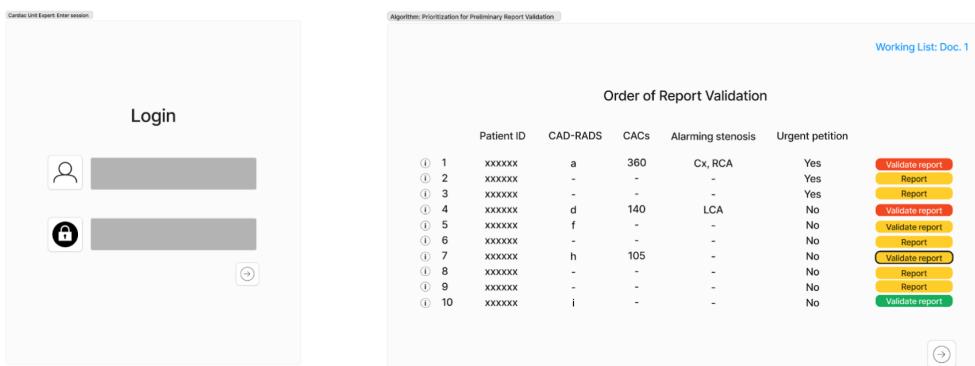


The screenshot shows a web-based form titled "Technician + Cardiac Unit Expert: Register technique data". It includes fields for "ID" (with a placeholder "XXXXXX"), "Age" (with a dropdown menu), "Sex" (radio buttons for "Female" and "Male"), "Center of origin" (text input), "History version" (text input), "Study date" (text input), "Urgent study" (checkbox), "Requesting physician" (text input), and "Service" (text input). There are tabs for "Clinical Data" and "Technique". Under "Image quality", there is a dropdown menu. A large text area for "Additional comments" is present. On the left, a list of "Study limitations" is shown with checkboxes: "Cardiac movement artifact", "Respiratory movement artifact", "Reconstructive artifact", "Venous interposition", "Poor opacification", "Granular image", "Excess coronary calcification", and "Metallic artifacts". At the bottom right is a circular save button with a checkmark.

Figure 10: System to report technique-related information.

#### 4.1.4 Interface for Cardiac Imaging Expert

After running the algorithm in the backlog, the Cardiac Imaging Expert will log in to their session (Figure 11) by introducing their ID, and their password and pressing enter or clicking on the arrow. Each session of each Cardiac Imaging Expert will have a worklist of ordered patients to evaluate that workday (Figure 12).



The screenshot shows two windows. The left window is a "Login" screen with fields for "User" (ID) and "Password". The right window is titled "Algorithm: Prioritization for Preliminary Report Validation" and "Working List: Doc. 1". It displays a table titled "Order of Report Validation" with 10 rows of patient data:

	Patient ID	CAD-RADS	CACs	Alarming stenosis	Urgent petition	
(i) 1	XXXXXX	a	360	Cx, RCA	Yes	<span style="background-color: red; color: white; border-radius: 5px; padding: 2px 5px;">Validate report</span>
(i) 2	XXXXXX	-	-	-	Yes	<span style="background-color: yellow; color: black; border-radius: 5px; padding: 2px 5px;">Report</span>
(i) 3	XXXXXX	-	-	-	Yes	<span style="background-color: yellow; color: black; border-radius: 5px; padding: 2px 5px;">Report</span>
(i) 4	XXXXXX	d	140	LCA	No	<span style="background-color: red; color: white; border-radius: 5px; padding: 2px 5px;">Validate report</span>
(i) 5	XXXXXX	f	-	-	No	<span style="background-color: yellow; color: black; border-radius: 5px; padding: 2px 5px;">Validate report</span>
(i) 6	XXXXXX	-	-	-	No	<span style="background-color: yellow; color: black; border-radius: 5px; padding: 2px 5px;">Report</span>
(i) 7	XXXXXX	h	105	-	No	<span style="background-color: yellow; color: black; border-radius: 5px; padding: 2px 5px;">Validate report</span>
(i) 8	XXXXXX	-	-	-	No	<span style="background-color: yellow; color: black; border-radius: 5px; padding: 2px 5px;">Report</span>
(i) 9	XXXXXX	-	-	-	No	<span style="background-color: yellow; color: black; border-radius: 5px; padding: 2px 5px;">Validate report</span>
(i) 10	XXXXXX	i	-	-	No	<span style="background-color: green; color: white; border-radius: 5px; padding: 2px 5px;">Validate report</span>

Figure 11: Cardiac Imaging Expert Login (left). Cardiac Imaging Expert Working List and order of Report Assessment (right). CAD-RADS: coronary artery disease reporting and data system. CACs: coronary artery calcium score. Cx: circumflex artery. RCA: right coronary artery. LCA: left coronary artery.

Next to each patient to be evaluated, the clinician can see critical values that provide a reference for the resulting order. Moreover, the clinician can click on the information button to have a detailed explainability as to why that patient is in that particular order. The explainability of each result varies if the patient has undergone or not the automatic workflow (Figure 12 and Figure 13).

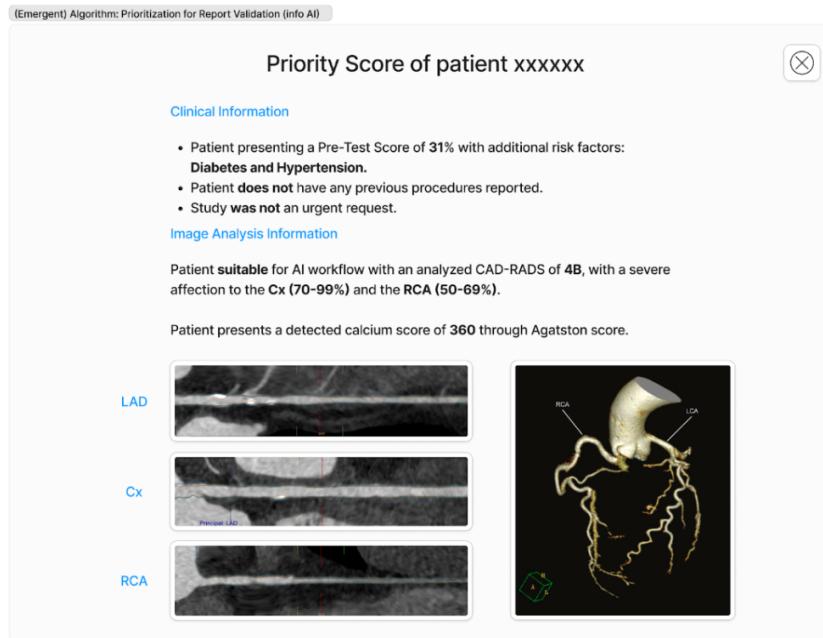


Figure 12: Explainability of the position in the reporting list for patients undergoing the automatic image analysis. AI: artificial intelligence. CAD-RADS: coronary artery disease reporting and data system. Cx: circumflex artery. RCA: right coronary artery. LAD: left coronary artery.

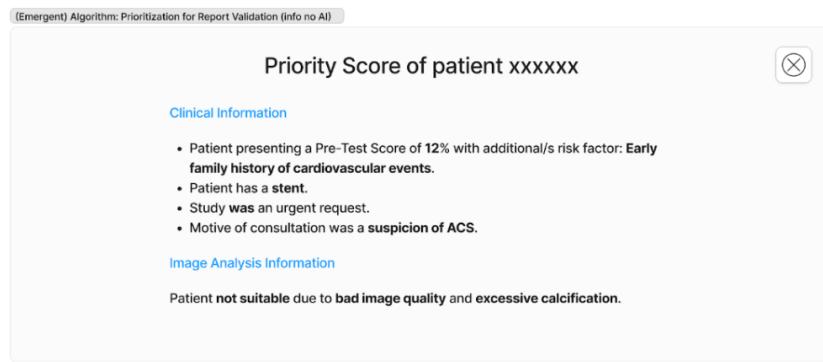
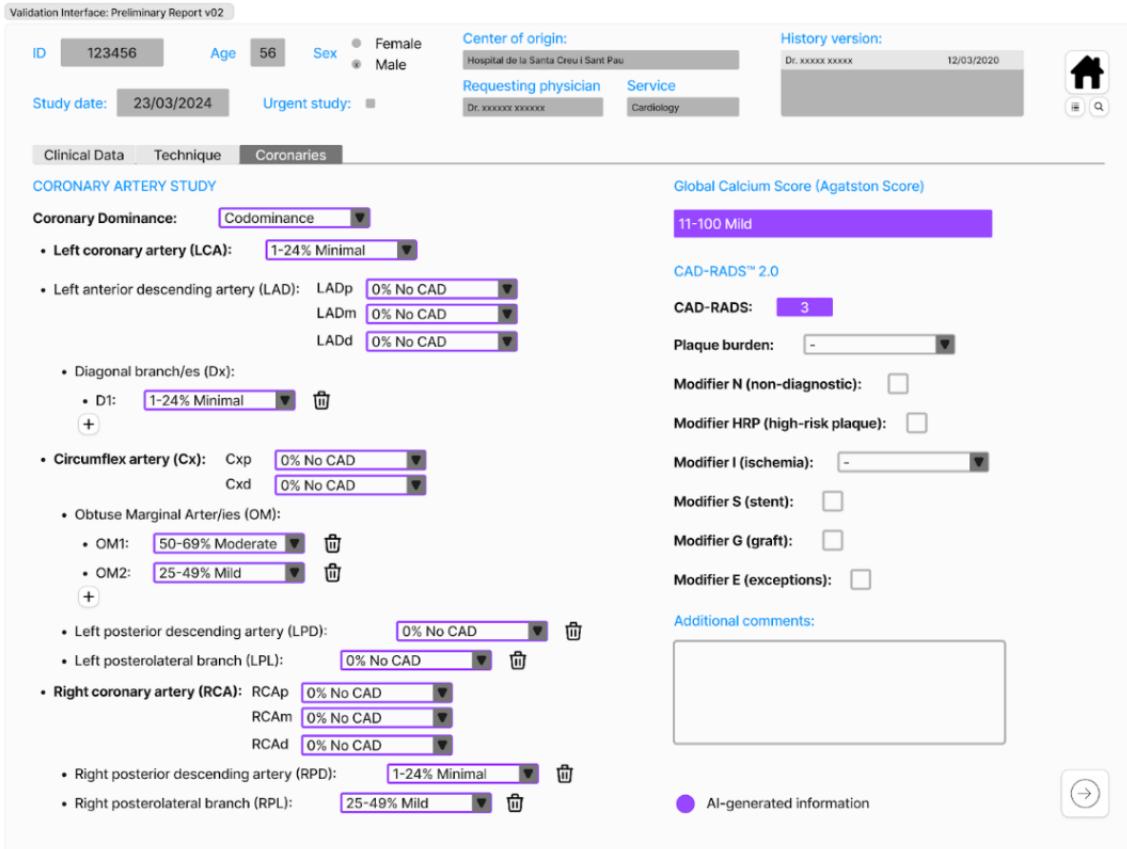


Figure 13: Explainability of the position in the reporting list for patients not undergoing the automatic image analysis. ACS: acute coronary syndrome.

The Cardiac Imaging Expert can choose which patient they want to report by clicking on the 'Validate report' or 'Report' buttons. For the chosen patient, the corresponding database will open with all the information registered (Figure 14).

Filled fields are non-modifiable while non-filled ones should be checked and validated by the Cardiac Imaging Expert.

To validate the image information, the clinician will be shown another window with the original CCTA coronary tree with the superposed automatic segmentation and the labeled segments (Figure 15).



Validation Interface: Preliminary Report v02

ID: 123456    Age: 56    Sex: Female    Center of origin: Hospital de la Santa Creu i Sant Pau    History version: Dr. XXXXXXXX 12/03/2020

Study date: 23/03/2024    Urgent study:

Clinical Data    Technique    Coronaries

**CORONARY ARTERY STUDY**

Coronary Dominance: Codominance

- Left coronary artery (LCA): 1-24% Minimal
- Left anterior descending artery (LAD):
  - LADp: 0% No CAD
  - LADm: 0% No CAD
  - LADD: 0% No CAD
- Diagonal branch/es (Dx):
  - D1: 1-24% Minimal
- Circumflex artery (Cx):
  - Cxp: 0% No CAD
  - Cxd: 0% No CAD
- Obtuse Marginal Arteries (OM):
  - OM1: 50-69% Moderate
  - OM2: 25-49% Mild
- Left posterior descending artery (LPD): 0% No CAD
- Left posterolateral branch (LPL): 0% No CAD
- Right coronary artery (RCA):
  - RCAp: 0% No CAD
  - RCAm: 0% No CAD
  - RCAd: 0% No CAD
- Right posterior descending artery (RPD): 1-24% Minimal
- Right posterolateral branch (RPL): 25-49% Mild

Global Calcium Score (Agatston Score): 11-100 Mild

CAD-RADS™ 2.0: CAD-RADS: 3

Plaque burden: -

Modifier N (non-diagnostic):

Modifier HRP (high-risk plaque):

Modifier I (ischemia): -

Modifier S (stent):

Modifier G (graft):

Modifier E (exceptions):

Additional comments:

AI-generated information 

Figure 14: Reporting system with the case information automatically filled. -p: proximal. -m: medial. -d: distal. AI: artificial intelligence. CAD-RADS: coronary artery disease reporting and data system.

The clinician can change the necessary information from the automatic preliminary report such as the coronary tree dominance (Figure 16) or stenosis degree range of segments. Upon clicking on one segment of the visual support window, the corresponding cMPR will be shown and the clinician will be able to correct the label and the stenosis range if needed (Figure 17).

Moreover, the Cardiac Imaging Expert can delete non-existing segments by clicking the ‘trash’ button and add non-detected vessels by clicking the ‘+’ button (Figure 18 and Figure 19).

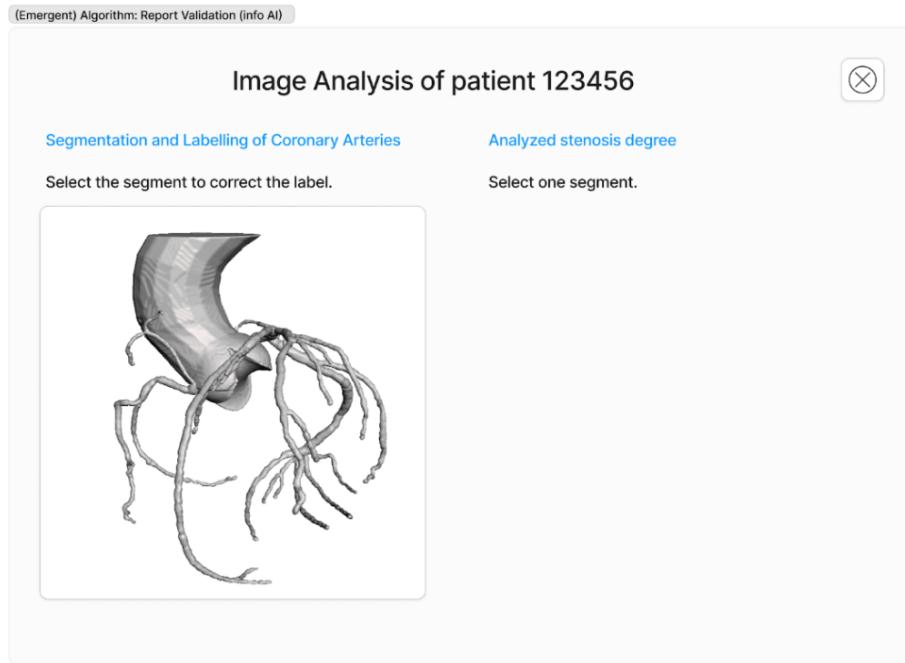


Figure 15: Visual support window.



Figure 16: Correction of the coronary tree dominance. -p: proximal. -m: medial. -d: distal. AI: artificial intelligence. CAD-RADS: coronary artery disease reporting and data system.

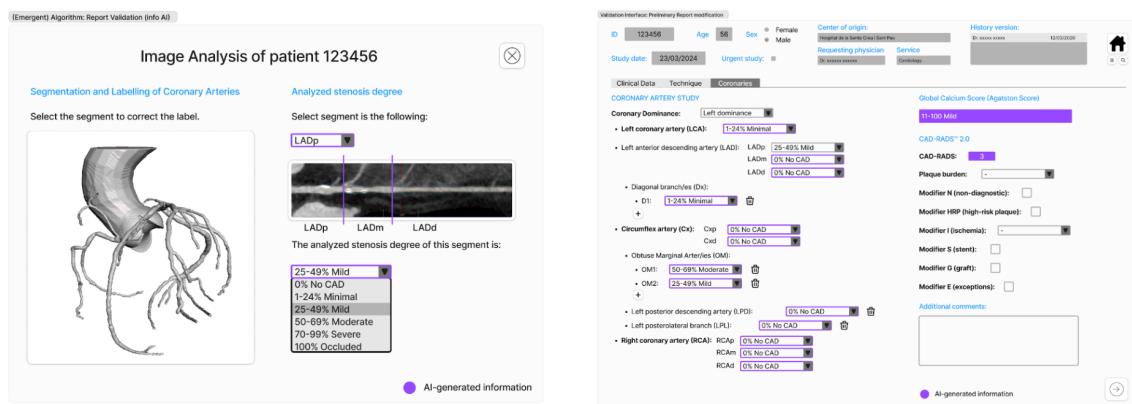


Figure 17: Correction of the proximal segment of the left anterior descending artery (LADp) stenosis degree range. -p: proximal. -m: medial. -d: distal. AI: artificial intelligence. CAD: coronary artery disease. CAD-RADS: CAD reporting and data system.

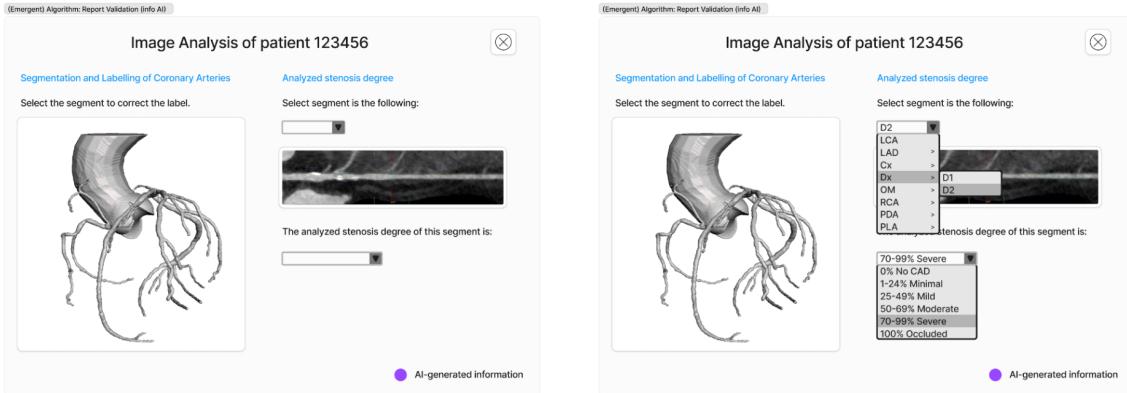


Figure 18: Addition of the coronary artery D2 using the visual supporting window. AI: artificial intelligence. LCA: left coronary artery. LAD: left anterior descending artery. Cx: circumflex artery. Dx: diagonal arteries. D1: first diagonal. D2: second diagonal. OM: obtuse marginal arteries. RCA: right coronary artery. PDA: posterior descending artery. PLA: posterolateral artery. CAD: coronary artery disease.

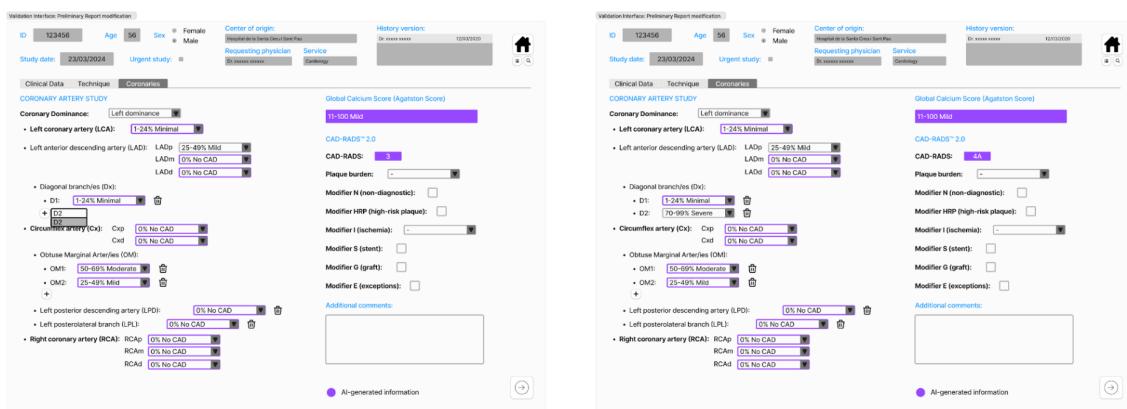


Figure 19: Addition of the coronary artery D2 using the reporting system. -p: proximal. -m: medial. -d: distal. AI: artificial intelligence. CAD-RADS: coronary artery disease reporting and data system.

## 4.2 Interface Mockup

The interface mockup has been developed using the PyQt library of Python, following the design proposed in the section above. Due to technical limitations and feedback from clinical implementation, the most recent version of the generated interface mockup may differ in some aspects from the original design presented in the section above.

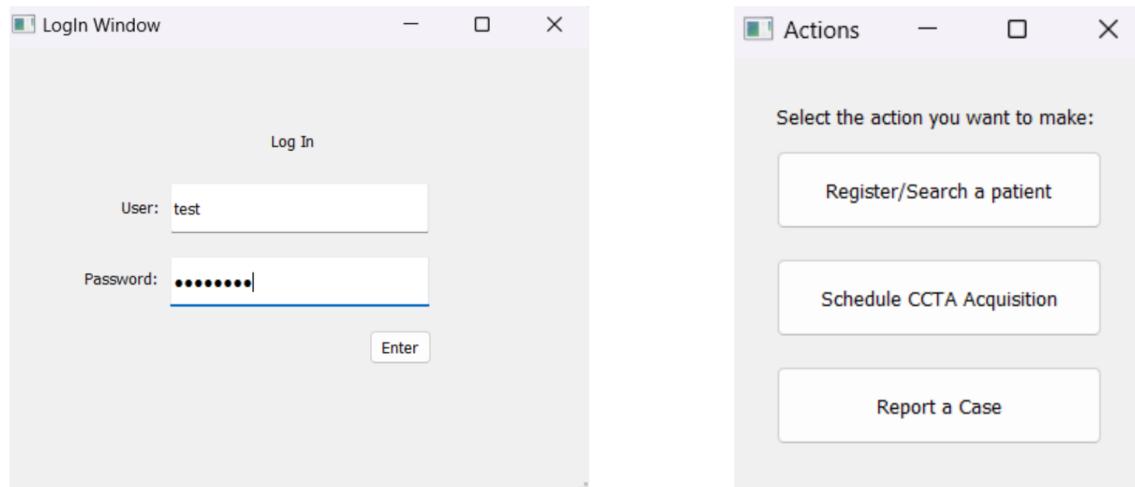


Figure 20: Login Window (left) and Actions to Perform (right). Depending on the user's permissions, access to the requested actions may vary. CCTA: coronary computed tomography angiography.

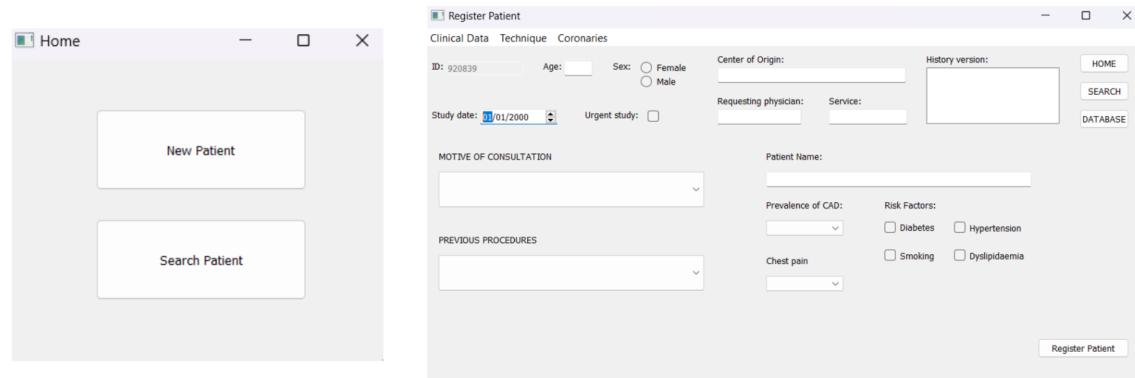


Figure 21: Register/Search a patient window (left). System to register patients by entering all the clinical data necessary (right). CAD: coronary artery disease.

Search Patient

Clinical Data Technique Coronaries

ID: <b>920835</b>	Age: 67	Sex: <input type="radio"/> Female <input checked="" type="radio"/> Male	Center of Origin: Hospital de la Santa Creu i Sant Pau	History version:	<b>HOME</b>
Study date: 26/02/2023	Urgent study: <input checked="" type="checkbox"/>	Requesting physician: Abdel Moustafa	Service: Emergency Room	<b>SEARCH</b>	<b>DATABASE</b>
MOTIVE OF CONSULTATION <input type="text" value="Other"/>			Patient Name: Loreto Benavent		
			Prevalence of CAD: Low	Risk Factors: <input checked="" type="checkbox"/> Diabetes <input type="checkbox"/> Hypertension	
PREVIOUS PROCEDURES <input type="text" value="Stent/ACTP"/>			Chest pain <input type="text" value="Typical"/>	<input type="checkbox"/> Smoking	<input checked="" type="checkbox"/> Dyslipidaemia
<b>SEARCH</b>					

Figure 22: System to search a patient and all the clinical data related to the patient search. ACTP: percutaneous transluminal coronary angioplasty. CAD: coronary artery disease.

CCTA Acquisition List

CCTA Acquisition Order

Order	ID	Age	Sex	Chest pain	Diabetes	Hypertension	Dyslipidaemia	Smoking	CACs	Model	%risk
1 (before: 14)	920835	67	Male	Typical	Yes	No	Yes	No	-	Clinical	68.85
2 (before: 4)	920831	82	Male	Non-specific	No	No	Yes	No	-	Clinical	58.61
3 (before: 10)	920836	54	Male	Typical	No	Yes	No	Yes	-	Clinical	48.45
4 (before: 13)	920826	69	Male	Atypical	No	No	Yes	Yes	-	Clinical	39.82
5 (before: 5)	920825	57	Male	Typical	No	No	No	No	-	Clinical	33.74
6 (before: 8)	920838	55	Male	Typical	No	No	No	No	-	Clinical	31.02
7 (before: 7)	920833	74	Male	Non-specific	No	No	Yes	No	-	Clinical	23.2
8 (before: 3)	920832	85	Female	Atypical	No	No	Yes	No	-	Clinical	22.9
9 (before: 9)	920834	69	Male	Atypical	No	No	No	No	-	Clinical	21.48
10 (before: 1)	920837	79	Male	Non-specific	No	No	No	No	-	Clinical	21.27
11 (before: 15)	920824	57	Male	Atypical	No	No	No	Yes	-	Clinical	17.09
12 (before: 6)	920830	60	Male	Non-specific	No	Yes	Yes	No	-	Clinical	15.1
13 (before: 11)	920829	72	Female	Non-specific	No	No	No	Yes	-	Clinical	6.82
14 (before: 2)	920827	61	Female	Non-specific	No	No	No	No	-	Clinical	2.28
15 (before: 12)	920828	45	Female	Non-specific	No	Yes	No	No	-	Clinical	1.2

Figure 23: CCTA acquisition list ordering the synthetic patients. CCTA: coronary computed tomography angiography. CACs: coronary artery calcium score.

Working List									
Urgent study	Order	Patient	Priority	CAD-RADS	Clinical info	Notes	Explainability		
True	1 (before: 4)	Vidal Alarcón	CRITICAL	4A*	Assessment of known coronary artery disease (not revascularized)		+ Validate		
True	2 (before: 9)	Gracia Hoz	CRITICAL	4A*	Other		+ Validate		
False	3 (before: 8)	Lalo Merino	CRITICAL	4A*	Other		+ Validate		
True	4 (before: 14)	Loreto Benavent	HIGH	-	Other	Stent/ACTP	+ Report		
False	5 (before: 12)	Amilcar Córdoba	HIGH	4B	Other		+ Validate		
False	6 (before: 7)	Augusto Cervera	MEDIUM	3	Screening for coronary artery disease in cardiomyopathy		+ Validate		
True	7 (before: 5)	Plácido Alegria	MEDIUM	3	Other		+ Validate		
True	8 (before: 1)	Iris Berrocal	MEDIUM	3	Other		+ Validate		
True	9 (before: 3)	Ileana Armengol	MEDIUM	3	No information		+ Validate		
False	10 (before: 11)	Fabio Andrés	MEDIUM	3	Other		+ Validate		
True	11 (before: 13)	Rodolfo Roselló	MEDIUM	-	Chest pain/atypical symptoms in patient without known CAD		+ Report		
True	12 (before: 2)	Reinaldo Carrasco	MEDIUM	-	Nonspecific ECG/Holter alteration	Suboptimal	+ Report		
False	13 (before: 10)	Evita Bas	LOW	2	Other		+ Validate		
True	14 (before: 15)	Jose Antonio Lucena	LOW	2	Chest pain/atypical symptoms in patient without known CAD		+ Validate		
True	15 (before: 6)	Joel Carranza	LOW	2	Checkup, patient without cardiology symptomatology or known coronary artery disease		+ Validate		

Figure 24: CCTA assessment list in order of priority after conducting the automatic analysis of the CCTA images (if applicable). Patient names are randomly generated. CAD: coronary artery disease. CCTA: coronary computed tomography angiography. CAD-RADS: CAD reporting and data system. ACTP: percutaneous transluminal coronary angioplasty. ECG: electrocardiogram.

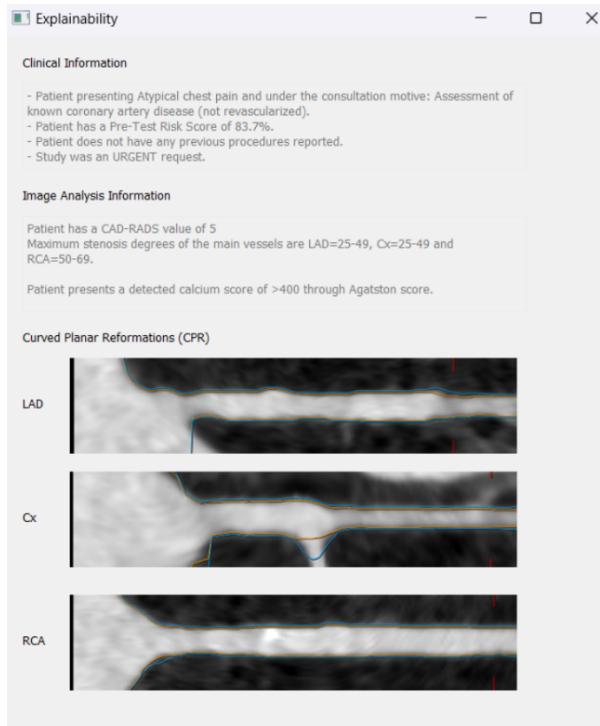


Figure 25: Explainability for the patient's order in the CCTA assessment list which has gone through automatic analysis of the CCTA image. CCTA: coronary computed tomography angiography. LAD: left anterior descending artery. Cx: circumflex artery. RCA: right coronary artery.

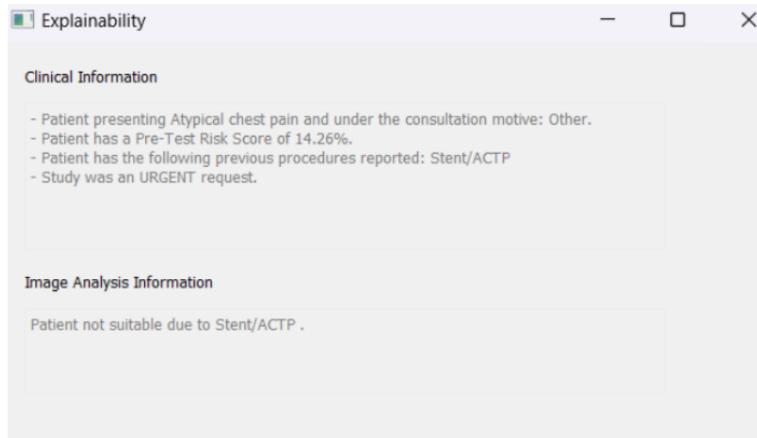


Figure 26: Explainability for the patient's order in the CCTA assessment list which has not gone through automatic analysis of the CCTA image. CCTA: coronary computed tomography angiography. ACTP: percutaneous transluminal coronary angioplasty.

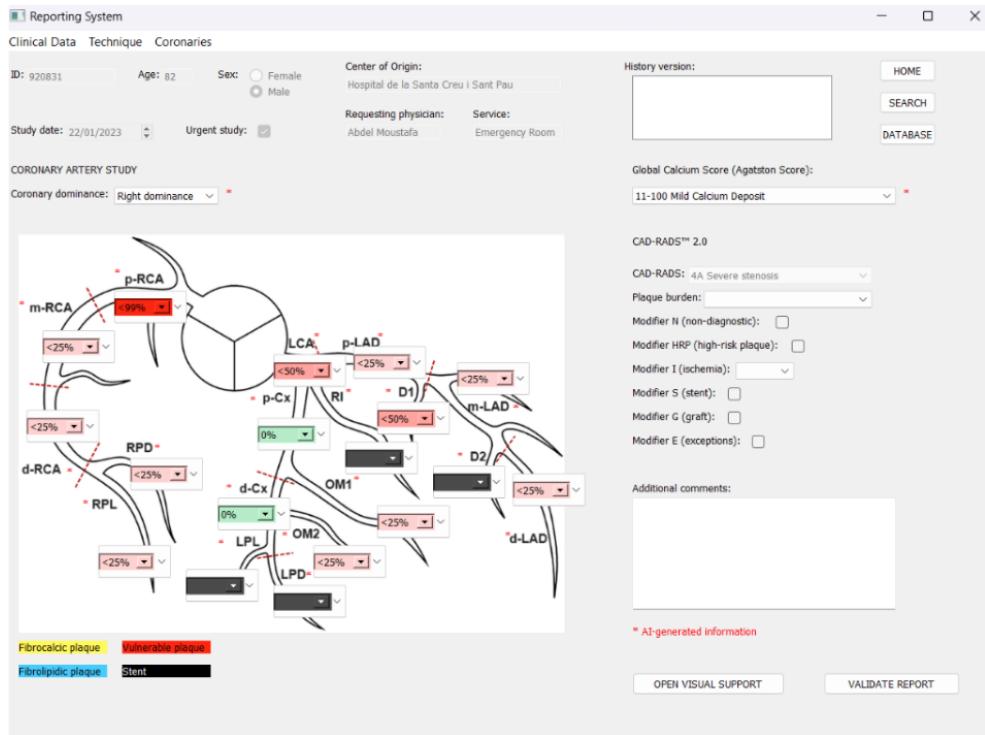


Figure 27: Snapshot of the interface displaying the integrated algorithm for validating preliminary case reports. This interface presents Cardiac Imaging Experts with the patient's clinical information alongside data theoretically automatically extracted from the CCTA image. CCTA: coronary computed tomography angiography. LCA: left coronary artery. LAD: left anterior descending artery. D1: first diagonal. D2: second diagonal. RI: ramus intermedius. Cx: circumflex artery. OM1: first obtuse marginal. OM2: second obtuse marginal. LPL: left posterolateral artery. LPD: left posterior descending artery. RCA: right coronary artery. RPL: right posterolateral artery. RPD: right posterior descending artery. p-: proximal segments. m-: medial segments. d-: distal segments. CAD-RADS: coronary artery disease reporting and data system. AI: artificial intelligence.

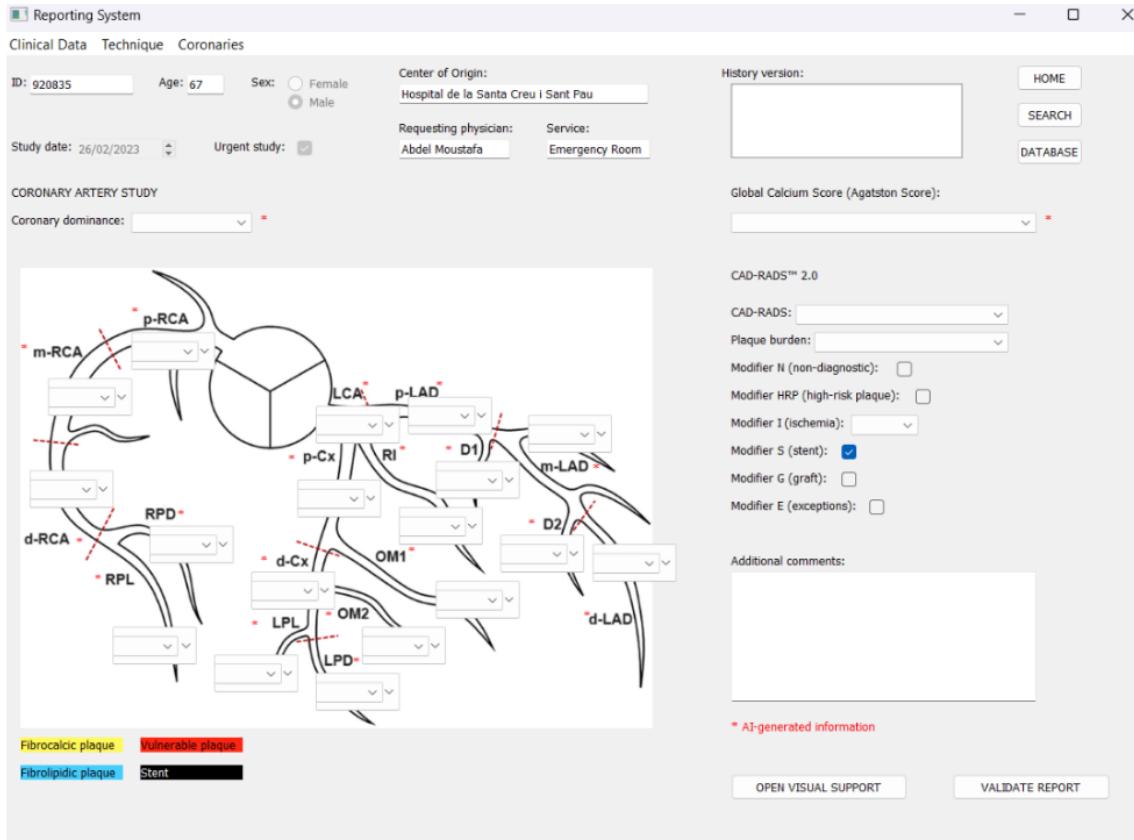


Figure 28: Snapshot of the interface displaying the integrated algorithm for generating preliminary case reports. This interface presents Cardiac Imaging Experts with only the patient's clinical information since data could not be automatically extracted from the CCTA image due to the stent. CCTA: coronary computed tomography angiography. LCA: left coronary artery. LAD: left anterior descending artery. D1: first diagonal. D2: second diagonal. RI: ramus intermedium. Cx: circumflex artery. OM1: first obtuse marginal. OM2: second obtuse marginal. LPL: left posterolateral artery. LPD: left posterior descending artery. RCA: right coronary artery. RPL: right posterolateral artery. RPD: right posterior descending artery. p-: proximal segments. m-: medial segments. d-: distal segments. CAD-RADS: coronary artery disease reporting and data system. AI: artificial intelligence.

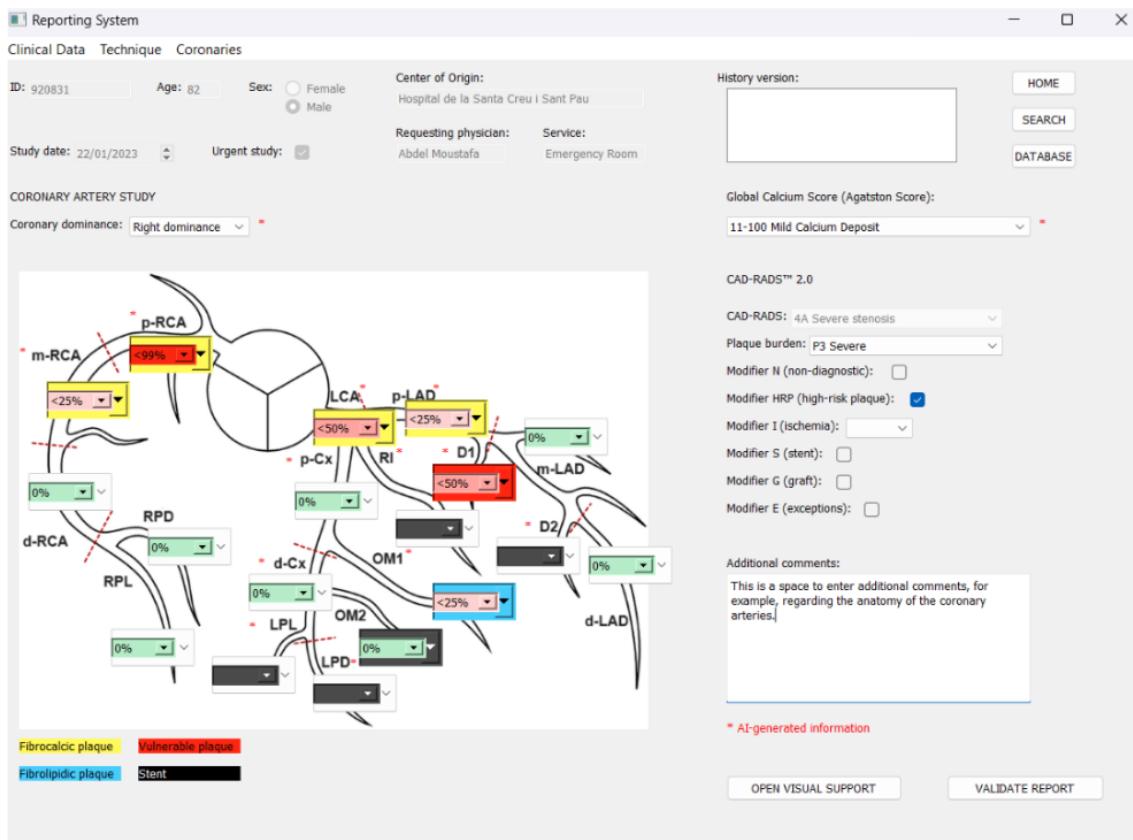


Figure 29: Corrections introduced in the reporting system regarding the stenosis degree range of some segments and the addition of plaque type. CCTA: coronary computed tomography angiography. LCA: left coronary artery. LAD: left anterior descending artery. D1: first diagonal. D2: second diagonal. RI: ramus intermedius. Cx: circumflex artery. OM1: first obtuse marginal. OM2: second obtuse marginal. LPL: left posterolateral artery. LPD: left posterior descending artery. RCA: right coronary artery. RPL: right posterolateral artery. RPD: right posterior descending artery. p-: proximal segments. m-: medial segments. d-: distal segments. CAD-RADS: coronary artery disease reporting and data system. AI: artificial intelligence.

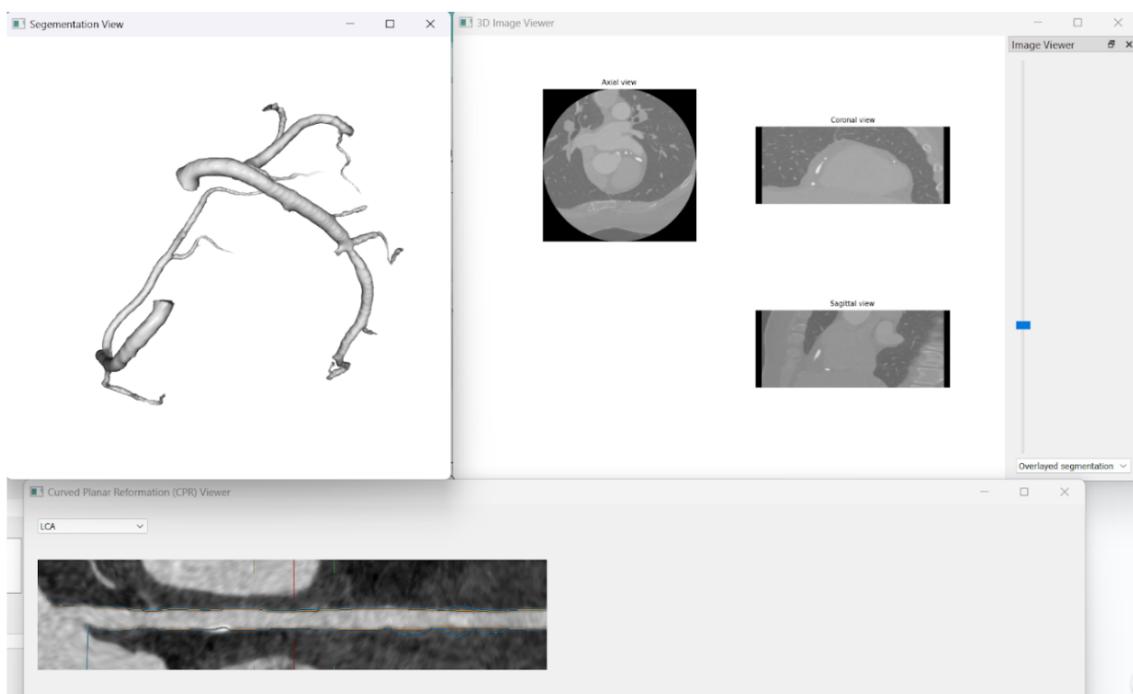


Figure 30: Visual support windows consisting of a 3D visualization of the segmented coronary tree (top left), original CCTA images in coronal, axial, and sagittal axes with overlapping segmented coronary vessels (top right), and cMPRs of selected vessels (bottom). CCTA: coronary computed tomography angiography. cMPRs: curved multiplanar reformations.

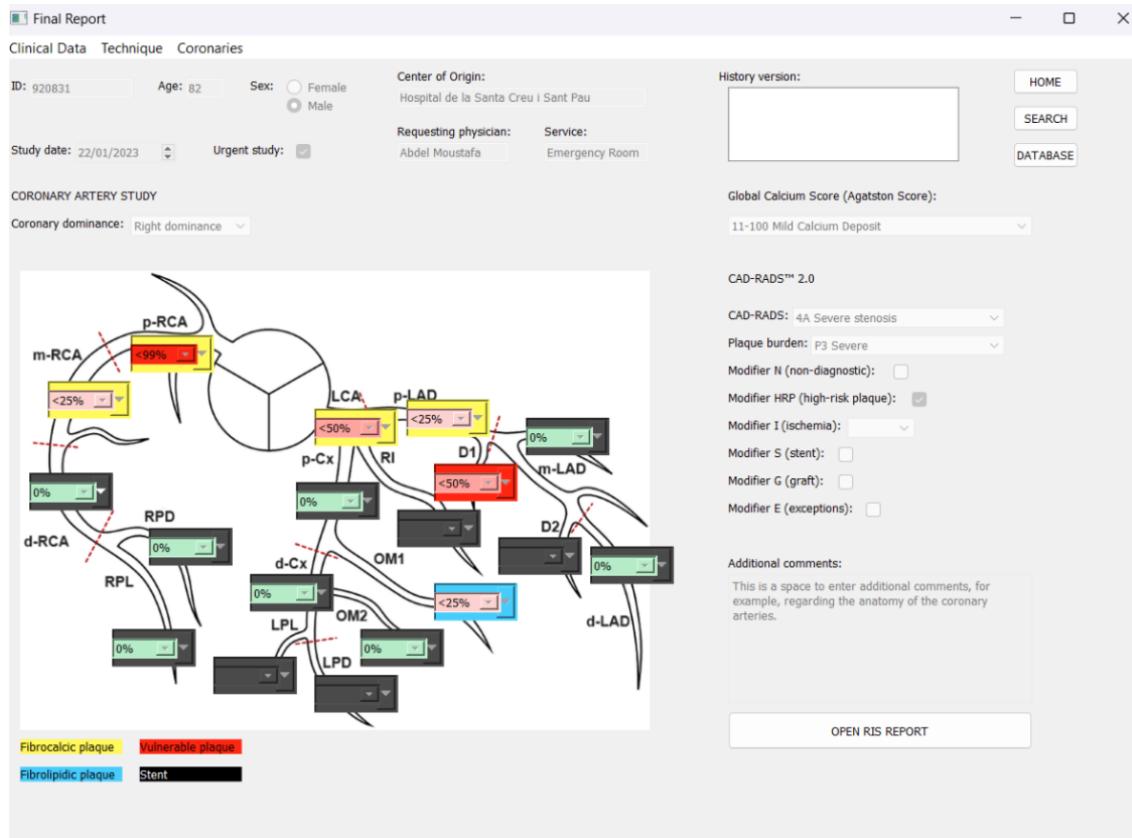


Figure 31: Final case report validated by the clinician with non-modifiable data. LCA: left coronary artery. LAD: left anterior descending artery. D1: first diagonal. D2: second diagonal. RI: ramus intermedium. Cx: circumflex artery. OM1: first obtuse marginal. OM2: second obtuse marginal. LPL: left posterolateral artery. LPD: left posterior descending artery. RCA: right coronary artery. RPL: right posterolateral artery. RPD: right posterior descending artery. p-: proximal segments. m-: medial segments. d-: distal segments. CAD-RADS: coronary artery disease reporting and data system.

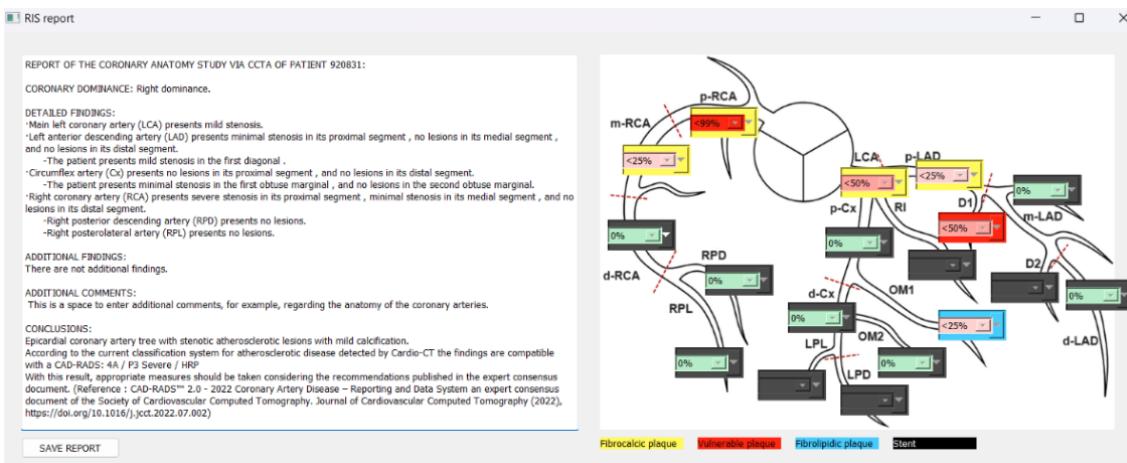


Figure 32: Final case report for RIS upload. RIS: radiology information system. CCTA: coronary computed tomography angiography. LCA: left coronary artery. LAD: left anterior descending artery. D1: first diagonal. D2: second diagonal. RI: ramus intermedium. Cx: circumflex artery. OM1: first obtuse marginal. OM2: second obtuse marginal. LPL: left posterolateral artery. LPD: left posterior descending artery. RCA: right coronary artery. RPL: right posterolateral artery. RPD: right posterior descending artery. p-: proximal segments. m-: medial segments. d-: distal segments. CAD-RADS: coronary artery disease reporting and data system.

## 5 Annex 5: Templates for clinical assessment

### 5.1 Template for evaluation of the global implementation of the prioritization algorithms

This template is intended for clinicians, and its goal is to register the semi-quantitative clinical assessment of the global implementation focusing mainly on the prioritization methodologies used to optimize the workflow. It follows the JBI Critical Appraisal Checklist for Case Reports with a modified set of questions adapted to the evaluation of the solution.

This template, as the other JBI templates, records a set of information consisting of the name of the clinician performing the review, the author of the solution being evaluated, the date and the year of review, and the number of the record. The questions to evaluate the solution assess, among others, factors such as solving the problems present in the currently used workflow, alignment of the solution with clinical objectives and guidelines, and enhancement of the decision-making process and patient outcomes. These are close-ended response questions that can have a positive, negative, unclear, or non-applicable result. Each positive answer is counted as a full point while unclear answers are counted as half point for the scoring out of the 6 questions. Moreover, clinicians can also add comments to further explain their answers or make suggestions for improvement.

Reviewer: _____	Date: _____		
Author: _____	Year: _____	Record Number: _____	
Which problems/areas of improvements (AOI) do you identify in your current CAD diagnosis workflow? <hr/> <hr/>			
Yes    No    Unclear    Not applicable			
1 Do you think that the proposed optimized workflow (partly) addresses these problems/AOI? <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> 2 The optimized workflow aligns with the objectives of your daily practice? <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> 3 The workflow aligns with established clinical guidelines? <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> 4 Do you think that this workflow would enhance your decision-making process? <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> 5 Do you think that this workflow could improve patient outcomes? <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> 6 Do you think that this workflow could impact patient care, resource allocation, or other relevant clinical outcomes? <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>			
Comments: <hr/> <hr/> <hr/>			
Score: ___ /6			

Figure 33: Template for clinical evaluation of the global implementation of the algorithm.  
CAD: coronary artery disease.

## 5.2 Template for clinical evaluation of the interface

This template is intended for clinicians, and its goal is to register the clinical feedback on the positive and negative features of the interface in which the optimization workflow is deployed.

This template records the name of the clinician performing the review, the author of the solution, the date of revision, and the year. The questions to evaluate the interface assess, among others, factors such as usability and intuitiveness. These are close-ended response questions that can have a positive, negative, unclear, or non-applicable result. Each positive answer is counted as a full point while unclear answers are counted as half point for the scoring out of the 6 questions. Moreover, clinicians can also add comments to further explain their answers or make suggestions for improvement.

Reviewer: _____	Date: _____		
Author: _____	Year: _____	Record Number: _____	
Yes    No    Unclear    Not applicable			
1   Is the interface's information distribution clear?	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
2   Is the interface easy to use?	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
3   Is the interface intuitive?	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
4   Does the interface enhance report interpretation?	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		
Comments: _____ _____			
Score: ___ /4			

Figure 34: Template for clinical evaluation of the interface.

## 5.3 Clinical Feedback

In this section, a translated version of the original feedback given by two cardiologists at Hospital de la Santa Creu i Sant Pau can be found.

Reviewer: [Dr. Abdel Hakim Moustafa](#)

Date: [22/05/2024](#)

Author: [Eva Ferrer Beltran](#)

Year: [2024](#)

Record Number: [NA](#)

Which problems/areas of improvements (AOI) do you identify in your current CAD diagnosis workflow?

Prioritize, automate the working list and structured reporting.

		Yes (+1)	No (+0)	Unclear (+0.5)	Not applicable (+0)
1	Do you think that the proposed optimized workflow (partly) addresses these problems/AOI?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2	The optimized workflow aligns with the objectives of your daily practice?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3	The workflow aligns with established clinical guidelines?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4	Do you think that this workflow would enhance your decision-making process?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5	Do you think that this workflow could improve patient outcomes?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6	Do you think that this workflow could impact patient care, resource allocation, or other relevant clinical outcomes?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Comments:

[Our workflow is very fragmented where we use several solutions for it and usually generate unstructured reports that are not linked to the EHR or RIS.](#)

Score: [6/6](#)

Figure 35: Clinical feedback about the global implementation of the proposed workflow registered in the aforementioned template. CAD: coronary artery disease.

Reviewer: [Dr. Abdel Hakim Moustafa](#)

Date: [22/05/2024](#)

Author: [Eva Ferrer Beltran](#)

Year: [2024](#)

Record Number: [NA](#)

		Yes (+1)	No (+0)	Unclear (+0.5)	Not applicable (+0)
1	Is the interface's information distribution clear?	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
2	Is the interface easy to use?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3	Is the interface intuitive?	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
4	Does the interface enhance report interpretation?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Comments:

[Use the diagram of the coronary arteries and have easier access to the CPRs.](#)

Score: [3/4](#)

Figure 36: Clinical feedback about the interface in which the proposed workflow has been deployed, registered in the aforementioned template.

Reviewer: Dr. Rubén Leta Petracca      Date: 28/05/2024

Author: Eva Ferrer Beltran      Year: 2024      Record Number: NA

Which problems/areas of improvements (AOI) do you identify in your current CAD diagnosis workflow?

Prioritization of studies of suboptimal quality.

	Yes (+1)	No (+0)	Unclear (+0.5)	Not applicable (+0)
1 Do you think that the proposed optimized workflow (partly) addresses these problems/AOI?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2 The optimized workflow aligns with the objectives of your daily practice?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3 The workflow aligns with established clinical guidelines?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4 Do you think that this workflow would enhance your decision-making process?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5 Do you think that this workflow could improve patient outcomes?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6 Do you think that this workflow could impact patient care, resource allocation, or other relevant clinical outcomes?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Comments:  
This prioritization system clearly improves workflow and optimizes the analysis time of coronary studies, allowing a larger number of patients to be addressed more efficiently.

Score: 6/6

Figure 37: Clinical feedback about the global implementation of the proposed workflow registered in the aforementioned template. CAD: coronary artery disease.

Reviewer: Dr. Rubén Leta Petracca      Date: 28/05/2024

Author: Eva Ferrer Beltran      Year: 2024      Record Number: NA

	Yes (+1)	No (+0)	Unclear (+0.5)	Not applicable (+0)
1 Is the interface's information distribution clear?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2 Is the interface easy to use?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3 Is the interface intuitive?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4 Does the interface enhance report interpretation?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Comments:  
Each of the labels are displayed appropriate to the clinical information expected from the interface.

Score: 4/4

Figure 38: Clinical feedback about the interface in which the proposed workflow has been deployed, registered in the aforementioned template.

## 6 Annex 6: Effectiveness validation process

The following process describes the detailed method for evaluating the Key Performance Indicator (KPI) related to the reduction of time expected from the implementation of the optimized CAD diagnosis workflow.

### 6.1 Reduction in time in severe cases as a result of prioritization for image acquisition

This process aims to evaluate the number of days elapsed from patient consultation to CCTA image acquisition in severe cases (patients with a CAD-RADS equal to or over 3) in the traditional process and compare it to the potential duration under the proposed solution. The following steps are taken:

1. Take a patient cohort of approximately 5 patients scheduled for image acquisition on the same day.
2. Annotate the acquisition day and the order in which the patients will undergo CCTA acquisition.
3. Annotate, for each patient, the consultation date on which this CCTA acquisition was requested. This information can be found in the hospital's management system.
4. Calculate, for each patient, the number of days elapsed between the CCTA acquisition request and the CCTA acquisition.
5. Use the proposed prioritization algorithm to determine the most optimal order for CCTA acquisition.
6. Reorder the patients by the order proposed by the algorithm and order the elapsed times from CCTA acquisition request to CCTA acquisition increasingly. This will exemplify that, in principle, the prioritized patients move faster through the diagnosis process.
7. Reassign the elapsed times for each of the patients with the new order.

### 6.2 Reduction in time in severe cases as a result of prioritization for case report validation

This process aims to evaluate the number of days elapsed from CCTA image acquisition to the CAD diagnosis in severe cases in the traditional process and compare it to the potential duration under the proposed solution. The following steps are taken:

1. Take the previous patient cohort of approximately 5 patients scheduled for image acquisition on the same day.

2. Annotate the acquisition day (which will be the same date on which the case will be reported) and the order in which the patients will have the CCTA reported.
3. Annotate, for each patient, the next date on which consultation with the referring physician will take place. This information can be found in the hospital's management system.
4. Calculate, for each patient, the number of days elapsed between CCTA acquisition and the next visit with the referring physician.
5. Use the proposed prioritization algorithm to determine the most optimal order for CCTA reporting.
6. Reorder the patients by the order proposed by the algorithm and order the elapsed times from CCTA acquisition to diagnosis increasingly. This will exemplify that, in principle, the prioritized patients move faster through the diagnosis process.
7. Reassign the elapsed times for each of the patients with the new order.

### 6.3 Reduction in time in severe cases as a result of the implementation of the prioritization algorithms

1. For each patient, calculate the total time elapsed from the CCTA acquisition request to diagnosis in the original workflow.
2. For each patient, Calculate the total time elapsed from CCTA acquisition request to diagnosis once patients have been prioritized and the elapsed time has been reordered.
3. Compare these times for every patient and determine the percentage change in the original elapsed time.
4. If for severe cases ( $CAD-RADS \geq 3$ ) the solution generates a substantial time reduction in at least 50% of the cases, it will be considered effective.

## Bibliography - Additional Information

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- [2] *Reglamento (UE) 2017/745 del Parlamento Europeo y del Consejo, de 5 de abril de 2017, sobre los productos sanitarios, por el que se modifican la Directiva 2001/83/CE, el Reglamento (CE) n.º 178/2002 y el Reglamento (CE) n.º 1223/2009 y por el que se derogan las Directivas 90/385/CEE y 93/42/CEE del Consejo (Texto pertinente a efectos del EEE).* ) Legislative Body: CONSIL, EP. Apr. 2017. URL: <http://data.europa.eu/eli/reg/2017/745/oj/spa>.
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- [4] Jaume Marrugat et al. “Estimación del riesgo coronario en España mediante la ecuación de Framingham calibrada”. In: *Revista Española de Cardiología* 56.3 (Mar. 2003). Publisher: Elsevier, pp. 253–261. ISSN: 0300-8932. DOI: [10.1157/13043951](https://doi.org/10.1157/13043951). URL: <http://www.revespcardiol.org/es-estimacion-del-riesgo-coronario-espana-articulo-13043951>.
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