Research Protocol:

High-Risk Plaques Identification using Coronary Computed Tomography and Computational Fluid Dynamics

Submitted to:

Institutional Review Board

BUET, Dhaka-1000, Bangladesh.

Principal Investigator

Prof. Dr. Muhammad Tarik Arafat

Department of Biomedical Engineering

BUET, Dhaka, Bangladesh.

Co-Principal Investigator:

Prof. (Dr.) M G Azam
Professor of Cardiology
MBBS, MD (Cardiology), FSCAI (USA)
Clinical and Interventional Cardiologist
Fellow, Interventional Cardiologist, Germany Professor of Cardiology
National Institute of Cardiovascular Diseases (NICVD)
LABAID Limited (Diagnostics)

Date of Submission:28.08.24

DOCUMENTS TO BE SUBMITTED FOR ETHICAL APPROVAL

01. Filled-up Ethical Clearance Application Form. (*Annexure - A*)

02. Signature of Principal Investigator (s) & Co-investigator (s) with details address. (*Annexure – A*)

03. Abstract for BME Ethical Review Committee (BMEERC) (*Annexure - B*)

04. BMRC format for Submission of the Proposal for Ethical Approval (*Annexure - C*)

05. Informed consent form (Both Bangla and English) from participants or from the Parent / legal guardian. (*Annexure - D*)

06. Budget (*Annexure - E*)

ANNEXURE - A

Application for Ethical Clearance

1. Principal Investigator(s):

Name: Dr. Muhammad Tarik Arafat

Qualification: Professor

Detail Address: Department of Biomedical Engineering, BUET, Dhaka, Bangladesh.

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2. Co-Investigator(s):

Name: Dr. M G Azam

Qualification: Professor of Cardiology, MBBS, MD (Cardiology), FSCAI (USA)

Detail Address: Room No-301, Middle Block, NICVD, Dhaka

3. Place of the Study/Institution(s): Department of Interventional Cardiology, National Institute of Cardiovascular Diseases & Hospital (Data Collection). Biomechanics Lab, BME, BUET (CFD & statistical analysis)

4. Title of Study: High-Risk Plaques Identification using Coronary Computed Tomographic Angiography and Computational Fluid Dynamics.

5. Type of Study: Observational Study

6. Duration of Study: 6 months

7. Total Cost: Tk**.** 80,000/-

8. Funding Agency: N/A

Circle the appropriate answer to each of the following
(If not Applicable write NA)

1. Source of Population:

(a) ill Participant — (Yes) No

(b) Non-ill Participant — Yes (No)

(c) Minors or persons under guardianship — Yes (No)

2. Does the study involve?

(a) Physical risks To the subjects — (Yes) No

(b) Social Risks — Yes (No)

(c) Psychological Risks to subjects — Yes (No)

(d) Discomfort to Subjects — (Yes) No

(e) Invasion of the body — Yes (No)

(f) Invasion of Privacy — Yes (No)

(g) Disclosure of Information damaging to Subject or others — Yes (No)

3. Does the study involve?

(a) Use of records, (Hospital, medical, Death, birth or other) — (Yes) No

(b) Use of fetal tissue Or abortus — Yes (No)

(c) Use of organs or Body fluids — (Yes) No

4. Are subjects clearly informed about?

(a) Nature and purposes of study — (Yes) No

(b) Procedures to be followed including — (Yes) No

(c) Physical risks — (Yes) No

(d) Private questions — Yes (No)

(e) Invasion of the Body — Yes (No)

(f) Benefits to be Derived — (Yes) No

(g) Right to refuse to participate or to withdraw from study — (Yes) No

(h) Confidential handling of data — (Yes) No

(i) Compensation where there are risks or loss of working time or privacy is involved in any particular procedure — N/A

5. Will signed consent form/verbal consent be required?

(a) From Subjects — (Yes) No

(b) From parent or guardian (if subjects are minors) — N/A

6. Will precautions be taken to protect anonymity of subjects — (Yes) No

Note: If the final instrument / questionnaire is not completed prior to review, the following information should be included in the abstract.

1. A description of the areas to be covered in the questionnaire or interview which could be considered either sensitive or which would constitute an invasion of privacy.
2. Examples of the type of specific question to be asked in the sensitive areas.
3. An indication as to whom the questionnaire will be presented to the committee for review.

We agree to obtain approval of the Ethical Review Committee for any changes involving the rights and welfare of subjects or any changes of the Methodology before making any such changes.

Signature

Prof. Dr. Muhammad Tarik Arafat

Professor, Department of Biomedical Engineering

BUET, Dhaka, Bangladesh.

Date:

Name of Co-investigator (S) **Signature:**

1. Name:
Prof. (Dr.) M G Azam
Qualification:
Professor of Cardiology, MBBS, MD (Cardiology), FSCAI (USA)
Detail Address: Room No-301, Middle Block, NICVD, Dhaka

ANNEXURE - B

PREPARATION OF AN ABSTRACT

The Ethical Review Committee will not consider any application which does not include a specific abstract/summary for the committee. The abstract should summarize the purpose of the study, the methods and procedures to be used, by addressing each of the following items. If an item is not applicable, please note accordingly:

1. Describe the requirements in respect of the population and explain the rationale for using population of special groups such as children, Incompetent person or groups whose ability to give voluntary informed consent is questionable.

   Response: This study was a single center observational study who underwent Computed Tomography (CT) for coronary artery disease in our institute. Patients who had advanced kidney disease, hemodialysis, severe liver disease, hyperthyroidism, and a history of coronary bypass surgery were all excluded.

2. Describe and assess any potential risks - physical, psychological, social, legal or other and assess the likelihood and seriousness of such risks. If methods of research create potential risks, describe other methods, if any, that were considered and why they cannot be used.

   Response: CFD analysis often requires imaging techniques like CT or MRI. Repeated imaging can expose patients to radiation, potentially increasing the risk of radiation-induced conditions. Use of contrast agents in imaging can cause allergic reactions or kidney damage. Patients diagnosed with cardiovascular diseases might face social stigma, affecting their personal and professional relationships. Handling sensitive patient data poses risks of data breaches and unauthorized access.

   Despite the potential risks, the use of imaging techniques combined with CFD provides unparalleled precision in identifying plaque rupture risks. The benefits of accurate diagnosis and the ability to tailor treatment plans outweigh the potential risks, provided that stringent safety protocols are followed. This includes minimizing radiation exposure, using non-invasive methods when possible, ensuring thorough patient education and consent, and protecting patient data.

   Alternative Methods Considered: -

   i. **Non-Invasive Imaging (e.g., Ultrasound):-** While safer, these methods may not provide the detailed information required for accurate CFD analysis.

      Reason for Not Using: Insufficient detail and accuracy for CFD modeling.

   ii. **Biomarkers:-** Blood tests for inflammatory markers can indicate risk but cannot provide detailed spatial information about plaque stability.

Reason for Not Using: Lack of spatial resolution and precision.

3. Describe procedures for protecting against or minimizing potential risks and assessment of their likely effectiveness.

   Response: Use of low-dose imaging protocols, and limiting the frequency of imaging to essential instances only. Advances in imaging technology have significantly reduced radiation doses while maintaining image quality. Pre-screening patients for allergies and renal function, using non-contrast imaging techniques when possible, and ensuring adequate hydration before and after the procedure. Proper pre-screening and hydration can significantly reduce the risk of adverse reactions. Utilize non-invasive imaging methods whenever possible, and strictly adhere to aseptic techniques during invasive procedures. Non-invasive imaging methods like MRI or CT can often replace invasive procedures, significantly reducing risks.

   Legal risks: Implementing robust data encryption, access controls, and regular audits to ensure compliance with data protection regulations. Strong data protection measures can significantly reduce the risk of data breaches. Developing comprehensive and easily understandable consent forms, and ensuring thorough discussions with patients about the risks and benefits. Properly informed consent processes can effectively mitigate legal risks.

   The effectiveness of all procedures is generally high, ensuring patient safety while maintaining diagnostic accuracy.

4. Include a description of the methods for safeguarding confidentiality or protecting anonymity.

   Response: The data collected by the study physicians will be kept confidential at all times. Remove or anonymize personally identifiable information (PII) from datasets used for CFD analysis. Ensure patients are fully informed about how their data will be used, and obtain explicit consent for data use in research and analysis. Include details about anonymization and confidentiality measures in the consent process. The confidentiality and anonymity of patient data in CFD studies can be effectively safeguarded. These measures ensure that patient information is protected from unauthorized access and misuse while allowing for the accurate identification of plaque rupture risks in acute coronary syndrome. The combination of these procedures provides a robust framework for maintaining the highest standards of data privacy and patient confidentiality.

5. When there are potential risks to the subject, or the privacy of the individual may be involved, the investigator is required to obtain a signed informed consent from the participant. For minors, informed consent must be obtained from the authorized legal guardian or parent of the subject. Describe consent procedures to be followed including how and where informed consent will be obtained.

   (a) If signed consent will not be obtained, explain why this requirement should be waived and provide an alternative procedure such as a verbal consent.

Response: Informed consent will be obtained.

(b) If information is to be withheld from a subject, justify this course of action.

Response: No information will be withheld from the subject.

(c) If there is a potential risk to the subject or privacy of the individual or loss of work time is involved in any particular procedure, include a statement in the consent form stating whether any compensation will be available.

Response: Not applicable since there is a minimal risk of privacy and loss of work time. This will be mentioned in the consent form.

6. If the study involves an interview, describe where and in what context the interview will take place. State approximate length of time required for the interview.

   Response: This study will not require an interview.

7. Assess the potential benefit to be gained by the individual subject as well as the benefits which may accrue to society in general as a result of the work. Indicate how the benefits may outweigh the risks.

   Response: computational fluid dynamics is a promising non-invasive tool that can help identify high-risk coronary plaques destined to cause acute coronary syndrome. CFD provides detailed analysis of blood flow and plaque characteristics, leading to a more accurate diagnosis of plaque rupture risk. Early identification and treatment of high-risk plaques can lead to a decrease in the incidence of acute coronary syndrome events. While there are physical risks associated with imaging and contrast agents, these are generally outweighed by the significant health benefits of accurate diagnosis and effective treatment. The use of non-invasive techniques and preventive measures can mitigate these risks, leading to better patient outcomes. With appropriate risk management strategies, the implementation of CFD in clinical practice offers a promising advancement in the fight against cardiovascular disease.

8. Incase of an experimental drugs, provide information about its status of registration for open sale in Bangladesh and in other developed countries.

   Response: N/A

9. For experimental 'new' drugs* which are not registered in Bangladesh provide full information about the toxicity studies carried out in animals or human volunteers. Published papers on this regard shall be annexed.

   Response: N/A

10. If placebo is to be used justify its uses and why the study cannot be done without its use.

    Response: N/A

11. If an experimental 'new' drug* is to be used state its sponsorship and the conditions for such sponsorship.

Response: N/A

12. State if the activity requires the use of records (hospital, medical, birth, death or other), organs, tissues, body fluids, the fetus or the abortus.

    Response: Yes. The study will use the medical records, including: date of birth, CT angiogram, body fluids etc.

The statement to the subject should include information specified in items 2, 3, 4, 5(c) and 7, as well as indicating the approximate time required for participation in the activity.

**** a 'new' drug means one which is not registered for free and open sale in Bangladesh.***

ANNEXURE - C

Project Title: High-Risk Plaques Identification using Coronary Computed Tomography and Computational Fluid Dynamics.

- **Summary:**

The study investigates the use of advanced imaging techniques and computational methods to identify high-risk plaques in coronary arteries. These plaques are significant because they have the potential to cause acute coronary syndrome (ACS), a condition that includes heart attacks and unstable angina. The research focuses on the integration of Coronary Computed Tomography (CCT) with Computational Fluid Dynamics (CFD) to provide detailed insights into plaque characteristics and their hemodynamic environment.
The primary aim of the study is to enhance the early detection and characterization of high-risk coronary plaques that could lead to ACS. By combining CCT, a non-invasive imaging technique, with CFD, which stimulates blood flow dynamics, the study seeks to: Identify High-Risk Plaques, Apply CFD to analyze the blood flow around these plaques, Improve Prediction of ACS, Inform Clinical Decision-Making.
Computational fluid dynamics (CFD) analysis of CCT data can also provide a noninvasive hemodynamic assessment to identify high-risk plaques destined to cause acute coronary syndrome [1]. Patients with adverse plaque characteristics like positive remodeling or low-attenuation plaque have a greater risk of future coronary events [2-4].

- **Introduction:**

Globally, Cardiovascular diseases (CVDs) are responsible for the highest fatalities where ACS is recognized to contribute to a good many of these effects [5-7]. ACS which involves myocardial infarction and unstable angina is mainly caused by the rupture or erosion of plaques in the arteries of the heart. So, early detection of the higher risk plaques that can cause an acute event and thereby, ACS is useful in optimizing patient's survival data [8-11].

New imaging technology and computing methods have made it extremely easier to identify and evaluate these dangerous plaques. Coronary computed tomographic angiography or CCT is the most recent imaging technique specifically used for diagnoses of coronary artery diseases because of features such as better accuracy, minimally invasive imaging of the coronary arteries along with the characterization of plaque. Clinicians use CCT to signal elements such as positive remodeling, low attenuation plaque, napkin-ring sign, and spotty calcium.

As useful as CCT is for plaque visualization, it doesn't inform the analysis of hemodynamic loads on the plaques, which are paramount to plaque destabilization. This is the role of computational fluid dynamics (CFD) tools step in playing into this reason. CFD is a strong application imitating blood flow within the coronary arteries, whereby assessment of values such as WSS and plaque stress can be done[12-21]. All these parameters play a pivotal role in dissecting the biomechanical milieu of the plaques and in stratifying the lesions most prone to causing ACS.
The combination of CCT with CFD assists in evaluating not only the major anatomic but also the hemodynamic facets that underlie plaque instability[22-25]. This approach does not only help to improve the identification of high-risk plaques, but it also helps to split the patients into groups according to their risk of development of ACS. Thus, the detection of patients with vulnerable plaques may enable clinicians to apply prevention and therapeutic approaches more efficiently and

effectively and prevent acute coronary events.

To sum it up, the application of both coronary CTA and CFD should be regarded as a major progress in diagnosing CAD through noninvasive means.

- **Objectives:**
  1. Identify High-Risk Plaque Features Using CCT. To compare the prevalence and distribution of the high-risk characteristics of the plaque among varying types of patients.
  2. To CFD to predict blood flow patterns in coronary arteries and quantify WSS and plaque stress environments.
  3. To associate the observed high-risk plaque features and hemodynamic data with clinical outcomes which include the rate of the future ACS.
  4. Improved risk stratification of patients with coronary artery disease to identify those at greatest risk of future ACS events.
  5. Enhance Non-Invasive Assessment Techniques: This would pave the way to the improvement of the knowledge in non-invasive cardiovascular imagining and computational modeling through the introduction of integrated CCT-CFD technique.

  To set best practice consensus documents regarding the application of CCT and CFD into clinical operative practice for the diagnosis of CAD.

Study Hypothesis:

The synergistic application of CCT and CFD helps to identify high-risk atherosclerotic plaques, which would be prone to causing ACS in the future, by assessing not only the morphological characteristics but also the hemodynamic factors, which helps in better risk estimation and management of the particular patient along with preventive and curative measures. the study's purpose is to verify that CCT + CFD is highly effective for non-invasive diagnostic assessment of high-risk plaques, thus improving the capacity to anticipate and avoid acute coronary syndrome.

- **Rationale:**

In cardiovascular medicine, it is a major challenge to identify and prevent further progression of unstable atherosclerotic plaques that predispose to rupture and formation of ACS. ACS including myocardial infarction and unstable angina occurs when these tears or erosions of these susceptible plaques form thrombus and occlude the coronary blood flow. This study aims to determine the current level of ACS and the complications that occurred to identify the early detection and prevention of ASC in Bangladesh. Coronary computed tomography (CCT) combined with computational fluid dynamics (CFD) may solve these challenges in the Bangladeshi care setting.

The incidences of CVDs such as the ACS have been on the rise in the last few decades in Bangladesh mainly due to urbanization, gradual change in many aspects of life such as diet and physical activity, and an aging population. The problems of CVDs due to their high prevalence pose a great economic and health care burden to a country such as Bangladesh.

CCT is an invasive and cheap procedure compared to surgical one, and it can provide the physician with valuable information about the anatomical features of the coronary arteries and the plaques. CCT allows imaging of the lumen of the coronary arteries and the vessel wall at the same time, which means that it can distinguish between the plaques that do not cause such a significant

narrowing of the arteries as to be detected using other methods, but that are prone to rupture. Other quantifiable characteristics that are linked with plaque stability and risk of rupture are WSS or wall shear stress, and atherosclerotic plaque stress that are not implanted as well as cannot be assessed by CCT alone. As it has been mentioned before, it may be stated that CFD can model blood flow behavior in the coronary arteries which provides needed information about the specific given hemodynamical features. Therefore, it can be stated that applying CFD in combination with CCT provides the possibility to receive extensive information about particular anatomical features and biomechanical conditions contributing to the formation of plaques. Integration of CCT and CFD may assist in the identification of specific high-risk plaque and the prognosis of the development of ACS, thus benefiting patients' outcomes. Implementation of this approach in the health facilities of Bangladesh will ensure a combination of the so-often practiced medical work and the newly developed diagnostic techniques. From the current trends of CVDs in Bangladesh, it is clear that new strategies for early identifying and improved preventive methods need to be developed. The integration of CCT and CFD programs into the structures of nationwide health care can play a great role in combatting the rise of the public health issue of ACS. Applying this concept of high-end diagnostic technologies can foster local research on cardiovascular diseases for the enrichment of humanity's body of knowledge. Another way is that close cooperation with international research organizations will also be effectively useful for developing the competencies of Bangladeshi healthcare workers and researchers. This approach can overcome the shortcomings of the current diagnostics, give solutions at a lower cost, and create a huge difference in the public health of the country – Bangladesh.

- **Methodology:**

The locally adapted workflow for the identification of high-risk atherosclerotic plaques that may cause Acute Coronary Syndrome (ACS) based on the integration of CCT and CFD is carried out systematically. These are the steps in the presented methodology, namely, the patient cohort, imaging, data handling and analysis, CFD simulation, and clinical implementation.

Firstly, select patients based on symptoms of coronary artery disease (CAD), high-risk factors (e.g., family history, hypertension, diabetes), or those requiring further evaluation after preliminary tests and then Preparation: Give drugs to achieve proper rate of heartbeat.The order includes checking the patient's habits for proper hydration and contraindications to the use of contrast media. If we read this then follow CCT imaging protocol. Conduct CCT with the help of a multi-detector CT scanner only. Take detailed images of the coronary arteries. Plan to administer iodinated contrast material to improve the visual display of coronary arteries. Moreover, electrocardiographic gating ensures the timely exposure of the patient's heart to radiation during the cardiac cycle to minimize motion. All the above processes have to be accomplished then the remaining work is taken care of by Mimics and Ansys Simulation software. Create reconstructions of the coronary arteries using Ansys software and out of the CCT data that was acquired. Grasp positive remodeling, low attenuation plaque, napkin ring sign, and spotty calcification in atherosclerotic plaques. Document the features you noticed about the plaques that are in the identified places; the sizes and the shapes and the location certainly. The working process is, to a large extent, sequential. When one of them is absent the other does not work, or does not operate within the protocol, we do not discover our

result. Following that, ‘‘Cut out’ the coronary artery regions of interest from the reconstructed 3D images. Develop a mesh based on the segmented coronary artery regions. This entails the segmentation of the artery into small parts that are useful in making a CFD analysis. CFD Simulation has some conditions that are important for the results of the research.

Boundary Conditions: Define physiological boundary conditions, such as blood flow rates, pressure, and viscosity, based on patient-specific data.

Simulation: Configure the CFD software with the segmented geometry and boundary conditions. Run the CFD simulations to calculate hemodynamic parameters, including wall shear stress (WSS), plaque stress, and flow velocity profiles.

Data Analysis: Analyze the CFD results to understand the hemodynamic environment within the coronary arteries and identify regions with abnormal hemodynamic forces.

After Completing the above processes, Integrate anatomical data from CCT (plaque characteristics) with hemodynamic data from CFD (WSS, plaque stress). Identify high-risk plaques based on combined criteria, including anatomical vulnerability and hemodynamic stress. Then, we Generate a detailed report summarizing the findings from CCT and CFD analysis. We Stratify patients into different risk categories (low, moderate, high) based on the comprehensive assessment. Finally, we will adjust the treatment plan based on the findings and analysis of the patient's response.

Phase-3- (A Pilot Study):

A pilot study is necessary to evaluate the accuracy and efficiency of Coronary Computed tomography (CCT) and Computational Fluid Dynamics (CFD) in helping distinguish high-risk plaques that may lead to Acute Coronary Syndrome (ACS). This pilot study will bring out some of the procedures to be used; fine-tune research procedures; and generate some data to be used in the main study.

Objectives

- To first determine whether CCT and CFD can be combined for proper identification of high-risk plaques.
- To assess the precision of this integrated method for early identification of ACS.
- To assess the realistic problems and constraints in a clinical center.
- To generate general data for forming more extensive and powerful research studies.

With regards to the decision of sample size for a pilot study, it depends on different strategies used depending on the purpose of the pilot study. As this pilot study aims to investigate the feasibility of interventions and acquisition of preliminary efficacy data, one of the recognizable practices of defining the sample size is by using certain rules of thumb or certain formulas for proportion / means estimation.

Estimation of sample size for a proportion

If the pilot study aims to estimate the proportion of patients with high-risk plaques accurately, the sample size can be calculated using the following equation: If the pilot study aims to estimate the

proportion of patients with high-risk plaques accurately, the sample size can be calculated using the following equation:

$$N = \frac{Z^2 \times p \times (1-p)}{d^2}$$

Where:

N = perfectly sized sample

Z = Z-value for the significance level e. g., for a 95% confidence level we use 1. 96.

p = Rate or prevalence; estimated proportion of the population with high-risk plaques (assumed to be 0.5 if unknown for maximum sample size)

d = required level of accuracy (for example, 0. 1 for 10%).

Thus, this calculation indicates that it would require 96 participants to have precision in estimating the proportion. However, for the pilot study aimed at establishing the feasibility of the study and collecting the first figures, the number can be reduced.

Since the purpose of this pilot study is to test survey efficacy and develop a sense of the magnitude of gender differences, a form of power analysis.

Final Sample Size Recommendation: 50 participants

- **Utilization of Results:**

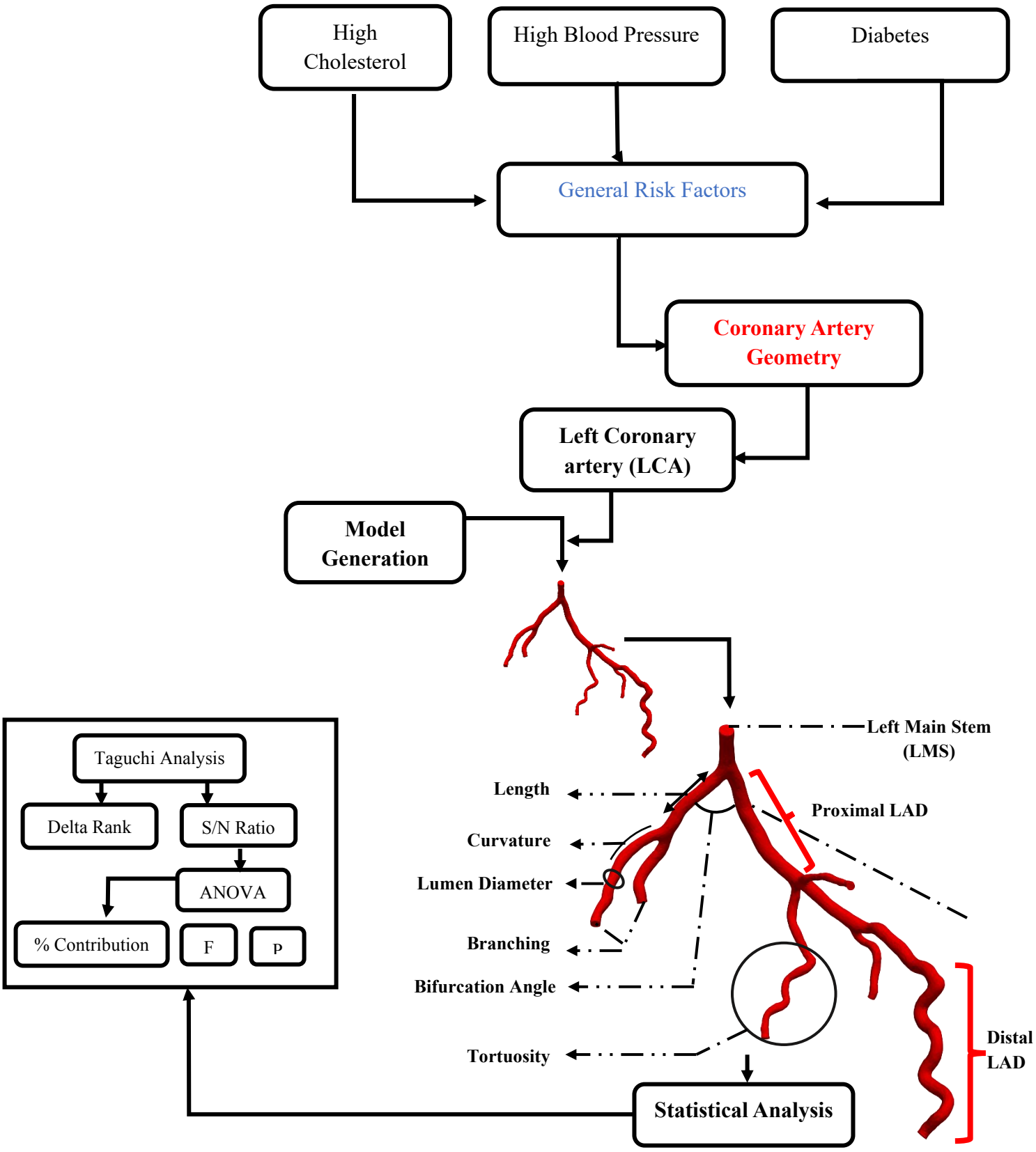
Applying these innovations in the form of CCT and CFD for risky plaque determination and ACS prevention can transform the treatment of cardiovascular diseases in Bangladesh. Therefore, this approach of early detection, accurate diagnostics, patient-tailored approaches, and better access to advanced diagnostics will allow for increasing the overall health and well-being of the population. Furthermore, it creates further chances of establishing and upgrading its capacity, research, and economic returns that are beneficial to the growth and development of the health sector in Bangladesh.

Table 1: Summary of the comparative pilot study: High-Risk Plaques Identification using Coronary Computed Tomography and Computational Fluid Dynamics

Aspect of the study	Description
Study Type	Prospective, observational pilot study
No of subjects	50
Objective	To evaluate the accuracy of this integrated approach in predicting ACS events.

Study Population	Inclusion Criteria: • Adults aged 40-70 years. • Presenting with symptoms of CAD (e.g., chest pain, shortness of breath) or having multiple risk factors (e.g., hypertension, diabetes, smoking). • Able to provide informed consent. Exclusion Criteria: • Severe renal impairment (due to contrast media risk). • Previous allergic reaction to iodinated contrast media. • Pregnant or lactating women.
Baseline Assessment	• Collect detailed medical history. • Perform a physical examination. • Conduct initial tests: ECG, blood tests, and echocardiography.
CCT Imaging	• Administer beta-blockers if necessary to achieve the target heart rate. • Perform CCT to acquire high-resolution images of coronary arteries. • Use iodinated contrast material to enhance imaging. Image Analysis and Plaque Identification • Reconstruct 3D images of the coronary arteries. • Reconstruct 3D images of the coronary arteries.
CFD Simulation	• Segment coronary artery regions from CCT images. • Generate computational mesh of segmented arteries. • Set up CFD simulations with patient-specific boundary conditions. • Run simulations to calculate hemodynamic parameters (e.g., wall shear stress, plaque stress). •
Integration of Data	• Combine anatomical data from CCT and hemodynamic data from CFD. • Identify high-risk plaques based on combined anatomical and hemodynamic criteria.
Data Collection and Analysis	• Record all patient data, imaging results, CFD parameters, and clinical outcomes. • Analyze data to evaluate the accuracy and predictive value of the integrated CCT and CFD approach. • Identify any practical challenges and limitations encountered during the study.
Ethical Considerations	• Obtain informed consent from all participants. • Ensure patient confidentiality and data security. • Seek approval from the institutional review board (IRB) or ethics committee.

- **Flow Chart:**


High Cholesterol
High Blood Pressure
Diabetes
General Risk Factors
Coronary Artery Geometry
Left Coronary artery (LCA)
Model Generation
Taguchi Analysis
Delta Rank
S/N Ratio
ANOVA
% Contribution
F
P
Left Main Stem (LMS)
Length
Proximal LAD
Curvature
Lumen Diameter
Branching
Bifurcation Angle
Tortuosity
Distal LAD
Statistical Analysis

- **References:**

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ANNEXURE - D

Project Title: High-Risk Plaques Identification using Coronary Computed Tomography and Computational Fluid Dynamics

Principal Investigator:

Dr. Muhammad Tarik Arafat, Professor
Department of Biomedical Engineering (BME), BUET, Dhaka - 1000, Bangladesh.

Location:

Biomechanics lab, Department of Biomedical Engineering (BME), BUET, Dhaka - 1000, Bangladesh.

Interviewer details:

The interview will be conducted by study investigators at the lab.

Purpose of the Study:

The purpose of the study's current investigation is to assess the initial efficiency and possible application of the CCT and CFD in defining the potential high-risk atherosclerotic plague prone to ACS. The critical nature of a patient's plaque can be established during its early formation, and before a particular plaque causes an ACS, medication or stent implantation procedure can be taken. This study could be useful in refining the way of sorting patients in terms of their potential for subsequent ACS occurrence. Hence, studying the composition of plaque and the movement of blood in and around the arteries of atherosclerosis enables the researchers to establish the specific predisposing factors toward ACS. Hence, the study concentrates on enhancing the techniques of recognizing and interpreting the factors of hazardous plaques to avoid progression to ACS, though not provoking it. To determine what technical and clinical issues arose within the study and whether logistics were an issue. Thus, the study protocols and methodologies could be fine-tuned in the case of subsequent, larger-scale studies.

Types of participation of the study respondents:

If you agree to participate in this study, you will be required to provide information on your demographics and medical history.

Duration of study:

The study will be performed for half an hour.

Procedures of the study:

The study concerns the application of imaging and computer modulization to detect high-risk plaques that can induce ACS individually. Here's a possible procedure for such a study: Here's a possible procedure for such a study:

1. Encompass patients with CAD and no recent ACS event, symptomatic CAD who have not had an ACS event over the last year. This might be for example for people with chest pain, a family history of CAD, or other risk factors.

2. Undergo CCT scans to check for structural abnormalities in the coronary arteries and the nature of the plaque formations. The CCTA images shall be evaluated by the Doctors in the context of risk-indicating features which include; Plaque composition, Plaque size & location, and Degree of stenosis in arteries.

3. Create 3D models of the coronary arteries based on CCT information, and operate using software.

4. Simulate blood flow through these models to calculate hemodynamic factors like Fractions Flow Reserve (FFR), Wall Shear Stress (WSS), and Axial Plaque Stress.

5. Integrate the results from CCT plaque characteristics and CFD flow analyses.

6. Determine values that may be considered critical or a switch from normal values for each of the factors that characterize high-risk plaques.

7. Propose a method for risk assessment to divide patients into those with high, moderate, or low risk for recurrent ACS.

Potential benefits:

The study offers significant potential benefits for both for you and society as a whole. Individually, you will receive your gait analysis report which will help the doctors to understand your gait impairments. The use of a BWSS ensures your safety during data collection.

Risks, hazards and discomforts:

It is imperative to note that the study will incorporate measures to enhance patients' safety as much as possible. Nonetheless, CCT scans use ionizing radiation, though the risk of cancer is very small but increases with the number of uses. Though this is a small risk meaning that its likelihood is low in the case of having a single scan it does however become slightly high when one has multiple scans. Some of the patients who undergo the process of CCT may develop an allergy to the contrast dye to be administered. Blockages can sometimes be seen on CCT scans even though they are not large enough to create symptoms. Thus, it can cause additional stress and may lead to additional and perhaps unjustified diagnostic and treatment steps. We also know that CFD is a computer modeling technique and that the results reclaimed hinge on the CCT scan input data and the assumptions put to the model. About any kind of test or operation, it is natural for individuals to feel anxious, especially when there is an issue of coronary artery disease.

Reimbursements:

Neither will you be reimbursed for any medical costs. Nevertheless, if any health risk occurs because of studying participation, appropriate measures will be provided by the study researchers. Once more, if you cannot pay for the travel cost and at the same time attend the study session, reimbursement will be provided for the cost. This compensation will be made after your involvement as a participant in this study is complete.

Confidentiality:

The confidentiality of about your information will be rigorously maintained throughout the study. Personal identifying information will be collected from you initially for contact but will be removed from the dataset after data collection to ensure anonymity. You will be assigned a unique identification code, which will be used in all data analysis and reporting.

Rights to withdraw from participation:

Participation in this study is voluntary and you may withdraw from the study for any reason at any time. You will not be penalized in any way for declining to take part in or withdrawing from the study. If you decide to withdraw, the gait data collection procedure will be discontinued.

I am consciously and voluntarily participating in the above research study entitled "**High-Risk Plaques Identification using Coronary Computed Tomography and Computational Fluid Dynamics**". I understand that I will not be given any financial benefit for my participation. The doctors assured me that participating in this study would not harm me physically or mentally and that at any time I would be able to voluntarily withdraw from the study and my treatment would not affect it. All my information will be kept confidential.

[Photographing / Video recording]

Photographing of a participant will be used to visualize experimental setups for the purposes including publication, grant application and public relations. Private information such as the participant's name will not be made available.

Do you agree with Photographing during the experiment?

Yes **No**

During any part of the experiment, whenever participants feel discomforts beyond tolerance, trials can be stopped.

Name of participant:	Signature/Thumb print of the participant:
Name of the witness:	Signature of the witness:
Name of the interviewer:	Signature of the interviewer:

[*please note: Where the participant/s are aged under 18, separate parental consent is required; where the participant/s are unable to answer for themselves due to disability, parental or guardian consent may be required.]

INFORMED CONSENT FORM

(English Version)

High-Risk Plaques Identification using Coronary Computed Tomography and Computational Fluid Dynamics

I am giving consent to take part in the above-mentioned research study of Department of Biomedical Engineering, BUET. The nature of the research has been explained to me.

I am ensuring that,

I am taking part in this study voluntarily ……. Yes No ☐ ☐

I am voluntarily giving my time to the research ……. Yes No ☐ ☐

I am giving my permission to let the researchers
of BME, BUET to keep the consent form as rec …… Yes No ☐ ☐

and I have been allowed to ask questions about this study and my participation in it. I understand that all my personal information will be kept confidential, and no part of this information that might reveal my identity will be published. I also understand that I can refuse to take part in this study any time I want, and I will not be accounted for any questioning or harm for my refusal.

Name of Participant …… Sign of Participant …….

Name of Investigator …….. Sign of Investigator ……

Date.....

[*please note: If the participants are unable to answer for themselves due to disability, guardian consent may be required.]

Case Report Form

Project Title: High-Risk Plaques Identification using Coronary Computed Tomography and Computational Fluid Dynamics

Patients Characteristics			
Age (years)			
Male gender			
Heart Rate (bpm)			
Median interval between coronary CTA and ACS			
LVEF(%)			
	Presence of Ruptured plaques	**Absence of Ruptured plaques**	**P value**
Cardiovascular risk factors			
Diabetes mellitus			
Hypertension			
Dyslipidemia			
Current smoker			
Previous Myocardial Infection			
Clinical presentation			
NSTEMI			
STEMI			
Unstable angina			
Coronary CTA characteristics			
Minimal Lumen area, mm^2			
Diameter stenosis, %			

Distance from coronary ostium to MLA, mm			
Lesion length, mm			
Coronary CTA acquisition			
Heart rate (beats/min)			
Prospective acquisition			
Retrospective acquisition			
Lesion characteristics			
Lesion locations			
Left main to LAD			
LCx			
RCA			
Quantitative coronary angiography			
Reference vessel diameter (mm)			
Minimal lumen diameter (mm)			
Diameter stenosis (%)			
Lesion length (mm)			
Laboratory data			
Creatinine (mg/dl)			
eGFR (ml/min/1.73 m^2)			
HbAlc (%)			
Total-Cholesterol (mg/dl)			
HDL-Cholesterol (mg/dl)			
LDL-Cholesterol (mg/dl)			

Uremic Acid (mg/dl)			
CT findings			
Radius of arch curvature(mm)			
Aortic arch center lumen line length (mm)			
Aortic arch tortuosity index			
Diameter of proximal aortic arch (mm)			
Diameter of distal aortic arch (mm)			
Maximum diameter of aortic arch (mm)			

ANNEXURE - E

- **Total Budget:-** 80,000/- TK
- **Detailed Budget:-**

1. Personnel Cost: N/A
2. **Field Expenses/Laboratory Cost:-** 2,000/- TK
3. Supplies and Materials (Items & quantity to be specified): Included with Patients cost
4. **Patient Cost (If applicable):-**

Patients for CT (10)	**Doppler ultrasound (2)**	**FFR (1)**
45,000 TK	5,000 TK	25,000 TK

5. **Travel Cost (Internal travel cost only):-** 2,000/- TK
6. Office Stationery (Items & quantity to be specified): N/A
7. Data Processing/Computer Charges (If applicable) : N/A
8. **Printing and Reproduction:-** 500/- TK
9. Contractual Services (Other than manpower): N/A
10. **Miscellaneous:-** 500/- TK