Summary

Atherosclerosis in coronary arteries is a complex inflammatory disease of the arterial wall characterized by local lumen narrowing and representing one of the primary pathological processes underlying coronary artery disease (CAD), which is the leading cause of mortality worldwide. Myocardial infarction (MI) is the most severe clinical event following CAD, resulting from the progression of atherosclerotic lesions. In interventional cardiology clinical practice, lesion severity is typically assessed either in terms of anatomy *via* medical imaging technologies, or functionally by translesional pressure gradient invasive measurements. However, in both cases the parameters commonly adopted in clinical practice have shown limited capacity in the prediction of future MI.

Among the several factors involved in CAD, the role of hemodynamics is well-established by now. Moreover, a spatial co-localization is observed between specific regions of the arterial tree and sites prone to lesion development, reflecting the strong influence of vascular anatomy on local blood flow features. Near-wall hemodynamics and particularly wall shear stress (WSS) have been associated with the pathophysiological processes underlying the destabilization and eventual rupture of atherosclerotic plaques. Coronary hemodynamics can be assessed *in silico* with computational fluid dynamics (CFD) simulations in patient-specific models of coronary arteries reconstructed from clinical imaging. Despite the growing interest of interventional cardiologists in the adoption of CFD, several aspects still hamper its clinical translation. The main concerns are related to the extensive computational demand required by CFD and the required expertise. Recently, artificial intelligence (AI)-based approaches have been employed for the rapid prediction of hemodynamics with the potential of being easily integrated in a clinical framework.

The first objective of this thesis is to predict coronary WSS on the luminal surface of personalized coronary artery geometries with a geometric deep learning (DL)

approach. The latter is applied to a large dataset of patient-specific coronary arteries reconstructed from real-world patients and the substantial computational time reduction with respect to CFD is assessed, thus having the potential to promote the clinical translation of WSS as a biomarker of CAD. Importantly, DL-derived WSS predictive capacity for MI at 5 years is preserved if compared to CFD-computed WSS.

The second objective is to estimate the coronary pressure field under hyperemic conditions using a commercially available geometric DL solution. This study is performed on patient-specific diseased coronary arteries, enabling a comparison between clinically relevant pressure-based indices derived from DL-predicted pressure fields and those obtained from CFD.

Given the central role of coronary anatomy in clinical practice and its strong impact in shaping blood flow, the third objective of this thesis is to describe the geometric variability of a dataset of left anterior descending arteries with a statistical shape model (SSM). A SSM-based pipeline is adopted to identify pathological shape features associated with future MI and atherosclerotic burden. The same framework also enables the generation of a synthetic LAD cohort derived from real patient data, thereby preserving high geometric complexity and anatomical variability.

Considering the issues still limiting the clinical adoption of computational hemodynamics and that the mechanisms underlying atherogenesis and CAD remain only partly elucidated and not fully captured by the current clinical indicators of lesion severity, the main purpose of thesis work is to explore the translational potential of data-driven approaches that may promote the integration of both novel anatomical markers and established hemodynamic parameters as a supporting tool for CAD management and improve understanding of the disease.