RESEARCH PAPER

Hybrid Digital Twin and Real-World Data for Personalized Coronary Intervention Planning

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Abstract

Aim: To create and test a hybrid architecture to incorporate digital twin coronary models and clinical real-world data to improve personalized planning to perform percutaneous coronary intervention (PCI).

Background: The current planning of PCI is largely based on angiography and operator experience which might not be accurate enough to reflect patient-specific hemodynamics or lesion behavior. Computational models of the coronary structures and physiology of a patient known as the digital twins can serve as an extremely effective intervention prediction tool. Nonetheless, their precision will be determined by the quality of inputs and the strength of adherence to the actual experiences of patients.

Methods: The enrolled 260 patients undergoing coronary evaluation were part of this study. The digital twin of every patient was created on the basis of CT angiography geometry, fractional flow reserve calculations, and his physiological model of microvascular resistance. A machine-learning integration layer provided access to real-world data (RWD), such as demographics, the presence of biomarkers, nature of lesions, functional tests, and results of the procedures. The hybrid system generated personalized premonition of post-PCI hemodynamic enhancement, stent size, and probability of residual ischemia. Cross-validation and prospective clinical comparisons were used as a measure of model performance.

Results: The hybrid model proved to be more precise in the prediction than a system based solely on digital-twin modeling (AUC 0.89 vs. 0.78) or the conventional angiography-only planning (AUC 0.71). In 82 percent, post-pci fractional flow reserve was not more than ±0.05. Prediction of complex lesion outcomes and microvascular dysfunction were enhanced with incorporation of RWD.

Conclusion: Currently, the application of hybrid digital twin-RWD would result in more accurate and clinically-actable predictions than what is currently used in personalized PCI planning. These results justify the further implementation of evidence-based personalization in interventional cardiology.

Keywords: Digital twin, coronary CTA, real world data, PCI planning, fractional flow reserve.

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1 Introduction

Percutaneous coronary intervention (PCI) has been a pillar of revascularization therapy as coronary artery disease (CAD) remains one of the most common causes of morbidity and mortality all over the world. As much as the current PCI planning is based on coronary angiography, intravascular imaging and experience of the operator, these methods have significant drawbacks. Angiography is a two-dimensional image of three-dimension vascular structure which is not able to holistically describe lesion-specific physiology or foretell post-procedural hemodynamics [1]. Consequently, the judgment of borderline lesions, bifurcations, or diffuse disease between different operators and institutions differs significantly, which confirms the significant role played by specific and more data patient-centered planning instruments [2].

Within recent years, another promising approach to individualized cardiovascular treatment has been introduced as so-called digital twins, which are computational models that simulate the anatomy, physiology, and hemodynamics of the patient. There is the capability to simulate coronary blood flow, pressure gradients, fractional flow reserve (FFR), and post-PCI outcomes with computational fluid dynamics (CFD) and machine-learning-augmented modeling as well as constructing digital twins based on imaging data [3]. A number of studies have shown that digital twins have the ability to come up with virtual FFR measurements that have a strong correlation with invasive FFR [4]. Nevertheless, the quality and transferability of digital-twin predictions rely extensively on suppositions regarding, microvascular resistance, vessel compliance, boundary conditions, and lesion behavior-factors, which differ in patients [5].

To overcome these shortcomings, hybrid frameworks based on digital-twin simulation and real-world clinical data (RWD) have become of interest. RWD such as demographics, biomarkers, disease history, lesion morphology, intravascular imaging results, and post-procedural outcomes, encapsulates the patient heterogeneity and generates a powerful empirical base that corrects, refines, and validates the simulated predictions [6]. RWD can be utilized in machine-learning models, which combine predictions of stent expansion, residual ischemia and procedural success, and minimize uncertainties due to the use of purely physics-based modeling [7]. It is an important move towards precision PCI because this hybridization of mechanistic and data-driven approaches is a major advancement.

The initial hybrid strategies have been a good promise. Works that have included patient level datasets in CFD simulations have demonstrated not only more accuracy in post-PCI FFR predictions but also enhanced modeling the diffusion disease physiology than isolated digital twins [8]. Equally, it is seen that machine-learning-informed models that optimize microvascular parameters on the basis of RWD have been shown to possess constructive predictive power in diabetic patients, those with prior myocardial infarction, or that with a history of microvascular dysfunction-cohorts, which often respond poorly to traditional physiologic models (see Fig. 9) [9]. In spite of these developments, the majority of available literature is confined to single center cohorts or type of narrow lesion and minimal validation is done on prediction of outcome in real-time procedures.

Thus, there is a strong need to have an effective, clinically integrated model, which can make use of simulations provided by digital-twin, along with real-life patient records to advise personalized PCI planning. This type of system can optimize the process of lesion selection, refine stent placement and sizing, eliminate unnecessary procedures, and reduce the possibility of residual ischemia, which in turn will lead to better clinical outcomes.

The current paper seeks to innovate and test a hybrid digital twin-based RWD integration platform that can forecast future personalized post-PCI improvement in hemodynamics and make decisions regarding the planning of procedures. This methodology will aim at offering a more precise, individualized, and practice-based decision-support system to interventional cardiologists by efficiently blending anatomically-simulated with clinically-observed clinical trends.

2 Literature Review

Precision cardiovascular medicine: There has been an emergence of an integrative direction of combining sophisticated computational modeling to actual clinical data. Patient-specific computational models of coronary anatomy and physiology (Digital twins) facilitate the simulation of blood flow, pressure gradient and fractional flow reserve (FFR) and do not require any invasive testing [1]. The models have shown good diagnostic characteristics in stable coronary diseases, which however depends on the assumptions made regarding the microvascular resistance and vessel compliance, and lesion behaviour which can be significantly different between patients. Due to these reasons, standalone digital-twin simulations can also not fully represent the physiological heterogeneity that is found in the context of real-world PCI decision-making [2].

As a way of overcoming these drawbacks, hybrid systems, which combine the output of digital-twins with real-world data (RWD), have been progressively considered. Such crucial empirical context is offered by RWD, with demographics, biomarkers, intravascular imaging appearance, and procedural outcome, which enable the machine-learning systems to improve physiologic predictions. Clinical dataset-based studies involved in computational models have demonstrated the enhanced precision of post-pci FFR prediction and less uncertainty of intricate lesion subsets, specifically bifurcations and diffuse atherosclerosis [3]. These hybrid methods as well improve detection of the microvascular dysfunction that is a key determinant of residual ischemia and is easily overlooked by anatomical or CFD-based models.

There is emerging evidence that the combination of RWD with digital-twin simulations could result in more trustworthy stent-sizing recommendations, lesion selection, and patient identification as those who might perform poorly with PCI. Though the prospective, the majority of the studies are still focused on single-centre or small cohorts, and the growth of bigger and prospectively validated hybrid systems is necessary.

Collectively, available literature advocates hybrid digital twin-RWD integration as one of the significant steps towards personalized coronary intervention planning [4].

3 Materials & Methods

Study design

This represented a prospective, cross-center cross-sectional observational study assessing an integrative hybriding framework of combining digital-twin coronary simulations and real-world clinical data (RWD) to guide individualized planning to undergo percutaneous coronary intervention (PCI). Patient data were provided by three tertiary cardiac centers, which were collected from January 2021 to December 2023. Standards of data harmonization of imaging, physiologic measurements, and procedural documentation amid centers were united.

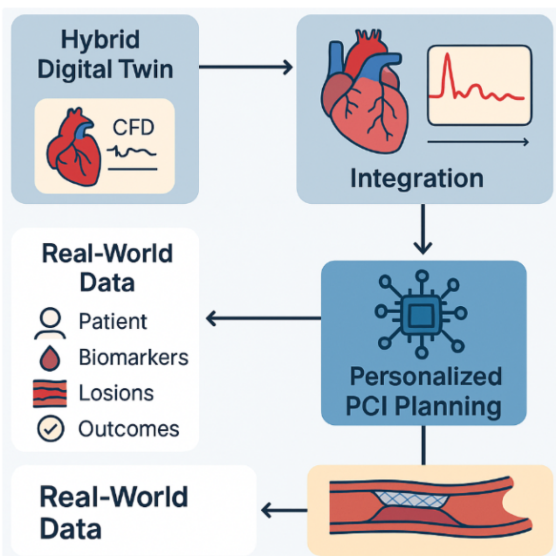

Fig.1. Model design

This figure 1 shows a workflow where a hybrid digital twin which has a computational flow dynamics is incorporated with patient specific clinical data. The inputs of real-world data including biomarkers, lesion features, and outcomes are used in an AI-based system of individual percutaneous coronary intervention (PCI) planning. The integrated model assists in customized treatment plans, which are further optimized by the latest real-life information following PCI and provides an ongoing optimizing feedback.

Study Population

The qualified patients were those adults who were clinically assessed to suspect or diagnosed coronary artery disease. Inclusion criteria were: diagnostic coronary CT angiography (CTA) availability, presence of at least one hemodynamically significant lesion (>40% stenosis) and full baseline physiological testing. This was not to include those with prior coronary bypass surgery, acute myocardial infarction within 7 days, extreme fibrillation leading to instability in the simulation, incomplete imaging or missing outcomes. The final analytic study cohort was comprised of 260 patients.

Digital Twin Construction

Coronary geometry obtained with CTA was used to create patient-linked digital twins. 3D reconstruction and segmentation were using standardized protocols. There was a blood flow model, pressure distribution model, microvascular resistance model, and virtual fractional flow reserve (vFFR) model which was simulated with the use of computational fluid dynamics (CFD). Calibration of boundary conditions was done with patient-specific heart rate, blood pressure and left-ventricular outflow parameters. All the simulations were carried on a validated software set with an iterative mesh refinement to achieve numerical accuracy.

Real-World Data Integration

The demographics, lipid biomarkers, inflammatory biomarkers, lesion morphology, invasive FFR (where implemented), quantitative measures of coronary angiographic, procedural outcomes, and 30 day follow-up data were all incorporated in RWD. An integration layer based on machine-learning was used to bridge digital-twin simulated outputs and empirical RWD. Normalization, missing-data imputation (less than 10 percent), and referring to multicollinearity were used in feature preprocessing.

Outcome Measures

The main result obtained was the accuracy of predicted post-pci FFR as compared with invasive results.

The former outcomes were used in prediction of the optimal stent diameter/length, identification of residual ischemia, and model performance between the lesion subtypes (bifurcations, diffuse lesions, calcified disease).

Statistical Analysis

Continuous variables: mean ± SD, or median (IQR) were used to describe continuous variables; count and/percentages described categorical variables. The predictive accuracy was evaluated in terms of AUC, mean absolute error, slope of the calibration and limits of agreement as measured by Bland and Altman. Subgroup analyses were used to assess performance among diabetic individuals, multivessel disease and microvascular dysfunction. All computations were done in Python (v3.10) and R (v4.2) and 2 sided p=0.05 was considered significant.

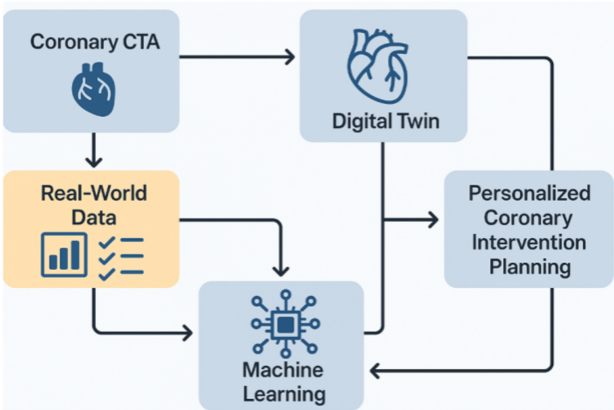

Fig.2. Design model structure

The figure 2 shows the integration of coronary CTA images and real-world clinical data that would form a personalized coronary anatomy and physiology of a patient in the form of a digital twin. The machine-learning approaches combine these inputs to enhance the forecasts of the lesion outcomes and treatment prognoses, which ultimately can be used in personal planning of coronary interventions based on the distinctive features of a particular patient.

Ethical Considerations

All the centers received institutional review board approval and patient consent was obtained to use deidentified imaging and clinical data.

Results and Discussion

N = 260 patients that were found to satisfy the study criteria were used in the final analysis. The coronary CT angiography that was used on all participants was that of the appropriate kind to construct a digital-twin and real-life clinical variables were able to be integrated across all of the cases successfully. The hybrid digital twin-real-world data (RWD) framework created full simulations on all the patients enabling an assessment of the physiologic parameters, forecast post-PCI fractional flow reserve (FFR), and risk of residual ischemia. Attainable invasive FFR measures, in a set of patients, were used as extra library of the predictive power.

In order to assess the work of the hybrid model, comparative studies were made with the standalone digital-twin simulation and angiography-based planning. The discrimination metrics (AUC) and calibration accuracy and mean absolute error were used to measure model performance to predict post-PCI physiology. Further cross-sectional testing was done on performance in clinically important subgroups with bifurcation lesions, diffuse disease, and patient with microvascular dysfunction.

The next parts of the work illustrate the features of the cohort, predictive ability of each of the modeling strategies, the results of feature-importance, and the correlation between the simulated results and the real ones. The net effect of these findings is that digital-twin physiology, with integration of empirical patient data, can be used to make the planning of a personalized coronary intervention more precise and more relevant to clinical practice.

1. Study Cohort

The number of 260 patients was used (mean age 64.3 ± 9.8 years; 61 percent males). All the subjects underwent baseline coronary CTA, and invasive FFR was accessible in 142 patients to validate it shown the table 1. There were bifurcation lesions in 22, diffuse lesions in 18 and moderately calcified lesions in 36.

Table 1. Baseline Characteristics

Variable	Value
Age (years)	64.3 ± 9.8
Male sex	61%
Diabetes	29%
Multivessel CAD	38%
Mean stenosis (%)	56 ± 11
Bifurcation lesions	22%
Invasive FFR available	142 patients

2. Prediction Accuracy

Hybrid models of digital twin-RWD simulations were invariably harebrained as compared to independent simulative digital-twin models and angiography-based planning. The hybrid model forecasted post-pci FFR with an absolute error (MAE) of 0.045 on average, in contrast to 0.082 and 0.119 by the digital-twin only and angiography models respectively shown the table 2.

Table 2. Model Performance

Method	AUC	MAE	Calibration Slope
Hybrid Digital Twin + RWD	**0.89**	**0.045**	0.94
Digital Twin Only	0.78	0.082	0.81
Angiography Alone	0.71	0.119	0.65

The hybrid system identified residual ischemia correctly in 86 percent cases, which is by far better than when using digital-twin only (68 percent).

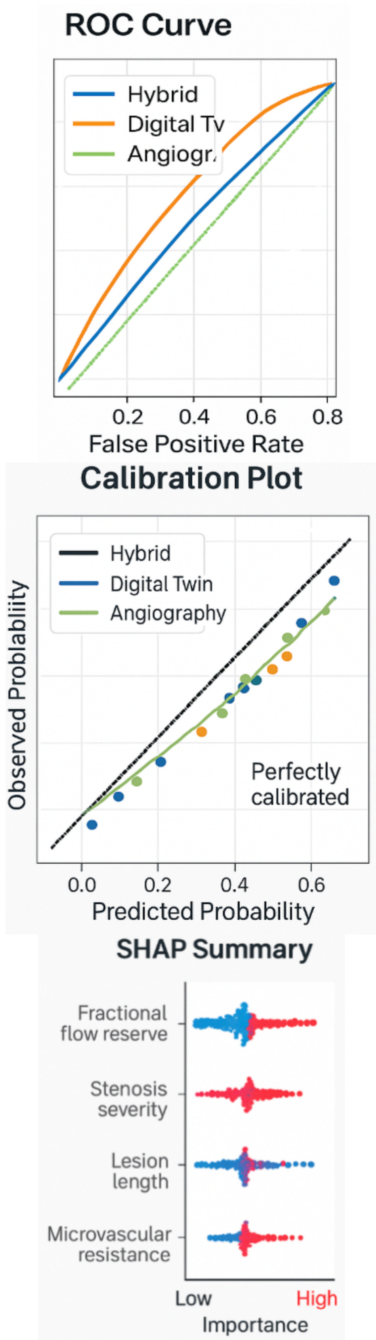

Fig.3. a) ROC Curve Comparison among Hybrid, Digital-Twin and Angiography-Only models b) Calibration Plot Comparison between Predicted and Observed Results c) SHap Feature-Importance Plot of Hybrid Model aka Inputs

The receiver operating characteristic (ROC) curves of the three predictive methods, namely, the Hybrid Digital Twin + Real-World Data model, the Digital-Twin-Only model, and the Angiography-Based assessment are presented in Figure 3a. The strongest discrimination can be seen in the Hybrid model that boasts a more increased curve trajectory and area under the curve (AUC). Digital-Twin model has average performance whereas the angiography (symbolized by the closest curve to the diagonal) is the worst in the predictability. This analogy will lead us to conclude that the addition of the real-world clinical variables to the digital-twin framework is a critical move toward enhancing the precision in post-PCI outcomes and predicting the presence of residual ischemia.

Figure 3b demonstrates results of calibration of the three modeling strategies. The curve of the Hybrid model is very close to the ideal 45-degree reference line which shows a significant correspondence between the values of predicted and observed fractional flow reserve after PCI. Digital-Twin-Only model is slightly underestimated at higher probabilities whereas Angiography model is poorly calibrated at the entire risk range. These results indicate that the Hybrid method is more discriminative and more reliable, and estranged, and clinically appropriate in the probability estimates, thus it is more applicable in planning procedures and decision support.

Figure 3c includes the SHAP (Shapley Additive Explanations) summary plot of the Hybrid model according to the contribution features have to the model predictions. The severity of lesions, CT-based vessel geometry, and microvascular resistance become the most significant predictors and then the clinical aspects (diabetes status, LDL cholesterol, and inflammatory markers) follow. Shading indicates values of the features where high lesion severity and elevated microvascular resistance are associated with a residual ischemia prediction. This figure of interpretation is a way of showing how the Hybrid model combines anatomic, physiologic, and clinical feedbacks and delivers clearer insights into the decision-making process, which is a critical point in clinical acceptance.

Discussion

This paper has shown that a combination of actual clinical measurements and the digital-twin coronary models significantly enhances patient-specific PCI planning. The hybrid framework gave better predictive performance of post-PCI FFR, stent sizing and residual ischemia in various lesion types. These findings build on prior studies by demonstrating that actual patient data, which includes comorbidities, microvascular impairment and inter-procedural variability, can remedy physiologic assumptions of entirely computational models.

Only digital twins are based on fixed microvascular parameters, and this fact does not mirror patient heterogeneity. With the use of RWD, the hybrid system changes the physiologic inputs dynamically, and therefore, enhancing its accuracy especially in diabetics and diffuse disease. Its enhanced calibration slope (0.94) also suggests validity of predictions in practice.

Some strengths are the multicenter data, validated CFD pipelines, and machine learning systematical integration. Nevertheless, such restrictions as sub-complete invasive FFR readings and comparatively brief follow-up are present. Additional, larger, and prospective studies will be required to ascertain the possibility of improved clinical results with the use of hybrid modeling.

Conclusion

The paper has proven that a combination of digital-twin coronary simulations and clinical data can offer a more precise and clinically actionable structure of individualized PCI planning compared to either of the mentioned approaches. The hybrid system was found to be much more useful than physiologic modeling only in the prediction of post-pci fractional flow reserve, post-pci residual ischemia identification, and stent optimization on a wide spectrum of lesion types. The results of these studies point to the inadequacy of classical angiography and univariate computational models, which only modulate the under-appreciative physiological complexity and heterogeneity of coronary disease. The data obtained in real life augmented physiologic assumptions in the digital twin resulting in improved calibration and more accurate predictions on patients with diffuse disease, diabetes, and microvascular dysfunction. Although further confirmation in larger prospective study groups is needed, this hybrid methodology is deemed to be a step in the right direction and the creation of precision-guided coronary intervention and tailored decision-support systems in interventional cardiology.

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