CFD-based Synthetic Data Generation for Machine Learning Based Pressure Drop Assessment in Aortic Stenosis

Teodor Ionut MATEI[1,2], Andreea Bianca POPESCU[1,2]*, Cosmin Ioan NITA[1], Costin Florian CIUSDEL[1,2], Lucian Mihai ITU[1,2]

[1] Transilvania University of Brasov, 29 Eroilor Boulevard, 500036, Brașov, Romania
teodor02matei@gmail.com, andreea.popescu@unitbv.com (**Corresponding author*),
cosmin.nita189@gmail.com, costin.ciusdel@siemens.com, lucian.itu@unitbv.ro

[2] Siemens S.R.L., 78, 15 Noiembrie Boulevard, Brașov, 500097, Romania

Abstract: Aortic stenosis occurs when the aortic valve does not fully open during the systole, which reduces and partially blocks the blood flow to the systemic circulation. The clinical diagnosis and treatment decision depend on the functional severity of the stenosis, which is assessed based on the trans-valvular peak pressure drop. The pressure drop is routinely estimated analytically, which may lead to sub-optimal results since certain hemodynamic aspects are not fully captured, like pressure recovery or blood flow turbulence. A promising solution lies in the use of machine learning (ML) for estimating the pressure drop based on patient-specific characteristics. Although a ML-based solution could provide the desired results in real time, the training of an accurate neural network would require a large database of invasively measured pressure drops, which is difficult and costly to set up. This study introduces a method for generating synthetic datasets based on a generic aortic valve model. This model is customized in order to create diverse yet physiologically normal valve shapes by modifying three anatomical parameters, namely the aorta diameter, blood velocity and valve area, by reducing it. High-fidelity computational fluid dynamics (CFD) simulations were conducted to compute reference pressure drop values. The efficacy of the generated dataset was assessed by employing it for training an ML model for pressure drop estimation.

Keywords: Synthetic Data, Computational Fluid Dynamics, Aortic Stenosis, Machine Learning.

1. Introduction

Aortic stenosis (AS) is one of the most common valvular heart conditions (Lindman et al., 2016). It occurs when the aortic valve does not fully open during systole, reducing blood flow to the systemic circulation. The treatment decision depends on the functional severity of the stenosis, which is assessed based on the trans-valvular peak pressure drop: typically, 20mmHg is used as a decision criterion, i.e. valves causing a pressure drop $\geq$ 20mmHg are treated invasively.

Non-invasively, the pressure drop is routinely estimated in an analytical manner, using a simplified form of the Bernoulli equation, which may lead to suboptimal results since certain hemodynamic aspects are not fully captured such as pressure recovery and blood flow turbulence (Hoeijmakers et al., 2022). Invasive cardiac catheterization may also be used to evaluate the hemodynamic burden of AS by measuring the net pressure drop across the aortic valve. This however is limited by its invasive nature, associated costs, and inherent risks (Manda & Baradhi, 2022).

Computational Fluid Dynamics (CFD)-based methods are often used in studies to simulate blood flow in various compartments of the cardiovascular system. A study conducted by Srinivasan and Madathil (2016) detailed the effects of a stenosis on blood flow turbulence by using CFD simulations. Blood vessels with various stenosis degrees were modeled and simulated using the open-source software OpenFOAM (OpenCFD Ltd., 2022). The results showed a direct correlation between the stenosis intensity and the blood flow turbulence. Research by Zakaria et al. (2018) used patient-specific geometries to simulate the blood flow through the aorta. The results were validated by comparing against an already existing experimental result. It was observed that this method was able to capture complex characteristics of the blood flow, suggesting that detailed flow physics could be extracted.

A recent study conducted by Hoeijmakers et al. (2020) indicated that training a meta-model for pressure drop estimation can be seen as a viable alternative to current clinical methods. Patient-specific meshes were created by performing image segmentation on Computer Tomography (CT) scans. The obtained meshes were used for building a statistical shape model (SSM) which enabled the generation of a synthetic dataset of meshes. Steady-state CFD simulations were performed in order to build a meta-model that could relate statistical shape variance and flow rate to pressure

https://doi.org/10.24846/v32i4y202305

drop. The obtained results suggest that, if enough training data is provided, the meta-model can capture the relevant features for pressure drop estimation. Average errors between 8.8% and 10.6% were observed for valve opening areas below 150 mm^2, with errors increasing for larger valve opening areas. This suggests that further improvements may be possible.

In addition to the CFD-based methods, machine learning models, such as neural networks (NN), have also seen an increased usage in hemodynamics and cardiovascular disease research. In a study conducted by Farajtabar et al. (2023), the pressure and velocity within a coronary arterial network were predicted based on its anatomical features. The data required to train the neural network was obtained from the CFD analysis of several geometries of arteries with specific features.

A study by Gamilov et al. (2023) also employed neural networks to estimate the pulse wave velocity (AoPWV) in the aorta. Given the limited number of clinical cases, the network was trained using a synthetic AoPWV database of virtual subjects. An additional dataset of real patient data was employed to validate the algorithm. The research of Long et al. (2021) also exploited a CFD-based synthetic dataset: CFD simulations were converted into synthetic 4D flow MRI data, and then this data was used to train various neural networks for image upsampling. Validation was performed on two sets of in-vivo 4D flow MRI data. The study proved that flow-image denoising was successful.

Machine learning (ML) models are considered to be a promising solution for pressure drop estimation in the cardiovascular system, using patient-specific characteristics as input (Nita et al., 2022). However, training ML models requires large datasets of invasively measured pressure drops. The previous studies used datasets created from patient-specific data collected through various modalities. Collecting such data is time-consuming and costly. This paper introduces an alternative method for generating purely synthetic datasets for developing a ML model capable of estimating pressure drop in aortic stenosis (AS). The approach proposed in this work uses a generic anatomical model of the aortic valve that can be customized, creating various valve shapes within normal physiological ranges, by adjusting three anatomical parameters (aorta diameter, blood velocity, and valve area reduction). Then, the ground truth pressure drop is computed by using high-fidelity CFD simulations. No actual patient data is employed during this process. Finally, the usefulness of this dataset is validated by using it for the development of a machine-learning model for pressure drop estimation.

The remainder of this paper is structured as follows. Section 2 presents the synthetic data generation process and the ML-based methodology. Section 3 provides an overview and detailed statistics of the resulting dataset and the performance analysis of the ML models. Section 4 discusses the advantages and the limitations of the proposed method, while also outlining the conclusion of this paper.

2. Methods

The following workflow is proposed for performing an automatic pressure drop assessment using ML:

1. Synthetic dataset generation:
   a. Physiological ranges and constraints are defined for the input parameters (valve diameter, blood flow velocity, and valve opening area reduction percentage). The cases which make up the analyzed dataset were randomly sampled, as it is detailed in subsection 2.1;
   b. A mesh representing the aortic valve is generated for each case, as it is described in subsection 2.2;
   c. A blood flow simulation is performed for each mesh, and the pressure drop is determined, as it is explained in subsection 2.3.
2. ML model development (subsection 2.4).

The parameter combination (step 1a) is used as the feature set (input to the ML model), while the pressure drop value (step 1c) is the ground truth value employed in training one of the models listed in subsection 2.4.

The focus was on synthetic data, since: (i) ML model training requires large amounts of data, and (ii) the limited amount of available clinical data is insufficient for such an approach. Moreover, another goal was to rely solely on open-source software (for CFD, etc.) during the entire dataset generation pipeline.

2.1 Parameter Sampling

Valve diameter, blood flow velocity, and valve opening area reduction percentage are the main characteristics that influence pressure drop in AS. Before selecting the parameter combinations for generating the analyzed subset, the potential ranges of the input parameters were defined. For the valve diameter (*D*), a range between 2 cm and 7 cm was chosen, with the blood flow velocity (*U*) ranging from 0.1 m/s to 0.6 m/s (Gabe et al., 1969). The valve opening area reduction percentage (*Ar*) represents the percentage difference between the inlet area and the valve opening area. Values between 60% and 85% were used to ensure a large number of samples are obtained around the point of interest (a 20mmHg pressure drop). The ranges were chosen such that they include the physiologically observed and clinically relevant ranges. However, even if each parameter value lies within the normal physiological range, their combination might still be physiologically impossible. To guarantee realistic parameter combinations, a constraint was added to the sampling process. The blood flow at the inlet must be at least 50 ml/s and it should not exceed 650ml/s (Hoeijmakers et al., 2020).

To compile a possible distribution of the analyzed cases, a mean for approximating the pressure drop was required. To this end, the formula in (1) was employed (Bessems, 2007), which was previously derived by combining analytical and experimental aspects. Because the formula does not generalize well in AS due to the irregular shape of the valve opening, its accuracy greatly decreases as the severity of the stenosis increases. However, these inaccuracies are acceptable in this context, since the distribution is only used for gathering general information, before constructing the actual dataset.

$$\Delta p_s = \frac{\rho K_t}{2A_0^2} \times \left(\frac{A_0}{A_s - 1} \right)^2 \times |q| \times q \,, \tag{1}$$

where ρ represents the blood density, while A_0 and A_s are the initial valve opening area and the minimum valve opening area, respectively. The blood flow rate is represented by the variable q, with K_t being the turbulence constant, set as equal to 1.5.

Despite only approximating the final dataset, this distribution provided valuable preliminary insights, such as the correlations between the parameters and their influence on the pressure drop, as it was detailed in subsection 3.2.

Finally, the set of synthetic cases was selected by randomly sampling the previously chosen intervals and discarding those that did not meet the flow rate constraint.

2.2 Aortic Valve Geometry

The aortic valve geometry was inspired by images depicting real valve anatomies. To facilitate both the mesh design process and the simulation step that follows, the open-source CFD software OpenFOAM was employed. The aortic valve geometry is represented as a hexahedral mesh by using the blockMesh utility. Furthermore, the quality of the mesh is assessed by using the checkMesh utility.

To ensure the quality of the resulting mesh, its geometry is modeled as two separate components that are merged afterwards (Figure 1). The first component renders the exterior of the aortic valve, alongside the left ventricular outflow tract and the ascending aorta. The second component contains only the internal geometry of the aortic leaflets.

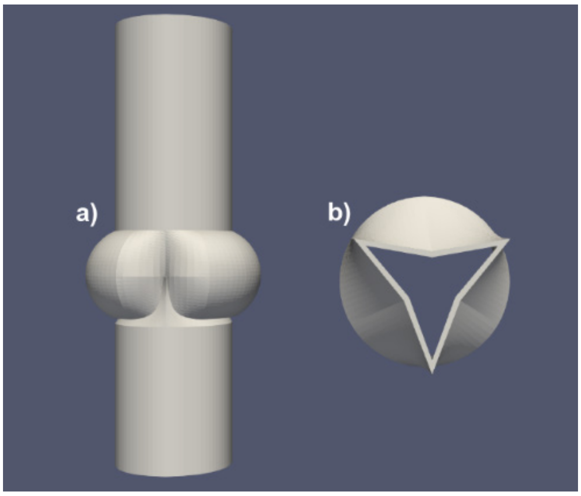

Figure 1. Valve geometry: a) exterior walls (left ventricular outflow tract, aortic valve, aorta); b) leaflets

To merge the two meshes, the snappyHexMesh utility was employed. This utility generates a three-dimensional mesh, by morphing a base mesh so as to conform to a surface geometry in the stereolithography (STL) format. The external mesh was used as the base mesh, while the leaflets were converted to the STL format.

Because the blockMesh utility uses dictionaries containing positional and relational information about the vertices comprising the mesh, this process can be parametrized, enabling the generation of different aortic valve geometries. Python scripts are employed to automate this process.

Using a parametrized mesh is advantageous since its geometry can be easily modified programmatically as needed, enabling the generation of different geometries for various simulation scenarios. The only parameters that changed across simulations were the valve diameter (*D*), the valve opening radius (*r*) and the blood flow velocity (*U*).

However, using the valve opening radius as one of the parameters posed a challenge. Clinically, it is not the valve opening radius that is being measured, but the valve opening area reduction percentage, relative to the area of the aorta. Therefore, the relationship between the valve opening area reduction percentage and the valve opening radius needs to be determined. This was achieved through the use of an interpolation algorithm. An auxiliary dataset containing a collection of three-dimensional points was generated. The coordinates of each point described the characteristics of a specific mesh: the valve diameter (*D*), the valve opening area reduction percentage (*Ar*) and the valve opening radius (*r*).

Before computing the area reduction percentage, the initial valve opening area (A_0) and the minimum valve opening area (A_s) need to be extracted from the generated meshes using the open-source visualization software ParaView (Ayachit, 2015). Once the two areas are extracted, the following formula can be used to determine the area reduction percentage:

$$Ar = 1 - \frac{A_s}{A_0} \times 100 \quad (2)$$

An experimental approach was employed to determine which interpolation algorithm performs best in this scenario. Among the algorithms provided by the open-source Python library SciPy (Virtanen et al., 2020), the CloughTocher2DInterpolator offered the most accurate predictions. The errors observed ranged within ±5%.

2.3 Anatomical Model and Flow Simulation Parameters

To determine the flow parameters that best describe the blood flow through the aorta, studies on the blood flow in the human arterial system (such as that of Thomas & Sumam, 2016) and blood flow simulations using CFD (Zakaria et al., 2018) were analyzed. Blood can be regarded as an incompressible Newtonian fluid, with a kinematic viscosity of 4×10^{-6} m_2/s and a density of 1500 kg/m_3. The most used model for blood flow turbulence is the K-epsilon turbulence model (Argyropoulos & Markatos, 2015). The formulas below were used to determine the turbulent kinetic energy *k* and the turbulent dissipation rate *ε* (Srinivasan & Madathil, 2016):

$$k = \frac{3}{2}(UI)^2, \quad (3)$$

$$\varepsilon = \frac{0.1643k^{1.5}}{l}, \quad (4)$$

where *U* represents the mean flow velocity and *I* the turbulent intensity. The turbulence length is represented by the variable *l*. Additionally, the outlet pressure was set at zero and a no-slip boundary condition was applied at the walls of the aorta.

Initially, blood flow simulations were carried out using a linear inlet velocity profile (LVP). A small dataset comprising six distinct scenarios was assembled and they were simulated with the pimpleFoam solver (Holzmann, 2016). The selected cases were decomposed using the decomposePar utility, enabling parallel runs on multiple CPU cores to speed up the simulations. The intermediate results were then concatenated using the reconstructPar utility.

To ensure convergence in a timely manner, the parameters of the control dictionary were fine-tuned. The simulation time was set at 5 seconds, with data being extracted every 0.1 seconds. A variable time step was enabled, allowing the solver to adjust the number of steps as required.

The relevant data was extracted from simulations using ParaView utilities (Figure 2). The simulated pressure drop was then compared against the analytically computed pressure drop. The analytically computed value was determined as in equation (1) (Bessems, 2007).

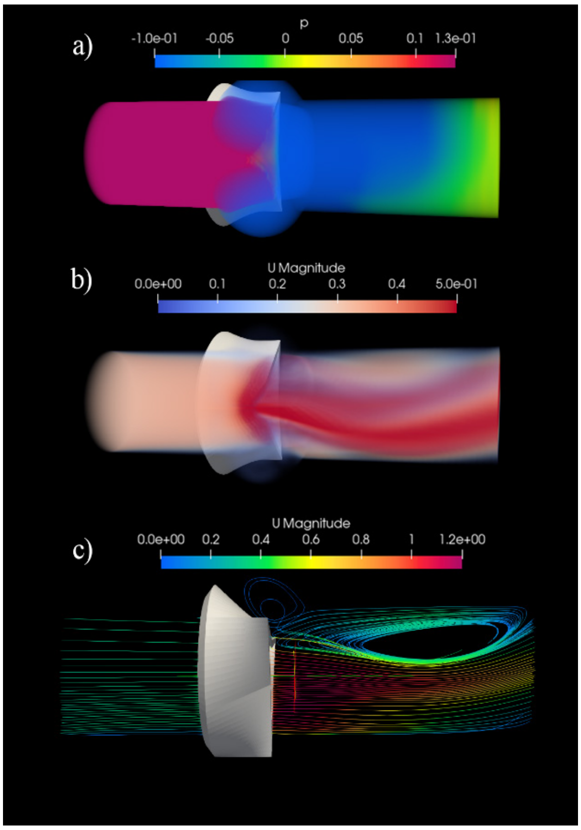

Figure 2. ParaView visualization: a) pressure; b) blood flow velocity; c) blood flow velocity (tracers)

To improve the accuracy of the simulation results, a parabolic velocity profile (PVP) was imposed at the inlet of the aortic valve, as it can be seen in Figure 3.

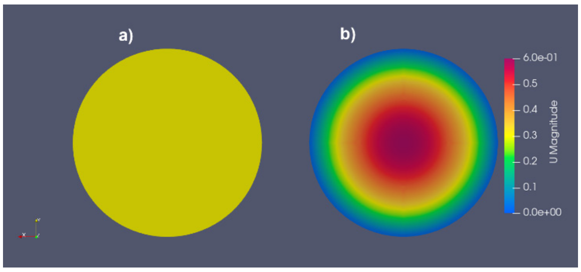

Figure 3. Valve inlet velocity: a) the linear profile; b) the parabolic profile

This assumption is based on the fact that there is no turbulence in the areas preceding the valve, meaning that the blood can be considered to have a laminar flow (Srinivasan & Madathil, 2016). Thus, the constant velocity was replaced with a location- (layer-) dependent velocity, which can be expressed by:

$$U(x) = U_{\max} \times \left(1 - \frac{(x-c_x)^2 + (y-c_y)^2}{2r^2}\right) \qquad (5)$$

In equation (5), the variable U_{max} represents the maximum velocity value, while r represents the radius of the valve inlet. The numerator of the fraction determines the position relative to the center of the inlet, with c_x and c_y representing the center coordinates.

2.4 Machine Learning-based Pressure Drop Estimation

After generating the dataset, the next step was to verify its viability in a machine learning (ML) application. The role of the ML model is to estimate the pressure drop value based on the other three parameters (diameter, velocity, and the valve opening area reduction percentage). Three approaches were considered: a polynomial regression model, a support vector regressor, and a neural network. Regardless of the chosen approach, the problem was formulated as a regression task, with the model's output representing the pressure drop.

The first approach, namely the polynomial regression model, was implemented using scikit-learn (Pedregosa et al., 2011). For the second approach, scikit-learn was used for implementing a Support Vector Machine (SVM) model. For implementing the neural network, the open-source framework PyTorch (Paszke et al., 2019) was used. The neural network is composed of three fully connected (FC) layers: one input layer with three neurons, one hidden layer with 32 neurons, and a single-neuron output layer. The first two layers use a Rectified Linear Unit (ReLU) activation function, while the output layer uses no activation function.

The specific parameters and hyperparameters were tuned using a grid search approach for each method. The optimal values are presented in subsection 3.4, along with the obtained results.

3. Results

3.1 Velocity Profile Comparison

The effect of modifying the velocity profile is highlighted in Table 1. In cases with mild stenosis (e.g., case A), the observed pressure drop was

Table 1. Comparison between pressure drop values extracted from linear velocity profile (LVP) simulations, parabolic velocity profile (PVP) simulations and analytically computed values

Case	D [cm]	Average U [m/s]	Area reduction [%]	Q [ml/s]	Pressure drop LVP [mm Hg]	Pressure drop PVP [mm Hg]	Analytical pressure drop [mm Hg]
A	6	0.3	46.81	847.44	0.73	0.42	0.41
B	2	0.3	53.13	94.16	2.13	1.75	0.68
C	4	0.3	59.72	376.64	2.07	1.75	1.17
D	4	0.1	60.31	125.55	0.25	0.21	0.14
E	4	0.5	60.31	627.74	5.62	4.71	3.41
F	4	0.3	73.64	376.64	9.81	9.39	4.15

much closer to the analytically computed value when using a parabolic velocity profile. As the severity of the stenosis increases (e.g., case F), the accuracy of the analytical formula decreases, which explains the large discrepancy relative to the observed values. Additionally, the increase in pressure drop for the cases simulated with a parabolic velocity profile is gradual (except for case D).

3.2 Convergence Analysis

Before proceeding with the dataset generation, a convergence analysis was performed with the aim of finding a tradeoff between mesh quality and simulation runtime. Two cases were chosen for the convergence analysis: one with a borderline pressure drop value (20 mmHg), and the other one with a high pressure drop value, of approximately 60 mmHg. Simulations were run for meshes with varying cell counts for each case. Figure 4 and Figure 5 indicate that a decrease in the relative cell count results in unpredictable oscillations in pressure drop values. Conversely, increasing the cell count maintains the pressure drop close to the expected range. These findings imply that the selected mesh resolution is adequate for this application.

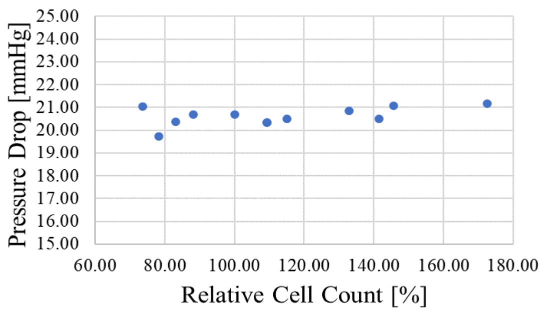

Figure 4. Convergence analysis results for a case with a pressure drop of approximately 20 mmHg

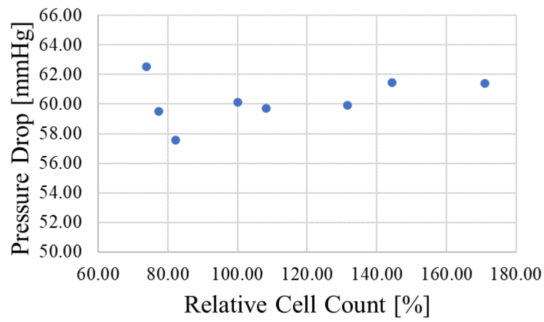

Figure 5. Convergence analysis results for a case with a pressure drop of approximately 60 mmHg

3.3 The Synthetic Dataset

A synthetic dataset comprising 241 samples was generated. The mean absolute difference between the predicted pressure drop and the analytically-derived value was computed to put the results into context. The mean difference of 6.35 mmHg suggests that the blood flow characteristics were captured as expected during the simulations. The largest differences were obtained for cases with a higher valve opening area reduction percentage, where the assumptions related to a circular area in the analytical formula no longer hold.

The distribution of the generated samples is presented in Figure 6.

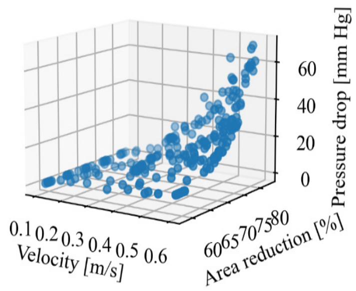

Figure 6. 3D representation of pressure drop as a function of velocity and valve opening area reduction percentage, for each sample in the analyzed dataset

The mean pressure drop value was 17.39 ± 16.18 mmHg, with a minimum of 0.21 mmHg and a maximum of 68.84 mmHg.

The correlation matrix depicted in Figure 7 indicates that as the blood flow velocity and the area reduction percentage increase, so does the pressure drop. While both parameters influence the severity of the pressure drop, an increase in velocity only leads to a marked increase in pressure drop for cases where the area reduction percentage is also high.

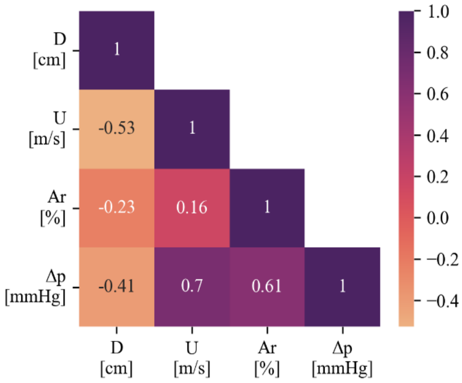

Figure 7. Correlation matrix for the generated dataset

3.4 Pressure Drop Estimation

To evaluate the performance of the employed models, a 5-fold cross-validation strategy was applied. The cross-validation performance metrics were computed for each ML approach, as it can be seen in Table 2.

The polynomial regression model performed best when implemented using a 3rd degree polynomial function. The SVM-based model offered the best results when using a 4th degree polynomial function as the kernel.

As it was mentioned previously, the models were trained using a regression formulation. However, the outputs can be post-processed by applying the clinical decision threshold, which would transform the regression task into a classification problem. In a clinical setting, a pressure drop value of 20 mmHg is applied as the lower limit when classifying severe stenosis (Baumgartner et al., 2017). By setting the threshold at 20 mmHg, the results can be split into two classes: healthy subjects/mild stenosis (under 20 mmHg), and severe stenosis (over 20 mmHg).

The neural network performed the best among the three employed approaches, achieving the highest R2 score, that is 0.9841. The obtained errors were also lower in comparison with those obtained by the other employed models and the classification performance was only slightly lower than that attained by the polynomial regression model.

Besides the usual regression-specific metrics, the correlation between the ground truth values and the predicted values was also assessed. The

Table 2. Optimal parameters for each approach, followed by the mean absolute error, minimum and maximum errors, absolute error standard deviation and mean error [mmHg], R2 Score and Pearson's correlation coefficient, Accuracy, Sensitivity, Specificity and area under the curve (AUC)

Cross Validation	5-Fold (241 samples)		
Algorithm	Polynomial Regression	Support Vector Regressor (SVR)	Fully Connected (FC) Neural Network
Kernel	N/A	Polynomial	N/A
Degree	3	4	N/A
MAE	1.7144	1.6220	1.2415
Min. Abs. Error	0.0046	0.0045	0.0016
Max. Abs. Error	11.1623	13.0340	9.5392
Abs. Error Std. Dev.	1.7178	1.8639	1.6244
Mean Error	0.0054	-0.2677	-0.0141
R2 Score	0.9762	0.9753	0.9841
Pearson's r	0.9887	0.9885	0.9920
Accuracy [%]	95.44	94.61	95.02
Sensitivity [%]	91.7	90.5	91.7
Specificity [%]	97.5	96.8	96.8
AUC	0.9951	0.9945	0.9947

Pearson correlation coefficient reflects a strong linear correlation, as it is illustrated in Figure 8. The Bland-Altman plot in Figure 9 shows that, at the worst, 95% of the prediction errors for the neural network should range between ±4 mmHg. A mean difference of only 0.01 indicates that the predictions were not biased.

The confusion matrix and ROC curve for each model are presented in Figure 10 and Figure 11, respectively. Additional classification metrics are displayed in Table 2.

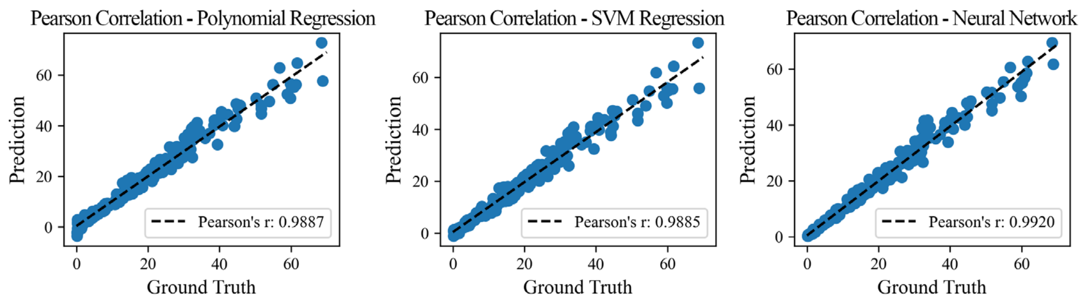

Figure 8. Pearson correlation: a) Polynomial regression; b) SVM Regression; c) Neural Network

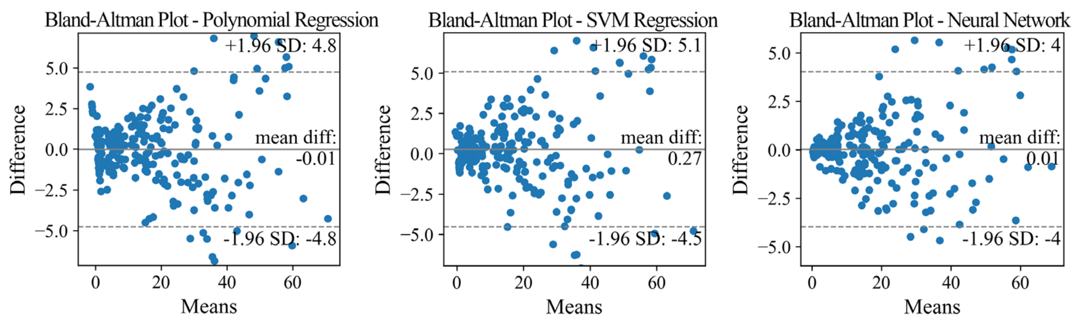

Figure 9. Bland-Altman plot: a) Polynomial regression; b) SVM Regression; c) Neural Network

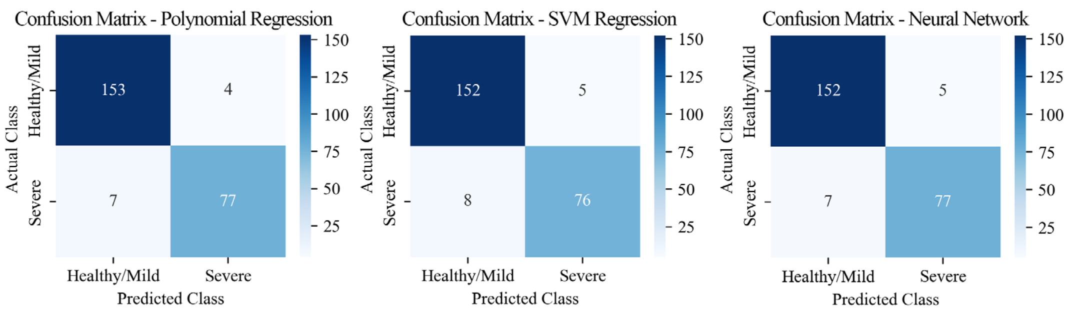

Figure 10. Confusion matrix: a) Polynomial Regression; b) SVM Regression; c) Neural Network

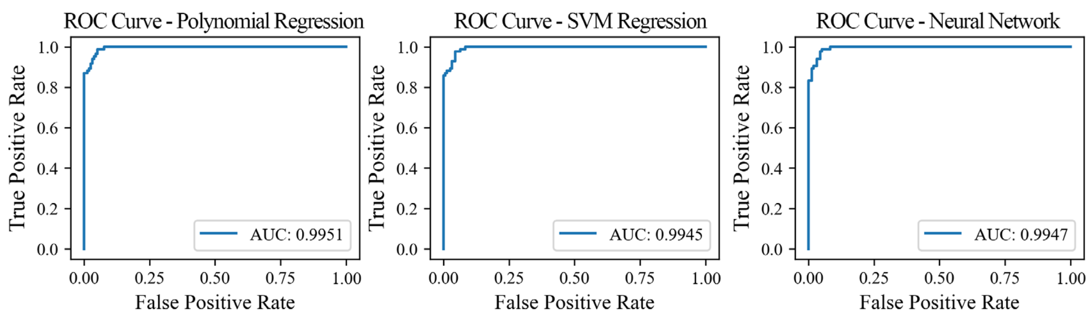

Figure 11. ROC curve: a) Polynomial Regression; b) SVM Regression; c) Neural Network

4. Discussion and Conclusion

With the trans-valvular peak pressure drop being one of the most important measurements in diagnosing AS, alternative estimation methods have become a popular research topic. Previous works have shown that meta-modeling can be used for capturing the relevant blood flow characteristics and estimating the pressure drop with reasonable accuracy. However, analytical approaches have their limitations, as they feature a decreased accuracy for larger valve areas.

By contrast, the approach proposed in this paper focuses on estimating the pressure drop by using machine learning models, such as neural networks. The results indicate that neural networks can effectively predict pressure drop by using synthetically generated data, with notable errors observed only in highly severe cases of AS. In this sense, it is important to acknowledge the inherent limitations of this approach.

In the context of the proposed approach, the dataset employed for both training and testing exclusively featured generic valve geometries. Although the employed model achieved a satisfactory performance for the synthetic dataset, the outcomes might differ when this model is applied to patient-specific data. These differences might also be caused by the fact that the synthetic geometries are idealized, e.g., there is no curvature in the aorta. Additionally, the Computational Fluid Dynamics (CFD) simulations were based on a turbulent flow model. In reality, blood flow through the aortic valve is pulsatile in nature, meaning it may fail to reach a completely turbulent state (Zhang & Zhang, 2018).

However, the proposed approach does hold significant advantages for use cases where real-world patient data cannot be readily obtained. With the introduction of stricter data privacy regulations such as GDPR, obtaining patient-specific data for ML model training has become more challenging, often requiring privacy preserving techniques. Synthetic data solves this issue, while also enabling the generation of large datasets faster than through the acquisition and segmentation of patient CT scans. Additionally, estimating the pressure drop value through CFD simulations can take up to several hours. By contrast, neural networks trained on synthetic data can provide the results almost in real time, with a high degree of accuracy.

This paper evaluated the viability of CFD-based synthetic data as an alternative to real-world data when training ML models for pressure drop assessment. The methodology detailed above has shown that large datasets can be obtained through CFD simulations of parametrized meshes. Furthermore, the neural network trained on the synthetic dataset was able to provide an accurate estimation of the pressure drop, being a promising non-invasive alternative to current clinical methods.

Ackwnowledgments

This work has been partly funded in the framework of the European Union's Horizon 2020 Research and Innovation Programme under Grant Agreement No. 101017578 (SIMCor: In-Silico testing and validation of Cardiovascular IMplantable devices). This work was also supported by a grant of the Romanian National Authority for Scientific Research and Innovation, CCCDI – UEFISCDI, ERA-NET-PERMED-RESPECT, within the PNCDI III program. The research leading to the obtained results has received funding based on the EEA Grants 2014-2021, under Project contract No. 33/2021.

REFERENCES

Ayachit, U. (2015) *The paraview guide: a parallel visualization application.* Clifton Park, NY, Kitware, Inc.

Argyropoulos, C. D. & Markatos, N. C. (2015) Recent advances on the numerical modelling of turbulent flows. *Applied Mathematical Modelling*. 39(2), 693-732. doi: 10.1016/j.apm.2014.07.001.

Baumgartner, H., Hung, J., Bermejo, J., Chambers, J. B., Edvardsen, T., Goldstein, S., Lancellotti, P., LeFevre, M., Miller Jr., F. & Otto, C. M. (2017) Recommendations on the echocardiographic assessment of aortic valve stenosis: a focused update from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. *European Heart Journal - Cardiovascular Imaging*. 18(3), 254-275. doi: 10.1093/ehjci/jew335.

Bessems, D. (2007) *On the propagation of pressure and flow waves through the patient specific arterial system*. PhD Thesis, Eindhoven University of Technology.

Farajtabar, M., Larimi, M. M., Biglarian, M., Sabour, D. & Miansari, M. (2023) Machine Learning Identification Framework of Hemodynamics of Blood Flow in Patient-Specific Coronary Arteries with Abnormality. *Journal of Cardiovascular Translational Research*. 16(3), 722-737. doi: 10.1007/s12265-022-10339-5.

Gabe, I. T., Gault, J. H., Ross Jr, J., Mason, D. T., Mills, C. J., Schillingford, J. P. & Braunwald, E. (1969) Measurement of instantaneous blood flow velocity and pressure in conscious man with a catheter-tip velocity probe. *Circulation*. 40(5), 603-614. doi: 10.1161/01.cir.40.5.603.

Gamilov, T., Liang, F., Kopylov, P., Kuznetsova, N., Rogov, A. & Simakov, S. (2023) Computational analysis of hemodynamic indices based on personalized identification of aortic pulse wave velocity by a neural network. *Mathematics*. 11(6), 1358. doi: 10.3390/math11061358.

Hoeijmakers, M. J. M. M., Waechter-Stehle, I., Weese, J. & Van de Vosse, F. N. (2020) Combining statistical shape modeling, CFD, and meta-modeling to approximate the patient-specific pressure-drop across the aortic valve in real-time. *International Journal for Numerical Methods in Biomedical Engineering*. 36(10), e3387. doi: 10.1002/cnm.3387.

Hoeijmakers, M. J. M. M., Morgenthaler, V., Rutten, M. C. M. & van de Vosse, F. N. (2022). Scale-Resolving Simulations of Steady and Pulsatile Flow Through Healthy and Stenotic Heart Valves. *Journal of Biomechanical Engineering*. 144(3), 031010. doi: 10.1115/1.4052459.

Holzmann, T. (2016) *Mathematics, numerics, derivations and OpenFOAM®. Loeben, Germany*, Holzmann CFD.

Lindman, B. R., Clavel, M.-A., Mathieu, P., Iung, B., Lancellotti, P., Otto, C. M. & Pibarot, P. (2016) Calcific aortic stenosis. *Nature Reviews Disease Primers*. 2, 16006. doi: 10.1038/nrdp.2016.6.

Long, D., McMurdo, C., Ferdian, E., Mauger, C. A., Marlevi, D., Young, A. A., & Nash, M. P. (2021). Non-invasive hemodynamic analysis for aortic regurgitation using computational fluid dynamics and deep learning. [Preprint] https://arxiv.org/abs/2111.11660 [Accessed 3rd October 2023].

Manda, Y. R. & Baradhi, K. M. (2022) *Cardiac Catheterization Risks and Complications*. Treasure Island, FL, StatPearls Publishing, LLC.

Nita, C. I., Puiu, A., Bunescu, D., Mihai Itu, L., Mihalef, V., Chintalapani, G., Armstrong, A., Zampi, J., Benson, L., Sharma, P. & Rapaka, S. (2022) Personalized Pre- and Post-Operative Hemodynamic Assessment of Aortic Coarctation from 3D Rotational Angiography. *Cardiovascular Engineering and Technology*. 13(1), 14-40. doi: 10.1007/s13239-021-00552-9.

OpenCFD Ltd. (2022) *ESI OpenCFD Release OpenFOAM® v2206*. https://www.openfoam.com/news/main-news/openfoam-v2206 [Accessed 27th November 2023].

Paszke, A., Gross, S., Massa, F., Lerer, A., Bradbury, J., Chanan, G., Killeen, T., Lin, Z., Gimelshein, N., Antiga, L., Desmaison, A., Köpf, A., Yang, E., DeVito, Z., Raison, M., Tejani, A., Chilamkurthy, S., Steiner, B., Fang, L., Bai, J. & Chintala, S. (2019) Pytorch: An imperative style, high-performance deep learning library. In: *Advances in Neural Information Processing Systems*, 32: *Proceedings of the 33rd International Conference on Neural Information Processing Systems, NIPS'19, 8-14 December 2019, Vancouver, Canada.* Red Hook, NY, Curran Associates Inc. pp. 8026-8037.

Pedregosa, F., Varoquaux, G., Gramfort, A., Michel, V., Thirion, B., Grisel, O., Blondel, M., Prettenhofer, P., Weiss, R., Dubourg, V., Vanderplas, J., Passos, A., Cournapeau, D., Brucher, M., Perrot, M. & Duchesnay, É. (2011) Scikit-learn: Machine learning in Python. *Journal of Machine Learning Research*. 12, 2825-2830.

Srinivasan, S. & Madathil, D. (2016) 3-dimensional computational study of blood flow in pathophysiologically affected arteries simulated in OpenFOAM. In: *2016 8th Cairo International Biomedical Engineering Conference (CIBEC), 15-17 December 2016, Cairo, Egypt.* IEEE. pp. 35-38.

Thomas, B. & Sumam, K. S. (2016) Blood flow in human arterial system - A review. *Procedia Technology*. 24, 339-346. doi: 10.1016/j.protcy.2016.05.045.

Virtanen, P., Gommers, R., Oliphant, T. E., Haberland, M., Reddy, T., Cournapeau, D., Burovski, E., Peterson, P., Weckesser, W., Bright, J., van der Walt, S. J., Brett, M., Wilson, J., Jarrod Millman, K., Mayorov, N. Nelson, A. R. J., Jones, E., Kern, R., Larson, E., Carey, C. J., Polat, I., Feng, Y., Moore, E. W., VanderPlas, J., Laxalde, D., Perktold, J., Cimrman, R., Henriksen, I., Quintero, E. A., Harris, C. R., Archibald, A. M., Ribeiro, A. R., Pedregosa, F. & van Mulbregt, P. (2020) SciPy 1.0: fundamental algorithms for scientific computing in Python. *Nature Methods*. 17(3), 261-272. doi: 10.1038/s41592-019-0686-2.

Zakaria, M. S., Ismail, F., Tamagawa, M., Fazli, A., Azi, A. F. A., Wiriadidjaya, S., Azriff, A. & Ahmad, K. A. (2018) Computational fluid dynamics study of blood flow in aorta using OpenFOAM. *Journal of Advanced Research in Fluid Mechanics and Thermal Sciences*. 43(1), 81-89.

Zhang, R. & Zhang, Y. (2018) An experimental study of pulsatile flow in a compliant aortic root model under varied cardiac outputs. *Fluids*. 3(4), 71. doi: 10.3390/fluids3040071.