

Research Article

Safety and Feasibility Using a Fluid-Filled Wire to Avoid Hydrostatic Errors in Physiological Intracoronary Measurements

Truls Råmunddal,^{1,2} Christian Dworeck,^{1,2} Petronella Torild,¹ Sofie Andréen,¹ Li-Ming Gan,^{1,2} Geir Hirlekar,^{1,2} Dan Ioanes,¹ Anna Myredal,^{1,2} Jacob Odenstedt,^{1,2} Petur Petursson,^{1,2} Tetiana Pylova,² Fanny Töpel,¹ Sebastian Völz,^{1,2} Mats Hilmersson,³ Björn Redfors,^{1,2} and Oskar Angerås ⁽¹⁾

¹Department of Cardiology, Sahlgrenska University Hospital, Gothenburg, Sweden ²Department of Molecular and Clinical Medicine, Institute of Medicine, Gothenburg University, Gothenburg, Sweden ³Cavis Technologies AB, Uppsala, Sweden

Correspondence should be addressed to Oskar Angerås; oskar.angeras@vgregion.se

Received 16 July 2023; Revised 13 December 2023; Accepted 18 December 2023; Published 2 January 2024

Academic Editor: Wei Zhang

Copyright © 2024 Truls Råmunddal et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Background. Using a fluid-filled wire with a pressure sensor outside the patient compared to a conventional pressure wire may avoid the systematic error introduced by the hydrostatic pressure within the coronary circulation. *Aims*. To assess the safety and effectiveness of the novel fluid-filled wire, Wirecath (Cavis Technologies, Uppsala, Sweden), as well as its ability to avoid the hydrostatic pressure error. *Methods and Results*. The Wirecath pressure wire was used in 45 eligible patients who underwent invasive coronary angiography and had a clinical indication for invasive coronary pressure measurement at Sahlgrenska University Hospital, Gothenburg, Sweden. In 29 patients, a simultaneous measurement was performed with a conventional coronary pressure wire (PressureWire X, Abbott Medical, Plymouth, MN, USA), and in 19 patients, the vertical height difference between the tip of the guide catheter and the wire measure point was measured in a 90-degree lateral angiographic projection. No adverse events caused by the pressure wires were reported. The mean Pd/Pa and mean FFR using the fluid-filled wire and the sensor-tipped wire differed significantly; however, after correcting for the hydrostatic effect, the sensor-tipped wire pressure correlated well with the fluid-filled wire pressure (R = 0.74 vs. R = 0.89 at rest and R = 0.89 vs. R = 0.98 at hyperemia). *Conclusion*. Hydrostatic errors in physiologic measurements can be avoided by using the fluid-filled Wirecath wire, which was safe to use in the present study. This trial is registered with NCT04776577 and NCT04802681.

1. Introduction

Using intracoronary pressure measurements to evaluate the clinical significance of coronary stenosis is recommended in European and American guidelines [1, 2]. The most common method to perform a pressure measurement is fractional flow reserve (FFR) using adenosine to accomplish hyperemia; however, resting indices, e.g., instant wave-free ratio (iFR), have been proven as effective as FFR to distinguish a significant from a nonsignificant lesion [3].

Several coronary wires are available to measure pressure inside the coronary artery, all with a pressure sensor in the distal part of the wire. The pressure sensor is calibrated to the aortic pressure by equalization of pressures when the pressure is measured at the same position, i.e., outside the guide catheter in the proximal part of the vessel or in the aorta. However, when advancing the wire into the coronary vessel, the hydrostatic pressure, due to the height difference between the coronary ostium and the distal part of the vessel, causes an unaccounted influence on the measured pressure. In a supine position, the left anterior descending artery (LAD) and posterior descending artery from the right coronary artery (PDA) ascend on average 5 cm, and the left circumflex artery (LCX) and posterior lateral artery from the right coronary artery (PLA) descend on average 3 cm (Figure 1). This results in a decrease in the measured pressure in the LAD and the PDA and an increase in pressure in LCX and PLA due to the hydrostatic pressure. CT studies measuring this height difference suggest a conversion factor of 0.77 mmHg/cm in order to adjust for differences in hydrostatic pressure [4–6].

The systematic error in conventional pressure measurements introduced by the hydrostatic pressure has been described previously but has not been accounted for in studies or guidelines when suggesting clinically used pressure ratio cutoffs for significance pre- and post-PCI regardless of type of pressure index [4].

The Wirecath (Cavis Technologies, Uppsala, Sweden) (Figure 2) is a novel fluid-filled 0.014" wire connected to an external pressure transducer with fixed height which makes the measurements by the Wirecath unaffected by the hydrostatic pressure difference in the coronary artery [7].

This first-in-human Wirecath study (ClinicalTrials.gov Identifier: NCT04776577) was designed to assess the safety and effectiveness of the novel fluid-filled wire as well as its ability to avoid the hydrostatic pressure error. The study was approved by the Swedish Ethical Review Authority (D-nr 2020-04421).

2. Methods

2.1. Patient Selection. Patients were recruited at Sahlgrenska University Hospital, Gothenburg, Sweden. Inclusion criteria were age 18 or above, signed informed consent, and clinical indication for coronary pressure assessment after coronary angiography. Exclusion criteria were known heparininduced thrombocytopenia, other allergy to heparin, contraindication for adenosine, or unstable condition by operator's judgment.

2.2. Study Design. As outlined in Figure3, 29 patients underwent simultaneous measurement with the fluid-filled wire (Wirecath 1, Cavis Technologies, Uppsala, Sweden) and a sensor-tipped wire (PressureWire X, Abbott Medical, Plymouth, MN, USA). At the discretion of the physician, 11 out of these 29 patients (38%) underwent bolus-thermoderived and within 14 days transthoracic ultrasound Doppler-derived coronary flow reserve (CFR) measurements in the LAD.

An additional 16 patients were enrolled who had coronary physiology assessment only using the fluid-filled wire (Wirecath 1, Cavis Technologies, Uppsala, Sweden). After each of the 45 procedures, a usability questionnaire pertaining to the use of the fluid-filled wire was filled out by the users.

The primary endpoint was the rate of adverse events, defined as an untoward medical occurrence, unintended disease or injury, or untoward clinical sign in any of the 45 studied subjects. The key secondary endpoints were the agreement between Pd/Pa and FFR measured with the fluidfilled (Wirecath) and sensor-tipped (Abbott PressureWire) before and after correction for the hydrostatic pressure by



FIGURE 1: Hydrostatic effects in ~99% of the population. Illustration of the influence of the height difference between the coronary ostia and distal coronary arteries and the measured pressure.

using the height measurements. Exploratory secondary endpoints included the correlations between fluid-filled and sensor-tipped wire-derived indices with CFR indices and the usability questionnaire score.

2.3. Procedure. Angiography was performed according to the local standard procedure. All patients received nitroglycerine prior to all physiology assessment. Hyperemia was induced by administering adenosine intravenous ($140 \,\mu g/kg/min$ over two minutes) or intracoronary ($200 \,\mu g$ for the left coronary vessel and $120-200 \,\mu g$ for the right coronary vessel). Whether the patients had simultaneous measurements with the fluid-filled and sensor-tipped wires or only had coronary physiology assessment using the fluid-filled wire was left to the discretion of the physician performing the procedure.

2.4. Simultaneous Measurements. The fluid-filled wire (Wirecath 1, Cavis Technologies, Uppsala, Sweden) and the sensor-tipped wire (PressureWire X, Abbott Medical, Plymouth, MN, USA) were placed simultaneously at the same location in the coronary artery. Simultaneous pressure measurements were then performed with both wires, both resting Pd/Pa and FFR.

The vertical height difference between the tip of the guide catheter and the wire measure point was measured in a 90degree lateral angiographic projection by first marking the position of the guide catheter tip with adhesive tape on the fluoroscopy screen, then adjusting the vertical position of the x-ray table until the measuring point of the wire on fluoroscopy reaches the tape mark on the screen, and finally assessing the total adjusted distance in centimeter between the two table positions on a tape measure attached to the patient table (Figure 4).

When the wires were withdrawn from the artery into the tip of the guide catheter, the observed "Pd/Pa" was recorded to allow quantification of any drift in pressure.

By multiplying each height difference, negative or positive, with the conversion factor 0.77 mmHg/cm, a correction for each pressure measurement by the sensor-tipped wire was established. By adjusting the sensor-tipped pressure with this correction, the pressure from the sensor-tipped wire was corrected for the hydrostatic effect.



FIGURE 2: Wirecath pressure wire with external transducer. Illustration of the design of the fluid-filled wire and transducer.



FIGURE 3: Enrollment flowchart.

2.5. Coronary Flow Reserve. A subset of patients who had simultaneous measurements by the fluid-filled and pressuretipped wires underwent bolus-thermo-derived coronary flow reserve (CFR) measurements in the LAD and was subsequently referred to transthoracic Doppler-echocardiography-derived CFR measurement (TDE-CFR), which has shown to be highly correlated with CFR derived from positron emission tomography [8] and to invasive Doppler guide wire-derived CFR [9, 10]. TDE-CFR was performed according to the standard procedure of the hospital [11]. The correlation between a pressure-derived CFR, bolus-thermo-derived CFR, and the echocardiography-CFR was investigated. To mimic the situation during the invasive physiology measurement, all patients received the same nitroglycerin dose 5 min prior to the TDE-CFR assessment measured during a denosine hyperemia (140 μ g/kg/min). Pressure-derived CFR was calculated by the formula 1-FFR/ 1-Pd/Pa [12].

2.6. Regular Use. In the regular-use study group, the fluidfilled wire was used as a regular pressure measurement tool, replacing the standard pressure wire.

2.7. Statistical Methods. The results are presented with descriptive statistics. Unless otherwise noted, all summed values are presented as mean \pm standard deviation. In the comparison of pressure measurements, the Pearson correlation factor and the intraclass correlation coefficient were calculated and regression plots were made for paired



FIGURE 4: Height measurement between the pressure measure point and the tip of the guide catheter. Example of an observed height difference between the pressure measure point and the tip of the guide catheter.

measurements. The CFR measurement comparisons were exploratory only and intended to give a first insight into the capability of pressure-derived CFR with a fluid-filled wire.

3. Results

Patients' age ranged from 54 to 82 years (mean 70 ± 6.5 years), and 31% were female. The indications for angiography were 14 patients with stable angina, 9 with unstable angina, 7 with non-ST elevation myocardial infarction, and the remaining with other indications.

No adverse events related to the use of the pressure wires were reported.

3.1. Comparisons of Pd/Pa and FFR after Simultaneous Measurements with Fluid-Filled and Sensor-Tipped Wires. 35 coronary arteries in 29 patients were included in the simultaneous measurements study group only.

24 lesions (69%) were located in the LAD artery, 4 (11%) in the LCX, and 7 (20%) in the right coronary artery (RCA).

The mean Pd/Pa at rest in the 29 simultaneous measurements, after removal of five drift cases (Pd/Pa >0.02) and one erroneous pressure data, using the fluid-filled wire and the sensor-tipped wire were 0.96 ± 0.03 and 0.94 ± 0.04 , respectively. The mean FFR in the same 29 simultaneous measurements using the fluid-filled wire and the sensortipped wire were 0.89 ± 0.07 and 0.87 ± 0.07 , respectively.

Successful height measurements were collected in 19 simultaneous measurements, after the exclusion of nine cases with missing height data and one erroneous height measurement. Data were missing due to difficulties in visualizing both the guide catheter tip and the wire position in the lateral view.

The 19 arteries consisted of 14 LAD, 2 LCX, and 3 RCA. The mean difference in height between the coronary ostium and the pressure measure point was 2.6 cm, corresponding to a mean hydrostatic pressure difference of 2.0 mmHg, using the conversion factor 0.77 mmHg/cm [6].

Table 1 summarizes the results showing that the difference between the two wires diminished when the sensortipped wire measurements were corrected. Table 2 presents which coronary vessel was measured, measured height difference, calculated hydrostatic pressure, and aortic and coronary pressure ratios.

Figure 5 shows that after correcting for the hydrostatic effect, the sensor-tipped wire pressure correlated well with the fluid-filled wire pressure (R = 0.74 vs. R = 0.89 at rest and R = 0.89 vs. R = 0.98 at hyperemia).

In the subgroup where measurements were made in the LAD, the mean Pd/Pa at rest were 0.96 ± 0.04 and 0.92 ± 0.04 for the fluid-filled wire and the sensor-tipped wire, respectively, and the mean FFR were 0.90 ± 0.05 and 0.86 ± 0.06 , respectively.

Out of the 29 valid measurements, the number of discordant classifications between the sensor-tipped wire and the fluid-filled wire was explored for the Pd/Pa at rest and the FFR measurements.

When applying the cutoff Pd/Pa \leq 0.92 [13], two LADs were significant according to the sensor-tipped wire but not according to the fluid-filled wire. Two RCAs were significant according to the fluid-filled wire but not according to the sensor-tipped wire.

When applying the cutoff $FFR \le 0.80$, three LADs were significant according to the sensor-tipped wire, but not according to the fluid-filled wire.

Drift was compared in 33 simultaneous measurements in 27 patients. The fluid-filled wire demonstrated less drift than the sensor-tipped wire (standard deviation 0.11 vs. 0.18). With an increasing number of cases, less drift was observed, possibly learning curve-related.

3.2. Correlations between Pressure Indices and CFR. Pressure-derived CFR with the fluid-filled wire correlated to TDE-CFR and thermodilution-CFR (R = 0.69 and R = 0.76, respectively (Figure 6(a))). Sensor-tipped wire pressure-derived CFR did not correlate positively to the reference methods; see Figure 6(b). When using the square root of 1-

		-								
Index		Sensor-tipped wire	Fluid-filled wire	Difference between sensor-tipped and fluid-filled wire	Difference between sensor-tipped and fluid-filled wire after correction of the sensor-tipped wire for the hydrostatic effec					
Pd/Pa	Mean ± SD	0.93 ± 0.041	0.95 ± 0.035	0.024 ± 0.028	0.002 ± 0.018					
	Median	0.93	0.97	0.036	0.003					
	Min	0.84	0.88	-0.04	-0.06					
	Max	1.01	1.00	0.05	0.03					
FFR	Mean ± SD	0.85 ± 0.066	0.87 ± 0.072	0.026 ± 0.033	0.0037 ± 0.017					
	Median	0.85	0.91	0.032	0.0016					
	Min	0.74	0.73	-0.035	-0.027					
	Max	0.96	0.96	0.072	0.03					

TABLE 1: Summary of simultaneous measurements including height measurements (n = 19).

FFR/1-PdPa, relationships get less proportional, and R values do not improve compared to not using square root.

3.3. Results of the Usability Questionnaire. 16 patients were included in the regular-use study group only. The fluid-filled wire was used as a regular pressure measurement tool, and in two cases, the fluid-filled wire was used for balloon and stent intervention during PCI.

Usability was evaluated by using a questionnaire filled in by the interventionalists in this group. The scoring was similar for the fluid-filled wire and the sensor-tipped wire when it came to perceived maneuverability, X-ray visibility, and signal quality. The preparation of the fluid-filled wire had a mean score of 2.8 compared to the sensor-tipped wire 3.0, on a scale from 1 (poor) to 5 (very good).

4. Discussion

The main findings of this study are that (i) the fluid-filled Wirecath wire (Cavis Technologies, Uppsala, Sweden) could be safely and reliably used to assess Pd/Pa and FFR for clinical decision-making in a typical patient population undergoing PCI; (ii) the differences between FFR and resting indices obtained by the sensor-tipped versus fluid-filled wires were explained by a hydrostatic pressure component related to the height difference between the coronary ostium and the distal vessel; and (iii) correcting the sensortipped values for the height difference almost completely aligned measurements derived by the sensor-tipped versus fluid-filled wires.

The hydrostatic pressure difference (which is the same value for resting and hyperemia measurements) has a larger impact on resting ratios since the true pressure reduction across the lesion is smaller at rest than during hyperemia (FFR). The effect is also larger on diastolic resting ratios compared to whole-cycle ratios, since the fixed hydrostatic pressure difference is relatively larger in diastolic versus mean blood ratios [5, 14].

A neglection of the hydrostatic error may have implications for clinical practice. The hydrostatic error causes lower measured values (i.e., overestimation) in the LAD or distal PDA, since these vessels in a supine patient position are located higher than the coronary ostium, i.e., the hydrostatic pressure falls. This measurement error might lead to false-positive pressure ratios and thus misclassification as clinically significant. Vice versa may the rise in hydrostatic pressure cause an underestimation in non-LAD vessels. This could be of special importance in patients where FFR is used to evaluate the result of the PCI exposing the patient to the risk of leaving an inadequate result or the risk of complication when trying to improve an already adequate stenting [15].

Coronary CT has previously been used for the measurement of height differences in coronary vessels [4, 5]. Another potential way to calculate the hydrostatic error, when a fluid-filled wire is not available, is to use quantitative coronary angiography (QCA) tools to measure the height in a lateral angiographic view and compensate for the height difference between the tip of the guide catheter and the measure point of the wire. This would simplify the height measurement compared to the method used in this study. The QCA method is currently evaluated in another study (ClinicalTrials.gov Identifier: NCT04802681).

When using a fluid-filled wire, pressure-derived CFR correlates to other CFR measurement methods as opposed to when using a sensor-tipped wire. This is presumably due to the avoidance of the hydrostatic error, which has also been shown in other explorative studies [16]. Due to the small sample size, no firm conclusion can be drawn, but the result may suggest that pressure-derived CFR can possibly be used as a screening tool for evaluating CFR and other CFR-related indices such as resistive reserve ratio (RRR) and microvascular resistance reserve (MRR).

4.1. Limitations. A larger dataset than available in this study would be needed to statistically evaluate the amount of discordance and misclassification caused by hydrostatic errors. Quantification of the size of errors caused by hydrostatic pressure has been explored in other studies [4, 5].

The reasons for drift were not explored in this study. Drift could be caused by both technical shortcomings of the measurement devices, but also by user mistakes caused by pitfalls when doing pressure measurements [7].

	Pd at hyperemia sensor-tipped after hydro correction (mmHg)	95.5	66.5	72.2	96.0	88.8	85.3	77.2	74.1	53.1	63.9	86.8	84.8	85.8	65.9	50.4	74.2	55.7	83.2	63.0	
	Pd at hyperemia sensor-tipped (mmHg)	86	62	68	92	85	82	74	71	50	61	84	82	84	65	52	76	58	86	66	
	Pa at hyperemia sensor-tipped (mmHg)	67	84	80	120	97	89	96	82	59	73	94	96	89	68	66	86	78	94	86	
	Pd at rest sensor-tipped after hydro correction (mmHg)	98.5	93.5	80.2	115.0	76.8	89.3	82.2	96.1	74.1	72.9	96.8	82.8	84.8	70.9	103.4	80.2	75.7	84.2	80.0	
	Pd at rest sensor-tipped (mmHg)	89	89	76	111	73	86	79	93	71	70	94	80	83	70	105	82	78	87	83	
	Pa at rest sensor-tipped (mmHg)	95	98	83	124	87	90	85	66	76	83	100	86	89	73	113	82	85	86	86	
	Hydrostatic error (0.77 mmHg/cm) (mmHg)	-9.5	-4.5	-4.2	-4.0	-3.8	-3.3	-3.2	-3.1	-3.1	-2.9	-2.8	-2.8	-1.8	-0.9	1.6	1.8	2.3	2.8	3.0	
	Height difference $\pm x$ (cm)	-12.4	-5.8	-5.5	-5.2	-4.9	-4.3	-4.2	-4.0	-4.0	-3.8	-3.7	-3.6	-2.4	-1.2	2.1	2.3	3.0	3.7	3.9	
	Vessel	LAD	LAD	LAD	LAD	LAD	LAD	LAD	LAD	LAD	LAD	LAD	LAD	LAD	LAD	RCA	LCX	RCA	RCA	LCX	

TABLE 2: Height measurements and correction of sensor-tipped wire measurements (n = 19).

6



FIGURE 5: Correlation between indices derived using the fluid-filled versus sensor-tipped wires. The correlation for both Pd/Pa (a) and fractional flow reserve (FFR) (b) between the two wires was greater when the hydrostatic error due to height was accounted for (right versus left). Passing-Bablok regression indicates that a small proportional bias was present between FFR derived using the fluid-filled wire versus the sensor-tipped wire after correction for hydrostatic pressure (slope 1.14 (95% CI) [1.01–1.38]) but not in the other comparisons.



FIGURE 6: Continued.



FIGURE 6: Correlation between pressure-derived coronary flow reserve (CFR) and CFR derived by echocardiography or thermodilution. (a) Correlation between pressure-derived CFR using the fluid-filled wire and CFR derived by echocardiography (left) and thermodilution (right). (b) Correlation between pressure-derived CFR using the sensor-tipped wire and CFR derived by echocardiography (left) and thermodilution (right).

5. Conclusions

Hydrostatic pressure introduces error in conventional intracoronary pressure measurements that has a particularly large impact on resting indices. Hydrostatic errors in physiologic measurements can be avoided by using the fluid-filled Wirecath wire, which was safe to use in the present study.

Data Availability

The study data used to support the findings of this study are available from the corresponding author upon request.

Disclosure

This work has been presented as an oral abstract at the European Society of Cardiology meeting in Barcelona 2022.

Conflicts of Interest

Oskar Angerås is a member of the advisory board of Cavis Technologies and a member of the advisory board of Abbott Vascular. He received research grant from Abbott Vascular and speaker fee from Abbott Vascular, Boston Scientific, and Medtronic. Petur Petursson received speaker fee from Medtronic. Sebastian Völz received speaker fee from Abbott Vascular and Boston Scientific. Mats Hilmersson is an employee at Cavis Technologies AB.

Acknowledgments

The study was financially supported by the Swedish Governmental Agency for Innovation Systems (Vinnova).

References

[1] J. Knuuti, W. Wijns, A. Saraste et al., "2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes," European Heart Journal, vol. 41, no. 3, pp. 407–477, 2020.

- [2] J. S. Lawton, J. E. Tamis-Holland, S. Bangalore et al., "2021 ACC/AHA/SCAI guideline for coronary artery revascularization: executive summary: a report of the American college of Cardiology/American heart association joint committee on clinical practice guidelines," *Circulation*, vol. 145, no. 3, pp. e4–e17, 2022.
- [3] J. M. Lee, T. M. Rhee, K. H. Choi et al., "Clinical outcome of lesions with discordant results among different invasive physiologic indices — resting distal coronary to aortic pressure ratio, resting full-cycle ratio, diastolic pressure ratio, instantaneous wave-free ratio, and fractional flow reserve," *Circulation Journal*, vol. 83, no. 11, pp. 2210–2221, 2019.
- [4] T. Härle, M. Luz, S. Meyer et al., "Effect of coronary anatomy and hydrostatic pressure on intracoronary indices of stenosis severity," *JACC: Cardiovascular Interventions*, vol. 10, no. 8, pp. 764–773, 2017.
- [5] F. Al-Janabi, G. Karamasis, C. M. Cook et al., "Coronary artery height differences and their effect on fractional flow reserve," *Cardiology Journal*, vol. 28, no. 1, pp. 41–48, 2021.
- [6] Y. Kawaguchi, K. Ito, H. Kin et al., "Impact of hydrostatic pressure variations caused by height differences in supine and prone positions on fractional flow reserve values in the coronary circulation," *Journal of Interventional Cardiology*, vol. 2019, Article ID 4532862, 9 pages, 2019.
- [7] N. H. J. Pijls, M. J. Kern, P. G. Yock, and B. De Bruyne, "Practice and potential pitfalls of coronary pressure measurement," *Catheterization and Cardiovascular Interventions*, vol. 49, no. 1, pp. 1–16, 2000.
- [8] M. Saraste, J. W. Koskenvuo, J. Knuuti et al., "Coronary flow reserve: measurement with transthoracic Doppler echocardiography is reproducible and comparable with positron emission tomography," *Clinical Physiology*, vol. 21, no. 1, pp. 114–122, 2001.
- [9] H. Lethen, H. P. Tries, J. Brechtken, S. Kersting, and H. Lambertz, "Comparison of transthoracic Doppler echocardiography to intracoronary Doppler guidewire

measurements for assessment of coronary flow reserve in the left anterior descending artery for detection of restenosis after coronary angioplasty," *The American Journal of Cardiology*, vol. 91, no. 4, pp. 412–417, 2003.

- [10] T. Wada, K. Hirata, Y. Shiono et al., "Coronary flow velocity reserve in three major coronary arteries by transthoracic echocardiography for the functional assessment of coronary artery disease: a comparison with fractional flow reserve," *European Heart Journal- Cardiovascular Imaging*, vol. 15, no. 4, pp. 399–408, 2014.
- [11] L. Gan, S. Svedlund, A. Wittfeldt et al., "Incremental value of transthoracic Doppler echocardiography-assessed coronary flow reserve in patients with suspected myocardial ischemia undergoing myocardial perfusion scintigraphy," *Journal of the American Heart Association*, vol. 6, no. 4, Article ID e004875, 2017.
- [12] J. M. Ahn, F. M. Zimmermann, N. P. Johnson et al., "Fractional flow reserve and pressure-bounded coronary flow reserve to predict outcomes in coronary artery disease," *European Heart Journal*, vol. 38, no. 25, pp. 1980–1989, 2017.
- [13] A. Jeremias, A. Maehara, P. Généreux et al., "Multicenter core laboratory comparison of the instantaneous wave-free ratio and resting P/P with fractional flow reserve," *Journal of the American College of Cardiology*, vol. 63, no. 13, pp. 1253–1261, 2014.
- [14] S. Sen, K. N. Asrress, S. Nijjer et al., "Diagnostic classification of the instantaneous wave-free ratio is equivalent to fractional flow reserve and is not improved with adenosine administration," *Journal of the American College of Cardiology*, vol. 61, no. 13, pp. 1409–1420, 2013.
- [15] Z. Piroth, H. Otsuki, F. M. Zimmermann et al., "Prognostic value of measuring fractional flow reserve after percutaneous coronary intervention in patients with complex coronary artery disease: insights from the FAME 3 trial," *Circulation: Cardiovascular Interventions*, vol. 15, no. 11, pp. 884–891, 2022.
- [16] K. Zsolt, "Novel microvasculature index: pressure bounded microvascular resistance reserve," https://eposter.europaorganisation.com/2022/europcr/index/slide/abstract/794.