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RESEARCH ARTICLE

Evaluation of Mechanical Hemolysis of Bare Metallic and Drug-Eluting Cardiovascular Stents

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Abstract

Objectives: To investigate the hemolytic potential of different types of experimental cardiovascular stents [Bare Metal Stents (BMS), Sirolimus Eluting Stents (SES), and Everolimus Eluting Stents (EES)] in an *in vitro* study using a bovine blood circulatory model. **Methods:** Fresh bovine blood was circulated through the loop containing the stents, using the peristaltic pump for 6 hours at 37°C at a constant flow of 200 mL/minute. Plasma Free Hemoglobin (PFH) was measured spectrophotometrically at defined intervals. The Normalized Index of Hemolysis (NIH) and the Modified Index of Hemolysis (MIH) were calculated from the PFH values. **Findings :** The PFH (mg/dL) of BMS ranged between 102 $\pm$ 22.4 at 1 hour and 560 $\pm$ 106.4 at 6 hours. Similarly for SES and EES, PFH (mg/dL) were between (116 $\pm$ 20.9 and 279.5 $\pm$ 61.5); and (124.5 $\pm$ 23.7 and 287.5 $\pm$ 57.5), respectively. Also, the MIH ranges for BMS, SES and EES were between 86.07 to 110.5, 47.19 to 88.83, and 57.618 to 64.528, respectively. SES and EES induced statistically less mechanical hemolysis compared to BMS. No statistically significant increase in mechanical hemolysis was observed over time in SES and EES, whereas BMS showed an increase in mechanical hemolysis over a period of 6 hours. **Novelty :** This study provides a comparative *in vitro/ex-vivo* hemolysis analysis of three commonly used stent types in a controlled circulatory system using bovine blood.

Keywords: Stent; Bovine blood; Plasma free hemoglobin; Normalized Index of Hemolysis (NIH); Modified Index of Hemolysis (MIH)

1 Introduction

Stents have become a critical intervention for the treatment of coronary artery disease, a leading cause of mortality worldwide. These devices, ranging from Bare-Metal Stents (BMS) to Drug-Eluting Stents (DES) and newer bioresorbable scaffolds, aim to restore blood flow and improve patient outcomes by addressing narrowed or obstructed coronary arteries through a minimally invasive procedure. Recent advancements in stent technology, such as thinner struts, improved drug coatings, and bioresorbable materials, have further enhanced their efficacy and safety. These developments address challenges like in-stent stenosis[(1)] and late stent thrombosis[(2,3)] while improving deliverability and biocompatibility[(4)]. For instance, drug-eluting stents[(5)] have

significantly reduced restenosis rates compared to earlier BMS [2].

Despite advancements, stent-induced hemolysis persists. Hemolysis, the rupture of red blood cells, can occur due to various factors, such as device geometry, direction of blood flow and mechanical stress. Stent Thrombosis is a particular concern for cardiovascular implants and devices, as the induced shear forces can lead to the destruction of erythrocytes, resulting in the release of hemoglobin and other intracellular materials.

Mechanical hemolysis, influenced by the stent design and blood flow dynamics is a key concern [6] BMS, while mechanically robust, can promote platelet adhesion and activation, potentially leading to thrombosis. DES were developed to mitigate this risk by releasing antiproliferative drugs. However, the impact of drug coatings and stent polymers on hemolysis remains an area of ongoing investigation. The authors of another publication suggest further research on the mechanical properties and long-term biostability of the new PET copolymers [7].

This ongoing risk of hemolysis can impact long-term patient outcomes, underscoring the need for further research in this area. This study seeks to fill this important knowledge gap by directly comparing the hemolytic properties of BMS, Sirolimus Eluding Stents (SES), and Everolimus Eluding Stents (EES) using a standardized *in vitro* bovine blood model. Although some research exists on individual stent types and hemolysis [8], a direct comparison between these three specific stent types in a standardized *in vitro* setting, using bovine blood, remains unstudied. This work addresses an important gap in the existing literature.

This study aims to:

1. To develop an *in vitro/ex vivo* model to study hemolysis of blood contacting medical devices.
2. Quantify and compare the hemolysis induced by BMS, SES, and EES in a controlled *in vitro/ex vivo* environment using a bovine blood model.
3. To analyze the progression of hemolysis over 6 hours, assessing any time-dependent variations between the stent types.
4. To determine if the drug-eluting coatings of SES and EES significantly alter the hemolytic properties compared to the bare metal surface of BMS.

This research seeks to provide insights into their respective safety profiles and potential clinical implications by assessing the degree of hemolysis induced by each stent type.

2 Methodology

2.1 Study Design

This study has developed an *in vitro/ex vivo* circulating blood loop method to test cardiovascular implants for their potential to cause mechanical hemolysis. Fresh bovine blood is circulated in the loop containing the implants for 6 hours at a flow rate of 200 mL/minute [9]. At the end of 6 hours period, various hemolysis parameters are measured.

2.2 Materials and Methods

2.2.1 Stent Tested

BMS, SES and EES were tested for mechanical hemolysis in this study.

2.2.2 Blood Collection and Preparation

Animal blood was obtained from an abattoir [10], hence, there were no need of ethical considerations. Blood was collected by controlled venipuncture to minimize the risk of contamination with debris or fluids other than blood. Blood was collected into a blood collection container containing 6000 IU of heparin per litre (Biological E. Limited, Hyderabad, India) of collected blood. On the day of the experiment, approximately 1000 mL of fresh heparinized blood was collected from the abattoir and transported to the laboratory at 2-8 °C. Once in the laboratory, the blood was stored at 2-8 °C and used. Before testing, the blood was warmed to 37±2 °C in a water bath. Visual inspection ensured that clot-free blood was used for testing. The blood remained in the water bath for the duration of testing. From that, a volume of 310 mL was used for each circulation. The blood was used in the experiments only if the free plasma hemoglobin was less than 50 mg/dL and hematocrit fell within 24.0 to 46.0 % (clinically relevant values for bovine blood) in the pooled blood sampling to qualify the blood.

2.2.3 Pump System

The experimental setup utilized a peristaltic pump (GX-LABV1-III/EP1-SC, Darwin Microfluidics, Paris, France) to replicate physiologically relevant blood flow patterns in the cardiovascular system. The pump settings were controlled to maintain a consistent flow rate that matched the typical blood flow observed in coronary arteries, enabling the simulation of realistic clinical conditions. This approach ensured that the mechanical forces exerted on the blood cells by the stents could be accurately evaluated. The flow rate was set to 200 mL/minute.

2.3 Experimental Procedure

2.3.1 The in vitro circulatory system consists of the following

Tubing : Platinum cured silicone tubing was selected for its biocompatibility and transparency. The inner diameter of the tubing was matched to the dimensions of a coronary artery to simulate realistic flow conditions. The tubing had an approximate wall thickness of 1.6 mm to provide structural integrity. A tubing length of 95 cm was used to ensure stable flow conditions.

Stent Deployment: Before testing, the tubing was sterilized, and the stent was carefully deployed using a deflated balloon catheter with the stent mounted on it. The stent was then expanded to a realistic configuration, matching the expected clinical deployment. After the deployment of the stent, the tubing was ready to be loaded onto the peristaltic pump.

2.3.2 Experimental Setup

The prepared tubing set-up was loaded to the peristaltic pump, which was set to a 200 mL/min flow rate (corresponding to the typical blood flow observed in coronary arteries). The tubing loaded with the stent was connected in a closed circuit to a 500 mL blood container (sterile borosilicate glass bottle) filled with 310 mL of blood. The use of glass containers didn't have any impact on the validity of the study. The container was placed in the water bath, with a temperature of 37 °C $\pm$ 2, to maintain an appropriate and constant blood temperature during the experiments. Before testing, phosphate buffered saline (PBS) was recirculated for approximately 5 minutes with the stent to rinse and wet all the blood-contacting surfaces. Each stent was run on the same day with the same collected bovine blood maintaining the hematocrit value standard. The experiments were repeated thrice.

2.3.3 Blood Circulation

All the air bubbles in the blood were eliminated to avoid air-blood mixing and bubble entrapment. The pump was operated at a 100 mL/min flow rate for approximately 5 minutes to ensure thorough mixing of the blood and removal of any air bubbles. After 5 minutes, when the blood reached its target test temperature (37 $\pm$ 2°C), the first blood sample (time = 0) was taken as the baseline control for analysis which includes hematocrit, total blood hemoglobin concentration, plasma free hemoglobin concentration (PFH)[11], pH and glucose. After the baseline (T = 0 minute) blood sampling, the blood pump was adjusted to the final flow of 200 mL/ minute. Blood samples were processed immediately for analysis to minimize any auto-hemolysis (see Figure 1).

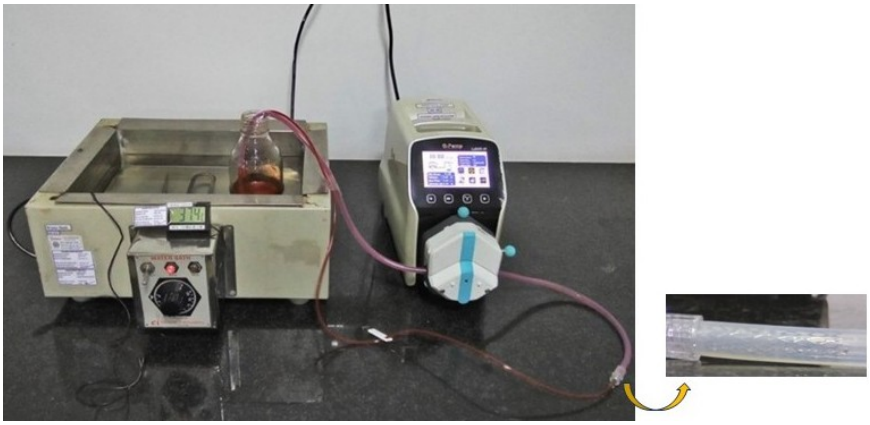

Fig 1. Flow loop setup with stent assembly

2.3.4 Sampling

Blood samples were collected hourly at the following time intervals: 0 (as above), 1 h ± 6 minutes, 2 h ± 6 minutes till 6 h ± 6 minutes. At each collection point the temperature of the water bath was also recorded. For each sampling, a 10 mL blood sample was collected and used to measure hematocrit, total hemoglobin concentration, and pH. To minimize auto-hemolysis, the blood samples were processed immediately. From the collected blood, 1 mL was used for hematology analysis, and 2 mL was used for pH measurement. The remaining blood was centrifuged at 2028 rcf for 15 minutes to isolate the plasma, which was then used to estimate PFH and glucose levels. The water bath temperature was recorded hourly throughout the experiment. Hematocrit and total hemoglobin concentration were reported for all observation points of the study.

2.3.5 Hemolysis Measurement

Haemoglobin Standard Preparation: A cyanmethaemoglobin standard (Arkray Healthcare Pvt. Mumbai, India) with a concentration of 60 mg/dL was diluted using Drabkin's reagent (Arkray Healthcare Pvt. Mumbai, India) to prepare six hemoglobin concentrations: 0.12, 0.18, 0.24, 0.30, 0.42, and 0.54 mg/mL. The absorbances of these solutions were measured against Drabkin's reagent using a microplate reader (Multiskan SkyHigh Microplate Spectrophotometer, Thermo Fisher Scientific, USA) at 540 nm. A standard curve was generated using the hemoglobin concentrations on the y-axis and the respective absorbances at 540 nm on the x-axis. The calibration coefficient (F) determined from the slope of the standard curve was then used for the study. The following measurements of hemolysis were then calculated using the following formulae:

Plasma Free Haemoglobin Concentration Determination (PFH) [11] **:** The plasma free hemoglobin (PFH) was calculated using the following formula

Plasma Free Haemoglobin (PFH) = APFH x F x 2

Normalized Index of Hemolysis (NIH) detection : Normalized Index of Hemolysis (NIH) was calculated using the following formula.

$$NIH(g/100L) = \frac{\Delta PFH \times V \times (100 - HCT)/100}{Q \times \Delta T \times 1000}$$

where:

Δ PFH = change in plasma free hemoglobin concentration (mg/dL) over the sampling time interval
V = blood volume in the loop (mL),
Q = flow rate (L/min),
Hct = hematocrit (%), and
ΔT = sampling time interval (min).

Modified index of hemolysis (MIH): The Modified index of hemolysis (MIH) was calculated using the following formula

$$MIH = \frac{\Delta PFH \times V \times (100 - HCT)/100}{Q \times \Delta T \times Hgb}$$

where:

Hgb = total blood hemoglobin concentration at time zero (g/dL).
Δ PFH = change in plasma free hemoglobin concentration (mg/dL) over the sampling time interval
V = blood volume in the loop (mL),
Q = flow rate (L/min),
Hct = hematocrit (%), and
ΔT = sampling time interval (min).

2.3.6 Statistical analysis

Non-parametric test (Friedman Test) used for comparing MIH values for different stents measured at repeated time points. This method is suitable when data do not meet the assumptions of normality or replication. Next Wilcoxon Signed-Rank Tests (Pairwise Comparisons) was used to compare MIH values between each pair of stents over the same time points. Probability values of p less than or equal to 0.05 were considered statistically significant.

3 Results and Discussion

The hemolysis data from the three stents are presented in Tables 1, 2 and 3.

Table 1. Overview of Readings for All Parameters – Bare Metal Stent

Parameters	Pooled blood	(Baseline) 0h	1h	2h	3h	4h	5h	6h
Mean PFH (mg/dL)	28±5.3	47.5±10.5	102±22.4	180±36.0	238.5±52.5	397±87.3	467.5±98.2	560±106.4
Mean HGB (g/dL)	13.7±2.9	12.7±2.8	12.75±2.4	13.2±2.9	12.8±2.4	13.35±2.8	13.65±2.9	13.1±2.5
Mean Hematocrit (%)	32.9±6.9	32.1±6.1	31.3±6.6	31.4±6.3	29.2±6.4	27.95±5.9	32.25±6.1	32.2±7.1
Glucose (mg/dL)	64.2±12.2	62.8±12.6	55±10.5	44.1±7.9	33.2±7.0	19.7±4.1	10.5±1.9	4.3±0.9
pH	7.56±0.1	7.44±0.1	7.36±0.1	7.34±0.2	7.3±0.1	7.28±0.1	7.23±0.1	7.09±0.1
Temperature (°C)	36.4±0.4	36.7±0.4	37±0.4	36.2±0.6	36.9±0.5	36.6±0.4	37.1±0.6	37±0.7
Normalized Index of Hemolysis (NIH) (g/100 L)*	-	-	0.94	1.14	1.13	1.57	1.42	1.45
Modified index of hemolysis (MIH)*	-	-	73.41	86.07	88.04	117.9	104.2	110.5

Flow rate 200 mL/min; volume of the loop was 300 mL
* Calculated from mean PFH and mean Hematocrit
PFH, Plasma Free Hemoglobin; HGB, Hemoglobin

Table 2. Overview of Readings for All Parameters – Sirolimus Drug Eluting Stent

Parameters	Pooled blood	(Baseline) 0h	1h	2h	3h	4h	5h	6h
Mean PFH (mg/dL)	34 ± 6.8	54.5 ± 12.0	116 ± 20.9	144 ± 27.4	180 ± 34.2	203 ± 44.7	231.5±44.0	279.5 ± 61.5
Mean HGB (g/dL)	12.1 ± 2.7	11.6 ± 2.2	11.9 ± 2.5	12.15 ± 2.3	12.4 ± 2.6	11.95 ± 2.3	12.65 ± 2.4	12.6 ± 2.8
Mean Hematocrit (%)	31.5 ± 6.6	31.2 ± 6.2	31.25±6.6	31.2 ± 5.9	31.2 ± 6.2	29.2 ± 6.4	32.55 ± 7.2	31.1 ± 5.9
Glucose (mg/dL)	57.5 ± 10.4	54.8 ± 11.5	50.2 ± 9.0	50.5 ± 10.1	37.1 ± 6.7	25.2 ± 4.8	15.1 ± 3.2	8.7 ± 1.7
pH	7.8 ± 0.2	7.54 ± 0.2	7.46 ± 0.1	7.51 ± 0.1	7.45 ± 0.1	7.34 ± 0.2	7.25 ± 0.1	7.07 ± 0.1
Temperature (°C)	37.1 ± 0.7	36.7 ± 0.6	35.6 ± 0.7	35.4 ± 0.6	37.2 ± 0.7	36.3 ± 0.6	37.3 ± 0.5	37.7 ± 0.4
Normalized Index of Hemolysis (NIH) (g/100 L)*	-	-	1.06	0.77	0.72	0.66	0.60	0.65
Modified index of hemolysis (MIH)*	-	-	88.83	63.35	58.03	54.99	47.19	51.269

Flow rate, 200 mL/min; volume of the loop, 300 mL
* Calculated from mean PFH and mean Hematocrit
PFH, Plasma Free Hemoglobin; HGB, Hemoglobin

Table 3. Overview of Readings for All Parameters – Everolimus Drug Eluting Stent

Parameters	Pooled blood	(Baseline) 0h	1h	2h	3h	4h	5h	6h
Mean PFH (mg/dL)	40 ± 8.4	90 ± 17.1	124.5±23.7	169 ± 37.2	195.5±39.1	227.5 ± 50.1	265±55.7	287.5 ± 57.5
Mean HGB (g/dL)	11.3 ± 2.3	10.8 ± 2.1	10.6 ± 2.3	10.95 ± 2.1	10.8 ± 2.2	10.65 ± 2.0	10.55±2.0	10.5 ± 2.1
Mean Hematocrit (%)	28.7 ± 5.7	28.7 ± 6.3	28.5 ± 6.0	28.45 ± 6.3	28.6 ± 5.7	28.6 ± 6.3	28.65±6.3	28.4 ± 5.4
Glucose (mg/dL)	67.1±12.1	63.2 ± 11.4	51.9 ± 9.3	46 ± 9.7	39.9 ± 7.6	35.6 ± 6.4	22.2±4.0	10.7 ± 1.9
pH	7.57 ± 0.2	7.44 ± 0.1	7.44 ± 0.1	7.37 ± 0.1	7.37 ± 0.1	7.36 ± 0.2	7.23±0.1	7.19 ± 0.1
Temperature (°C)	37.5 ± 0.6	35.4 ± 0.4	37 ± 0.4	37.2 ± 0.5	36.9 ± 0.6	37.2 ± 0.5	36.9±0.5	35.8 ± 0.5
Normalized Index of Hemolysis (NIH) (g/100 L)*	-	-	0.62	0.71	0.63	0.61	0.62	0.59
Modified index of hemolysis (MIH)*	-	-	58.18	64.528	58.128	57.618	59.18	56.12

Flow rate, 200 mL/min; volume of the loop, 300 mL
* Calculated from mean PFH and mean Hematocrit
PFH, Plasma Free Hemoglobin; HGB, Hemoglobin

Table 4: Statistical analysis of Modified Index of Hemolysis data

A. Non-Parametric Test (Friedman Test) for hemolysis effect between the stents and time duration

- Chi square $\chi^2(2) = 7.00$
- p = 0.030

B. Wilcoxon Signed-Rank Tests (Pairwise Comparisons)

Used to compare MIH values between each pair of stents over the same time points.

Comparison	Test Statistic	p-value	Significance
BMS vs SES	1.0	0.0625	Marginal
BMS vs EES	0.0	0.031	Significant
SES vs EES	6.0	0.4375	Not significant

Linear regression analysis of each PFH curve showed a linear relationship over time, with a regression coefficient greater than 0.95. NIH and MIH were also calculated. Since MIH is a better indicator of hemolysis to compare between devices, we performed statistical analysis to assess whether there are statistically significant differences in MIH values among three types of stents (BMS, SES, EES) across a 6-hour period. The dataset includes PFH values at 1hr, 2hr, 3hr, 4hr, 5hr, and 6hr time points for each stent type (see Figure 2).

However, each condition (stent x time) contains only a single value, making traditional parametric tests such as two-way ANOVA inapplicable due to lack of replicates. Therefore, a non-parametric test (Friedman Test) used for comparing multiple paired MIH values for different stents measured at different time points. This method is suitable when data do not meet the assumptions of normality or replication. The test yielded a chi-square statistic of 7.00 with 2 degrees of freedom, which corresponds to a p-value of 0.0302, indicating a significant difference in MIH patterns across the three stent types. Next Wilcoxon Signed-Rank Tests (Pairwise Comparisons) was used to compare MIH values between each pair of stents over the same time points. Statistically significant differences were observed between BMS v/s EES ($p<0.05$), with BMS showing more

mechanical hemolysis compared to EES at various time points. Differences between BMS and SES were marginal, even though not statistically significant, with SES showing less mechanical hemolysis compared to BMS. Mechanical hemolysis induced were similar between SES and EES. No difference in hemolysis pattern were observed over time for SES and EES, however BMS showed an increase in mechanical hemolysis tendencies over a 6 hour time period.

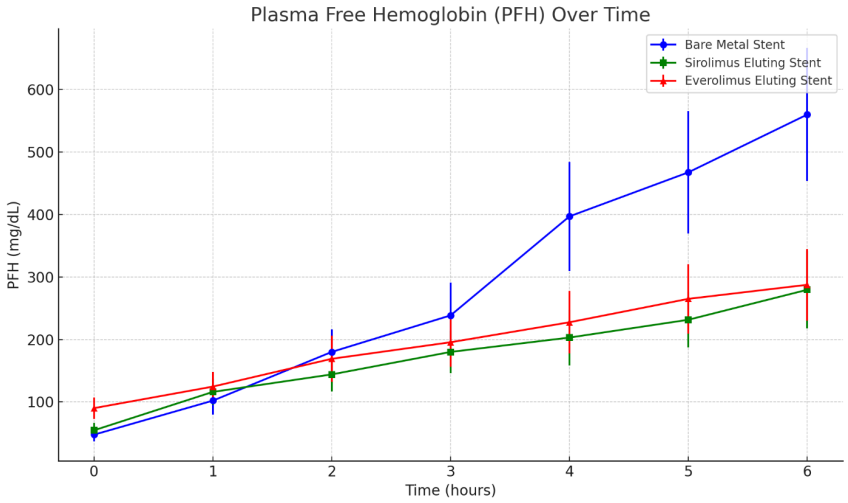

Fig 2. Comparative PFH Kinetics Over Time for Bare Metal, Sirolimus, and Everolimus Eluting Stents

The findings of this study align with previous research highlighting the potential for stent-induced hemolysis[12,13]. Von Petersdorff-Campen et al., (2022) explained about the challenges in achieving reproducible results in *in vitro* hemolysis testing due to various factors, including the inherent variability of bovine blood[12]. This study's use of bovine blood, also showed a similar variations. Jamiolkowski et al., (2022) focuses on updating ASTM F1841 testing standards for blood pumps, highlighting the importance of standardized protocols and the complexities of *in vitro* hemolysis assessment[13]. This study found challenges in reproducible *in vitro* hemolysis testing due to bovine blood variability. It also highlighted the importance of standardized protocols and the complexities of *in vitro* hemolysis assessment. The observed trends in PFH, hemoglobin, and hematocrit were consistent with hemolytic processes in *in vitro* settings. Further investigation could provide additional insights on stent-induced hemolysis mechanisms.

Our results were similar to some clinical studies like De Waha et al., 2011 and Bønaa KH et al., 2016 that have shown differences in clinical outcomes, particularly regarding restenosis rates, between different stent types.[14,15] Specifically compares EES and SES in a meta-analysis of randomized trials, finding no significant difference in major adverse cardiac events but highlighting the need for further research on long-term outcomes. De Waha et al., 2011 compares drug-eluting stents and BMS for coronary artery disease, finding lower rates of repeat revascularization with drug-eluting stents[14]. Lemos et al., 2009 directly compares two drug-eluting stents (paclitaxel and sirolimus) against bare metal stents, finding differences in angiographic outcomes[16]. These studies underscore the complex interplay of factors influencing clinical outcomes and the need to consider hemolysis alongside other factors like restenosis and thrombosis.

Understanding the hemolysis of different stent types is crucial for improving stents and reducing potential issues in clinical use. While this *in vitro* study did show some statistically significant differences between the tested stents, the observed hemolysis highlights the need for more research. Reducing hemolysis could improve long-term outcomes for patients receiving stents.

This study has several limitations. The use of bovine blood, while a common practice, may not fully represent human blood. The simplified *in vitro* system lacks the dynamic interactions of the *in vivo* environment. The decrease in blood volume from sampling could have influenced the results, especially at later time points. This study focused only on hemolysis and did not investigate other factors like thrombogenicity or endothelialization, which are crucial for stent evaluation. Future research using human blood, more complex *in vitro* models, or *in vivo* studies is needed to understand the clinical implications. Comparative studies with a range of stent materials and coatings, as well as computational fluid dynamics analysis, could provide further insights into stent-induced hemolysis.

4 Conclusion

In conclusion, this study has demonstrated that SES and EES were significantly more advantageous than BMS in *in vitro* models, primarily due to reduced mechanical hemolysis. However, further studies are needed to fully understand their clinical relevance.

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References

1) Bennett MR. In-stent stenosis: Pathology and implications for the development of drug-eluting stents. *Heart*. 2003;89(2):218–224. Available from: https://doi.org/10.1136/heart.89.2.218.
2) Windecker S, Meier B. Late coronary stent thrombosis. *Circulation*. 2007;116(17):1952–1965. Available from: https://doi.org/10.1161/CIRCULATIONAHA.106.683995.
3) Windecker S, Latib A, Kedhi E, Kirtane AJ, Kandzari DE, Mehran R. Polymer-based or Polymer-free Stents in Patients at High Bleeding Risk. *New England Journal of Medicine*. 2020;382(13):1208–1218. Available from: https://doi.org/10.1056/NEJMoa1910021.
4) Wu H, Yang L, Luo R, Li L, Zheng T, Huang K, et al. A drug-free cardiovascular stent functionalized with tailored collagen supports in-situ healing of vascular tissues. *Nature Communications* . 2024;15(1):1–19. Available from: https://www.nature.com/articles/s41467-024-44902-2#citeas.
5) Canfield J, Totary-Jain H. 40 years of percutaneous coronary intervention: History and future directions. *Journal of Personalized Medicine*. 2018;8(4):1–9. Available from: https://doi.org/10.3390/jpm8040033.
6) Schibilsky D, Takatani S, Schibilsky B, Graf T, Silva DMD, Wendel HP, et al. Hemocompatibility of new magnetically-levitated centrifugal pump technology compared to the CentriMag adult pump. *Scientific Reports* . 2020;10(1):1–8. Available from: https://doi.org/10.1038/s41598-020-78709-0.
7) Gawlikowski M, Fray ME, Janiczak K, Zawidlak-Węgrzyńska B, Kustosz R. In-Vitro Biocompatibility and Hemocompatibility Study of New PET Copolyesters Intended for Heart Assist Devices. *Polymers* . 2020;12(12):1–15. Available from: https://doi.org/10.3390/polym12122857.
8) Van Oeveren W, Schoen P, Maijers CA, Monnink SH, Van Boven AJ. Hemocompatibility of Stents. *Progress in Biomedical Research*. 1999;p. 17–22. Available from: https://www.msbt.nat.fau.de/PBMR/documents/199904010017.pdf.
9) Standard Practice for Assessment of Hemolysis in Continuous Flow Blood Pumps ASTM F1841-19ε1. *Annual Book of ASTM Standards*. 2021;13:1–2. Available from: https://cdn.standards.iteh.ai/samples/109047/ecda3b54cc2d4960823e11f99a756dd1/ASTM-F1841-19e1.pdf.
10) Standard Practice for Selection of Blood for In Vitro Evaluation of Blood Pumps, ASTM F 1830. *Annual Book of ASTM Standards*. 1998;17. Available from: https://store.astm.org/f1830-97r17.html.
11) Standard Practice for Assessment of Hemolytic Properties of Materials, ASTM F756-13. *Annual Book of ASTM Standards*. 2017. Available from: https://store.astm.org/f0756-13.html.
12) von Petersdorff-Campen K, Fischer P, Bogdanova A, Daners MS. Potential Factors for Poor Reproducibility of In vitro Hemolysis Testing. *ASAIO Journal*. 2022;68(3):384–393. Available from: https://doi.org/10.1097/mat.0000000000001577.
13) Jamiolkowski MA, Patel M, Golding MD, Malinauskas RA, Lu Q. Comparison of animal and human blood for in vitro dynamic thrombogenicity testing of biomaterials. *Artificial Organs*. 2022;46(12):2400–2411. Available from: https://doi.org/10.1111/aor.14366.
14) De Waha A, Dibra A, Byrne RA, Ndrepepa G, Mehilli J, Fusaro M, et al. Everolimus-eluting versus sirolimus-eluting stents : A meta-analysis of randomized trials. *Circulation: Cardiovascular Interventions*. 2011;4(4):371–377. Available from: https://doi.org/10.1161/circinterventions.111.963256.
15) Bønaa KH, Mannsverk J, Wiseth R, Aaberge L, Myreng Y, Nygård O, et al. Drug-Eluting or Bare-Metal Stents for Coronary Artery Disease. *New England Journal of Medicine*. 2016;375(13):1242–1252. Available from: https://doi.org/10.1056/NEJMoa1607991.
16) Lemos PA, Moulin B, Perin MA, Oliveira L, Arruda JA, Lima VC, et al. Randomized evaluation of two drug-eluting stents with identical metallic platform and biodegradable polymer but different agents (paclitaxel or sirolimus) compared against bare stents: 1-year results of the PAINT trial. *Catheterization and Cardiovascular Interventions*. 2009;74(5):665–673. Available from: https://doi.org/10.1002/ccd.22166.