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EVALUATION OF THE EFFECTIVENESS OF NOVEL POLYPROPYLENE MEMBRANES FOR EXTRACORPOREAL MEMBRANE OXYGENATION

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Objective: to assess the gas transport performance of new polypropylene (PP) membranes manufactured by Cobetter Filtration® (China) for use in extracorporeal circulation, and to compare their efficacy with the original 3M® PP membrane (USA) using both an extracorporeal hydrodynamic test bench and *in vivo* animal experiments. **Materials and methods.** Three experimental groups were established for bench and animal testing: a) Experimental – PP membrane 380/280 (n = 3); b) Experimental – PP membrane 300/200 (n = 3); c) Control – original 3M® PP membrane (n = 3). A total of 18 oxygenators were evaluated, including 12 experimental oxygenators with the Cobetter Filtration® membranes and 6 control oxygenators with 3M® membranes. The primary outcome was the oxygenation index (OI), reflecting the gas transport function of the membrane oxygenators. **Results.** During bench testing, the OI of the PP 300/200 membrane decreased from 509 ± 27 at baseline to 422 ± 31 after 240 minutes, showing no significant difference compared with the PP 380/280 membrane, which decreased from 487 ± 15 to 385 ± 20 ($p > 0.05$). In contrast, oxygenators with the original 3M® membrane exhibited significantly higher OI values, declining from 713 ± 46 to 612 ± 39 over the same period. In animal experiments, the initial OI in the 3M® control group exceeded the threshold of 300, measuring 439 ± 13, whereas the experimental groups recorded lower values: 392 ± 27 (PP 380/280) and 411 ± 8 (PP 300/200), with $p < 0.05$. By 60 minutes, OI values were similar across all groups ($p = 1$). At the end of the 5-hour acute observation, OI values were 325 ± 29 (PP 380/280) and 355 ± 33 (PP 300/200), with no statistically significant difference between the experimental groups ($p > 0.05$). **Conclusion.** The experimental PP membranes demonstrated comparable effectiveness to the original 3M® products, suggesting their potential for enhancing the safety and biocompatibility of extracorporeal circulation procedures.

Keywords: transplantology, perfusion physiology, artificial circulation, membrane oxygenation, polypropylene membrane.

INTRODUCTION

Today, membrane oxygenation is an essential technique for maintaining gas exchange during cardiac surgery. Despite the long evolution of this life-saving technology, polypropylene (PP) membranes have attracted intense research interest due to their unique properties, such as high chemical resistance, relatively low cost, and favorable mechanical strength [1].

Historically, research in the field of membrane oxygenation has been directed toward identifying the optimal material for gas exchange and achieving the ideal balance between biocompatibility and non-traumatic interaction with blood cells, which has been an enduring challenge. These efforts led to the development of disc, screen, bubble, and film oxygenators for extracorporeal gas exchange in cardiac surgery, paralleling the rapid rise of cardiac surgery as a distinct medical specialty [2–4].

In the early stages of development, various materials such as cellophane and polyethylene were used as gas exchange surfaces. However, the bubble direct-flow oxygenator, developed and commercialized by Richard DeWall and C. Walton Lillehei in 1955, became a life-saving device that dominated clinical practice for the next 25 years [5]. It was only natural that bubble oxygenators were eventually replaced by membrane oxygenators, a transition made possible by the introduction of microporous materials with unique properties [6].

The first commercially available microporous Teflon-based oxygenator, developed by Baxter-Travenol™ (USA), represented a major technological milestone. Distinguished by its pronounced hydrophobicity, it ensured complete separation between the gas phase and the

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patient's blood while also providing thermoregulatory functionality [7–9]. Shortly thereafter, Cobe Laboratories (USA) introduced the Variable Prime Cobe Membrane Lung™, based on a porous PP membrane, which closely resembles modern designs [10, 11]. From that point forward, within just 5–10 years, the global adoption of extracorporeal blood oxygenation technology based on PP membranes expanded rapidly – a dominance that continues to define clinical practice today.

The experience gained from commercially successful products and the findings of international research groups demonstrate that PP is a unique material with remarkable biocompatibility. It elicits no immune response upon contact with the body's internal environment and induces minimal production of pro-inflammatory cytokines. Furthermore, its pronounced hydrophobicity prevents the adhesion of blood cells, thrombus formation, and plasma proteins, thereby broadening the safe operational range of oxygenators utilizing PP membranes, even under challenging conditions such as high hematocrit or thrombocytosis. These properties are essential for ensuring the safety and efficacy of PP-based systems in extracorporeal circulatory support [12].

The chemical properties of PP play a crucial role in its suitability for medical applications:

1. Chemical inertness
   - PP has high chemical inertness, remaining resistant to a wide range of chemicals, including acids and alkalis. This stability prevents adverse reactions with blood components or other agents present within the oxygenation circuit.
2. Corrosion resistance
   - PP is not prone to corrosion, which makes it highly reliable for prolonged use. Since oxygenators operate in complex environments where various fluids may coexist with blood, corrosion resistance is a critical criterion.
3. Surface modifiability
   - The surface of PP membranes can be chemically modified to enhance their properties. For instance, increasing the hydrophilicity of the membrane surface improves its compatibility with blood and reduces the risk of thrombosis. Such modifications may involve the addition of specific functional groups or the use of polymeric or inorganic coatings.
4. Thermal stability
   - PP has a broad range of thermal stability, allowing its safe use under various temperature conditions. This is important because sterilization protocols typically involve exposure to high temperatures.
5. Porosity
   - PP membranes can be manufactured with controlled porosity, enabling optimization of their gas exchange capacity. The porous architecture enhances oxygen permeability, facilitating more efficient gas transfer between the blood and gaseous environments [13, 14].

At present, the leading global manufacturer of membranes and materials for extracorporeal blood circulation and oxygenation systems is 3M® (USA), which effectively maintains a dominant position in the production of polymer materials. However, interest in this field is expanding rapidly within the international medical device industry. Notably, Cobetter Filtration® (China) has achieved substantial progress through continuous refinement of the physical and chemical properties of PP membranes. The main directions of such improvements include optimization of structural porosity, as well as application of polymeric and inorganic surface coatings with tunable characteristics.

The objective of this international study is to investigate the performance of a modified PP membrane, assess its functional effectiveness, and conduct a comparative analysis of its gas exchange characteristics relative to the standard 3M® membrane.

RESEARCH DESIGN

Two types of PP membranes under investigation were supplied by Cobetter Filtration™, while the prototype oxygenators were assembled at a certified production facility with the technical support of Special and Medical Equipment™. The specifications of the test samples are presented in Table.

The tests were conducted at Shumakov National Medical Research Center of Transplantology and Artificial Organs in Moscow and included two sequential stages: bench tests and research on an experimental model of large animals. All membrane samples underwent molecular and microscopic diagnostics. The electron microscopy findings for PP membrane 300/200 are presented in Fig. 1.

In addition, infrared radiation analysis was performed during the membrane study (Fig. 2). The results confirmed that the quality parameters of all tested membranes were fully consistent with international reference data [15].

Table

Main characteristics of experimental polypropylene membranes

Specification	PP 380/280 membrane	PP 300/200 membrane
Wall thickness (μm)	50 ± 10	50 ± 10
Outer diameter (μm)	380 ± 20	300 ± 20
Inner diameter (μm)	280 ± 20	200 ± 20
Tensile strength (cN)	≥150	≥150
Elongation at break (%)	≥400	≥400
Nitrogen flow (ml/cm^2·min·bar)	50 ± 30	50 ± 30
Number of capillaries (cap/cm)	16.7 ± 1	20.5 ± 1
Angle ratio (°)	>12	>12

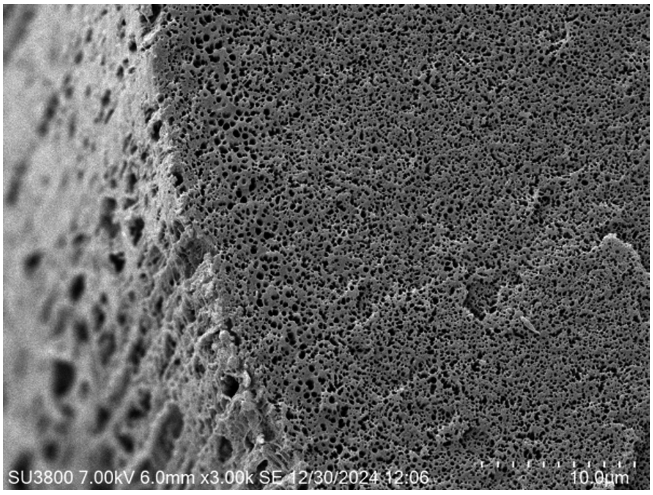

Fig. 1. Electron microscopy of PP 300/200 membrane

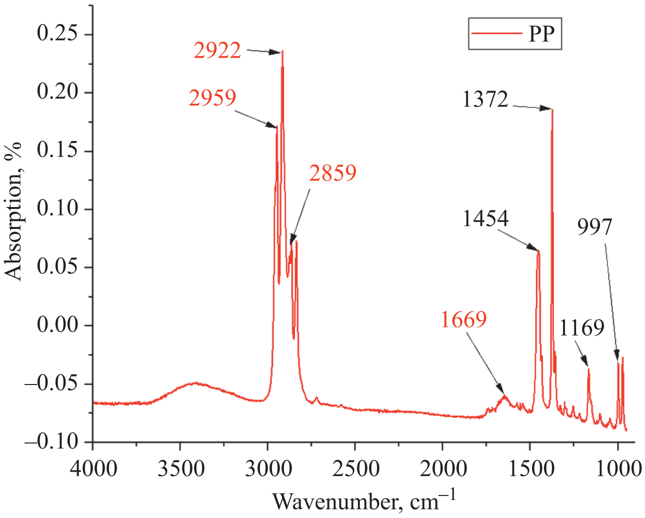

Fig. 2. Fourier transform infrared (FTIR) spectra of a PP fiber sample

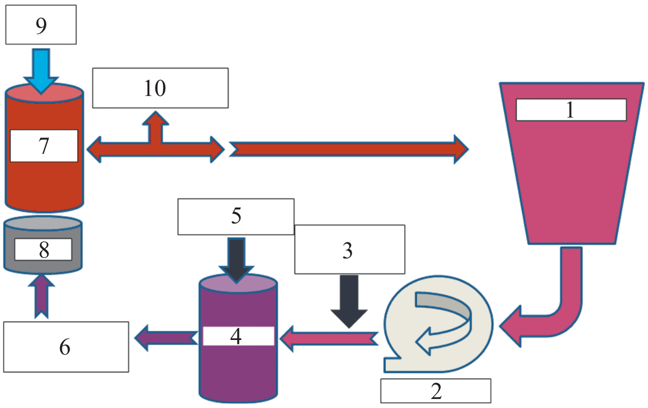

Fig. 3. Diagram of the low-volume hydrodynamic test bench. 1 – Reservoir with donor whole blood; 2 – Centrifugal pump of the ECMO device; 3 – Flow, temperature, and bubble sensor; 4 – Deoxygenator; 5 – Source of deoxygenated gas mixture; 6 – Pressure sensor #1 and sampling port #1; 7 – Tested oxygenator; 8 – Temperature control device; 9 – Oxygen mixture source; 10 – Pressure sensor #2 and sampling port #2

A sheep model was selected for the *in vivo* evaluation of the experimental membrane samples. A total of nine Romanov sheep (n = 9), each weighing 30–35 kg, were included in the study and divided into groups. All animal experiments were approved by the Committee on Biological Safety and Bioethics and conducted in accordance with the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes and Directive 2010/63/EU. The animals were maintained under controlled laboratory conditions: temperature 22 ± 2 °C, humidity 65%, and a 12-hour light/dark cycle. Feeding and access to sterilized water were regulated according to physiological needs. A two-week quarantine period was observed prior to experimentation. Three groups were identified for the study: experimental (group 1, PP membrane 380/280, n = 3), experimental (group 2, PP membrane 300/200, n = 3), control (group 3, original PP membrane 3M®, n = 3). For bench testing, corresponding membrane groups with identical sample sizes and names were used for comparison.

MATERIALS AND METHODS

The first stage of experimental testing involved laboratory bench testing. A custom low-volume hydrodynamic bench was constructed, incorporating an original Nipro® oxygenator (Japan) that enriched the blood with carbon dioxide to simulate venous blood (exhalation phase). The test oxygenator, equipped with a Cobetter Filtration™ membrane (Groups 1 and 2), and the reference oxygenator with a 3M® membrane (Group 3) were supplied with pure oxygen. The perfusion circuit was filled with whole donor blood treated with a citrate anticoagulant. The configuration of the hydrodynamic setup is shown in Fig. 3.

As shown in the diagram above, a gas mixture of 5% CO_2 and 95% N_2 was delivered to the Nipro® oxygenator at a flow rate of 700 mL/min, while pure oxygen was supplied to the test or control oxygenators at 1 L/min. Blood circulated continuously at 37 °C and 1 L/min. To evaluate the gas transport efficiency of each membrane – quantified as the oxygenation index (OI) – blood flow was increased to 3 L/min for 15 minutes. Pressure sensors were positioned before and after the oxygenator to monitor the pressure differential, which remained constant at 80 mmHg throughout the tests. Blood samples were collected hourly from both the inlet (venous) and outlet (arterial) ports for analysis. The test lasted 240 minutes.

After bench testing, we studied oxygenators on sheep in three groups, fully replicating the extracorporeal circulation technique (infrared and cardiopulmonary bypass) used in cardiac surgery (Fig. 4).

The cardiopulmonary bypass (CPB) system was connected following standard clinical protocols. The test lasted for five hours (300 minutes), with the volumetric perfusion rate adjusted according to each animal's weight and body surface area, ranging from 2.77 to 2.94 L/min. Gas flow rate was maintained at 1 L/min with an FiO_2 of 0.5. All blood parameters were kept within physiological limits. Pressure gradients were continuously recorded before and after the oxygenator. Heparin was administered as the anticoagulant, with activated clotting time (ACT) maintained below 400 seconds. Mechanical ventilation was discontinued during CPB.

Statistical analysis was conducted using StatTech v. 3.1.10 (StatTech LLC, Russia). The normality of quantitative variables was assessed with the Shapiro–Wilk test ($n < 50$). Normally distributed data were summarized as mean (M) ± standard deviation (SD) with 95% confidence intervals (CI). To compare three or more related groups, a one-way repeated-measures analysis of variance was used. Differences were considered statistically significant at $p < 0.05$.

RESULTS

As a result of bench testing, satisfactory blood oxygen saturation values were obtained for both types of new polypropylene membranes compared with the original 3M® membrane. Fig. 5 illustrates the dynamics of oxygen concentration changes, corresponding to the calculated OI, after blood passage through the oxygenators with the tested membranes relative to the 3M® reference membrane at a blood flow rate of 3 L/min.

No statistically significant difference in oxygenation performance was observed between the two experimental samples. The PP 300/200 membrane showed an OI of 509 ± 27 at baseline and 422 ± 31 after 240 minutes of testing, while the PP 380/280 membrane showed an OI of 487 ± 15 initially and 385 ± 20 at the final time point ($p > 0.05$).

In contrast, the oxygenators equipped with the original 3M® membrane exhibited significantly higher OI – 713 ± 46 at baseline and 612 ± 39 after 240 minutes ($p < 0.05$). Despite an average oxygen concentration difference of approximately 100 mmHg between the Cobetter Filtration® and 3M® membranes, all experimental membranes maintained oxygen levels exceeding normal physiological oxygen level.

Further *in vivo* testing on large animal models under infrared conditions with standardized perfusion and homeostatic parameters confirmed the high efficiency of Cobetter Filtration® membranes compared with the original 3M® oxygenators. Consistent with bench test results, arterial blood oxygenation index remained the principal comparative parameter, as shown in Fig. 6.

Although the initial OI values in the 3M® control group exceeded the threshold level (439 ± 13), the respiratory index values in groups 1 (PP 300/200) and 2 (PP 380/280) were slightly lower – 392 ± 27 and 411 ± 8, respectively ($p < 0.05$). However, by 60 minutes, the OI values across all groups had equalized, as indicated by $p = 1$, reflecting comparable oxygenation performance. At the end of five hours (300 minutes) of observation in the acute experiment, OI values in the PP 380/280 group were 325 ± 29, and in the PP 300/200 group 355 ± 33, with no statistically significant differences between these experimental groups ($p > 0.05$). In contrast, the control group with the 3M® membrane demonstrated a marked decline in oxygenation capacity by the end of the expe-

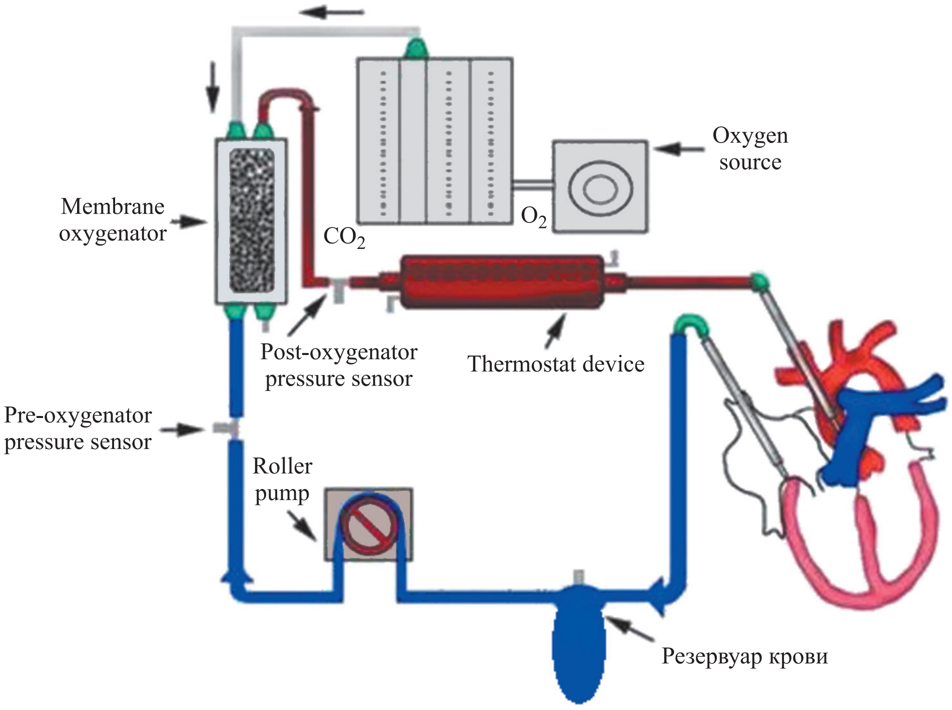

Fig. 4. Diagram of the extracorporeal circuit for artificial blood circulation

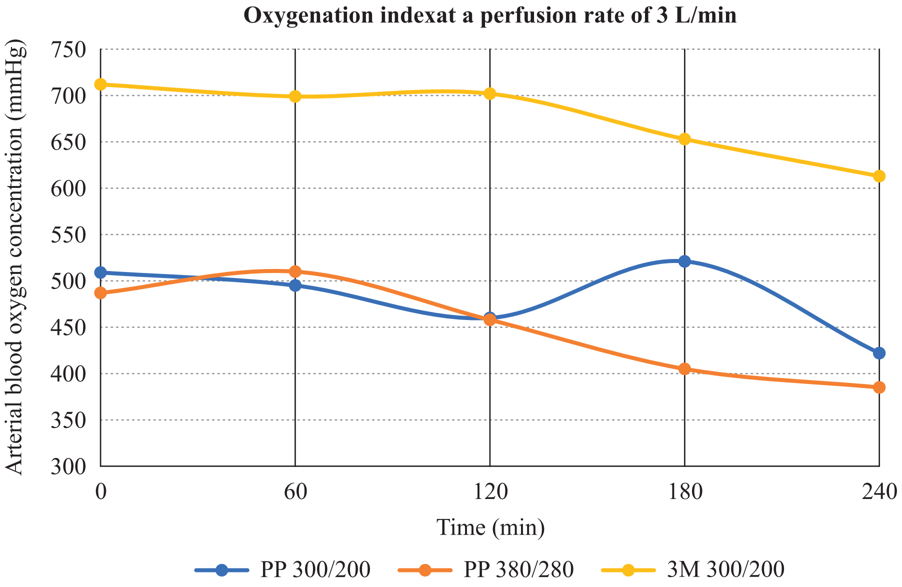

Fig. 5. Changes in oxygenation index in the tested membranes in bench tests

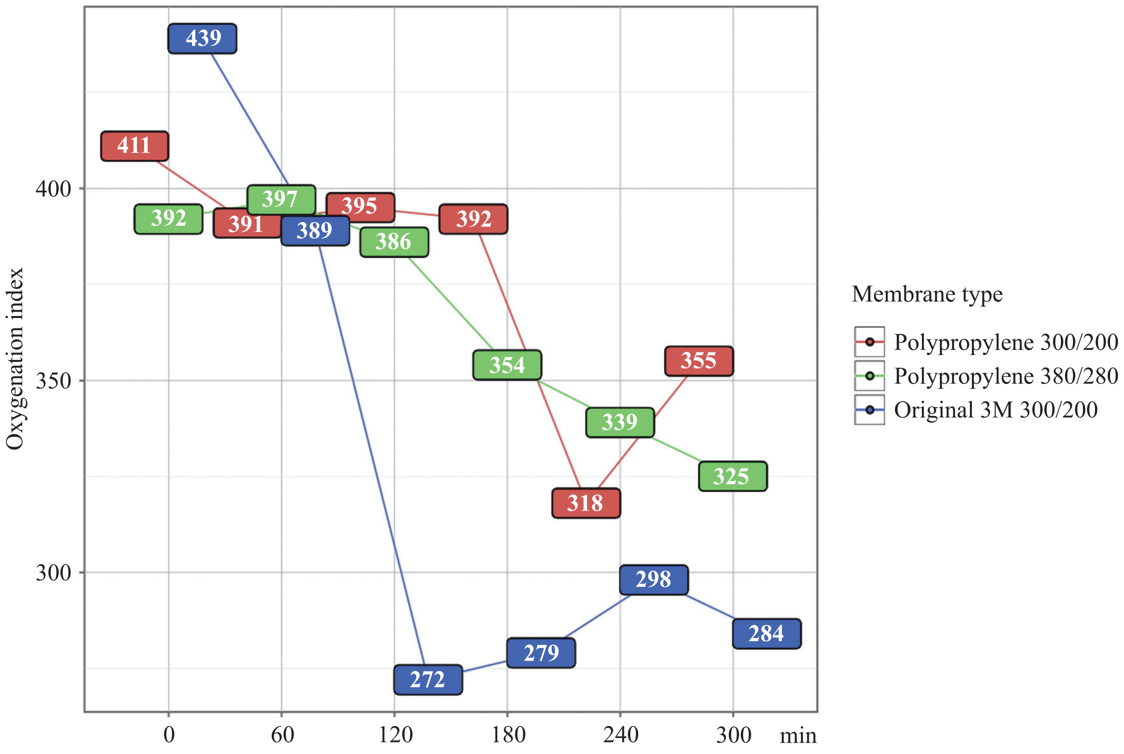

Fig. 6. Changes in oxygenation index in the tested membranes in the animal model

riment, with OI values dropping to 284 ± 18. The differences between the 3M® membrane and the Cobetter Filtration® membranes were statistically significant (p = 0), indicating a decrease in the oxygenating efficiency of the original 3M® oxygenator over time.

DISCUSSION

The results of this study demonstrate that Cobetter Filtration® polypropylene membranes are comparable in performance to the established 3M® polypropylene membranes, and under certain conditions, they even exhibit superior functional characteristics. In experimental settings that closely simulated clinical practice, oxygenators equipped with PP 300/200 and PP 380/280 membranes showed significantly higher OI values compared to those with the original 3M® membranes, maintaining consistently elevated OI levels throughout the 5-hour observation period.

This performance suggests that during prolonged cardiopulmonary bypass, Cobetter Filtration® membranes possess advantages over the 3M® membranes, including more stable gas exchange, lower plasma leakage, and reduced thrombus formation within the interstitial spaces. The results were further supported by data on carbon dioxide elimination: while bench tests showed comparable CO_2 removal rates across all three groups (8.93 ± 1.25 mmHg, $p > 0.05$), experiments in large animal models revealed a progressive decline in CO_2 elimination with the 3M® membrane – from 6.74 ± 0.83 to 3.29 ± 0.17 mmHg over five hours. In contrast, the Cobetter Filtration® oxygenators maintained stable CO_2 elimination values (7.51 ± 1.77 mmHg) throughout the entire 300-minute test, with the difference reaching statistical significance ($p = 0.039$).

Along with blood gas composition indicators, blood pressure before and after the oxygenators was evaluated. In the control group, the transmembrane pressure gradient increased notably, from 19 ± 6 mmHg at baseline to over 30 mmHg after 300 minutes. Meanwhile, in both experimental groups, the gradient remained stable throughout the 5-hour perfusion period (22 ± 4.7 mmHg), indirectly indicating lower intermembrane thrombosis in the Cobetter Filtration® membranes.

CONCLUSION

The evolution of extracorporeal circulatory support has a long and dynamic history, and the devices themselves have undergone significant changes and modifications. Nevertheless, the core element of membrane oxygenation – the gas exchange membrane – has remained largely unchanged since its first clinical application. Today, intensive research is focused on enhancing the mechanical strength and biocompatibility of polypropylene.

The findings of this study possess both scientific significance and commercial potential, demonstrating that the newly developed Cobetter Filtration® polypropylene membranes exhibit comparable effectiveness to the established 3M® membranes. This opens new avenues for advancing membrane oxygenation technologies, ultimately improving procedural safety for patients.

The authors declare no conflict of interest.

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