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Cardiopulmonary bypass: development of John Gibbon's heart-lung machine

Circulação extracorpórea: desenvolvimento da máquina de coração-pulmão de John Gibbon

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Abstract

Objective: **To provide a brief review of the development of cardiopulmonary bypass.**

Methods: **A review of the literature on the development of extracorporeal circulation techniques, their essential role in cardiovascular surgery, and the complications associated with their use, including hemolysis and inflammation.**

Results: **The advancement of extracorporeal circulation techniques has played an essential role in minimizing the complications of cardiopulmonary bypass, which can range from various degrees of tissue injury to multiple organ dysfunction syndrome. Investigators have long researched the ways in which cardiopulmonary bypass may insult the human body. Potential solutions arose and laid the groundwork for development of safer postoperative care strategies.**

Conclusion: **Steady progress has been made in cardiopulmonary bypass in the decades since it was first conceived of by Gibbon. Despite the constant evolution of cardiopulmonary bypass techniques and attempts to minimize their complications, it is still essential that clinicians respect the particularities of each patient's physiological function.**

Descriptors: **Cardiopulmonary Bypass. Oxygenation. Postoperative Complications.**

Resumo

Objetivo: **Relatar de forma simples e resumida o desenvolvimento da circulação extracorpórea.**

Métodos: **Realizada revisão de literatura sobre a evolução da circulação extracorpórea, seu papel fundamental para cirurgia cardiovascular e as complicações que podem surgir após o seu uso, dentre elas, a hemólise e a inflamação.**

Resultados: **O processo de desenvolvimento da circulação extracorpórea foi fundamental, diminuindo as complicações desencadeadas por ela, que acabam por repercutir no paciente, variando de lesões de graus variados até falência de múltiplos órgãos. Os pesquisadores estudaram quais as agressões que a circulação extracorpórea poderia suscitar no organismo humano. Possíveis soluções surgiram e, consequentemente, meios mais adequados para uma condução mais segura do pós-operatório foram propostas.**

Conclusão: **A circulação extracorpórea progrediu a passos firmes e seguros ao longo destas últimas décadas desde a sua concepção por Gibbon. Apesar da sua evolução e das condutas realizadas na tentativa de amenizar as complicações, o respeito aos detalhes das funções fisiológicas do paciente é fundamental.**

Descritores: **Circulação Extracorpórea. Oxigenação. Complicações Pós-Operatórias.**

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Abbreviations, acronyms & symbols	
ANC	Absolute neutrophil count
CP	Centrifugal pump
CPB	Cardiopulmonary bypass
IL	Levels of interleukin
LDH	Lactate dehydrogenase
MCV	Mean corpuscular volume
RP	Roller pump
TNFα	Tumor necrosis factor-alpha

THE ADVENT OF CARDIOPULMONARY BYPASS

In the 19th century, the interest of physiologists in the circulation of blood turned to the study of isolated organs. Many of the studies conducted at this time laid the foundation for the future development of cardiopulmonary bypass (CPB).

In 1813, Le Gallois formulated the first concept of what would constitute an artificial circulation[1]. In 1828, Kay showed that the contractility of muscle could be restored by perfusing with blood[2]. Between 1848 and 1858, Brown-Séquard obtained "oxygenated" blood by agitating it with air, highlighting the importance of blood in the perfusate solution to obtain neurologic activity in isolated mammalian heads[2-4]. In 1868, Ludwig and Schmidt built a device that could infuse blood under pressure, thus enabling better perfusion of isolated organs for study[5,6]. In 1882, Von Schroeder developed and built the first prototype of a primitive bubble "oxygenator", which consisted of a chamber containing venous blood; air was bubbled into the chamber and converted the venous blood to arterial blood[7].

In 1885, Von Frey and Gruber developed an artificial heart-lung system whereby the perfusate solution could be oxygenated without interrupting blood flow, an achievement that had not been attempted by their predecessor Von Schroeder.

Other discoveries played essential roles in the further development of research that would ultimately contribute to CPB. One such achievement was the discovery of the ABO blood group system by Landsteiner in 1900, which enabled prevention of many inconveniences related to incompatibility[8]. In 1916, Howell and McLean (the latter a medical student) serendipitously discovered heparin while studying animal liver extracts. This discovery would assist both in vivo and in vitro studies, which were made successful by inhibition of coagulation[9,10].

The later work of Gibbon, starting in 1937, piqued the curiosity of many other investigators, who were prompted to start similar projects and follow in his footsteps[11,15].

To Crafoord, who would later perform the first successful atrial myxoma removal surgery with CPB[16], artificial circulation was a necessity, as correction of intracardiac defects required that the surgeon be able to open the heart while maintaining blood flow to all organs and carrying out gas exchange. As a tool for circulatory support during cardiovascular surgery, CPB is a contemporary notion. On May 6, 1953, Gibbon – who devoted his life's work to obtaining a working heart-lung machine – performed an atrial septal defect repair that became a landmark in the development of this technology.

At the time, the University of Minnesota was considered the cradle of cardiovascular surgery, where innovative techniques made it a destination of choice for heart surgeons worldwide. Concepts such as hypothermic circulatory arrest, cross-circulation, and the bubble oxygenator, which became commonplace in the field, were first investigated at Minnesota[17]. This combined advent of cardiac surgery and cardiopulmonary bypass techniques constituted a major advance in the history of healthcare, as it enabled direct manipulation of the heart, thus providing a possibility of cure for a variety of conditions that were hitherto considered incurable[17,18].

In the meantime, Brazilian heart surgeons had started to exchange experiences with their foreign peers, ringing in a "Golden Age" for cardiovascular surgery at Hospital das Clínicas in São Paulo. One of the pioneering researchers in this field was Professor Hugo João Felipozzi, who was responsible for the very first heart-lung machine and for the first on-pump open-heart procedure in Brazil, performed in October 1955[17,19,20].

This watershed moment marked the start of a new age in Brazilian cardiac surgery. In São Paulo, the group headed by surgeon Euryclides Zerbini built Hospital das Clínicas into the largest cardiovascular surgery center in the country[17]. Mere months after Christiaan Barnard performed the first human heart transplant in December 1967, he assisted Professor Zerbini in conducting the first such procedure in Brazil, in May 1968, thus giving rise to the era of transplantation in Brazil[20].

However, such progress was not without its challenges. Supplies for surgery had to be imported at a high cost. This, compounded by the fear of being unable to match the pace of U.S. and European development in the field of cardiovascular surgery equipment, prompted Brazilian surgeons to design and construct their own devices so that procedures could continue unimpeded. Surgeons such as Adib Jatene, Domingos de Morais, and Otoni M. Gomes began developing domestic heart-lung machines, oxygenators, prosthetic valves, and pacemakers. Particular attention is warranted to the dedication of cardiovascular surgeon Domingo M. Braile, who established his own manufacturing plant to produce CPB circuits and machines, prosthetic valves, and endoprosthetic devices of the highest quality, building a reputation for Brazil at cardiovascular surgery centers the world over. The dedication of these professionals in the operating theater and in the laboratory, improving their surgical techniques through experimentation so as to contribute to the advancement of the field and ensure safer and more efficient care of patients with heart disease, speaks for itself.

This evolution also brought progress to CPB, making the procedure even more complex. Within this context, profes-

sionals responsible for CPB operation (i.e., perfusionists) needed new knowledge to enable rapid and appropriate decision-making. Experienced professionals such as perfusionist Maria Helena L. Souza and cardiovascular surgeon Décio O. Elias wrote peerless textbooks that provide a comprehensive, up-to-date overview of the techniques and methods required of those who devote themselves to restoring the health and quality of life of patients with cardiovascular disease[18].

Happy were – and still are – those who, by absorbing hard-won knowledge through years of sacrifice and experimentation, had the privilege of reading about the evolution of cardiovascular surgery in recent decades and witnessing the complete devotion of these providers, whose love and dedication have carved their feats in stone. Words cannot express the importance of their work.

EXTRACORPOREAL OXYGENATORS DEVELOPED FOR CARDIOPULMONARY BYPASS

The need for adequate oxygenation led Gibbon to continue his search for an enhanced method of blood arterialization. He noted many issues that occurred during the oxygenation process, such as foaming, hemolysis, and synthesis and release of vasoactive substances[21,22]. The first oxygenator models developed were classified according to the method used for oxygenation.

Film oxygenators performed gas exchange on a surface onto which blood was flowed in thin films, over a substrate exposed to an oxygen-rich atmosphere[3,23,24].

In 1885, von Frey and Gruber had developed a rotating cylinder that is considered the precursor of cylinder or drum oxygenators. Venous blood was spread over the inner wall of the rotating cylinder, where it came into contact with a stream of oxygen, thus accomplishing gas exchange. In 1957, Crafoord, Norberg, and Senning[25] developed a new oxygenator consisting of multiple spinning rollers, the rotation of which facilitated the exposure of filmed blood to oxygen (Figure 1).

In screen oxygenators, venous blood was flowed over a support containing mesh screens. Much of Gibbon's work used such a model of oxygenator, in which venous blood flowed down a series of vertical screens (Figure 2)[16,22,26,27].

Disc oxygenators were the next development. Briefly, these oxygenators consisted of a horizontal axis around which a series of metal discs were arranged. These discs rotated within a glass cylinder, through which venous blood was circulated and exposed to oxygen. Bjork[28] worked on the first disc oxygenator in 1948, but Kay and Cross[29] were the ones to enhance it and improve its effectiveness in 1956 (Figure 3). Disc oxygenators were an important landmark in the evolution of CPB, and their efficiency ensured they remained in use well into the 1970s.

The development of bubble oxygenators was plagued by the occurrence of bubbling and foaming, with the inherent

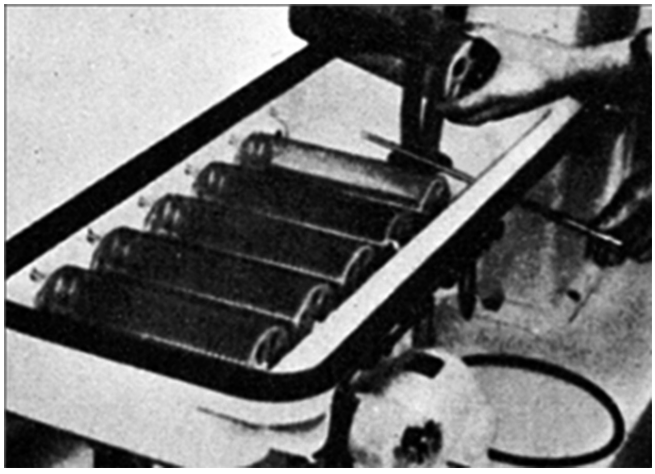

Fig. 1 - Cylinder (drum) oxygenator, 1957. Source: Correa Neto, 1988.

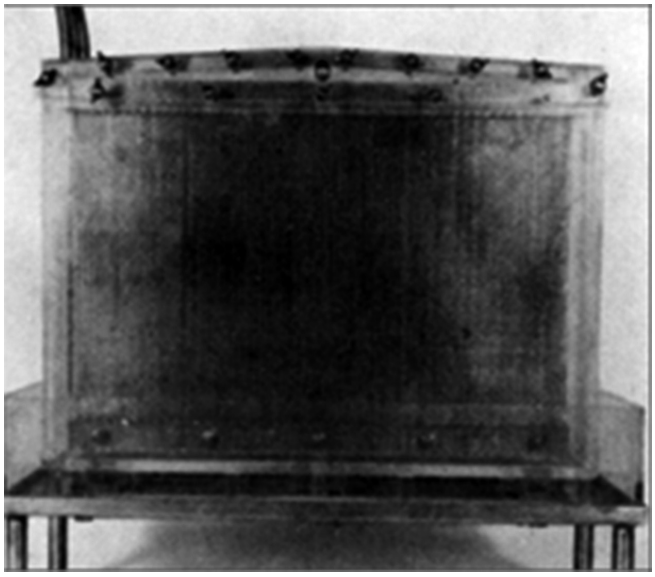

Fig. 2 - Screen oxygenator, 1946. Source: Correa Neto, 1988.

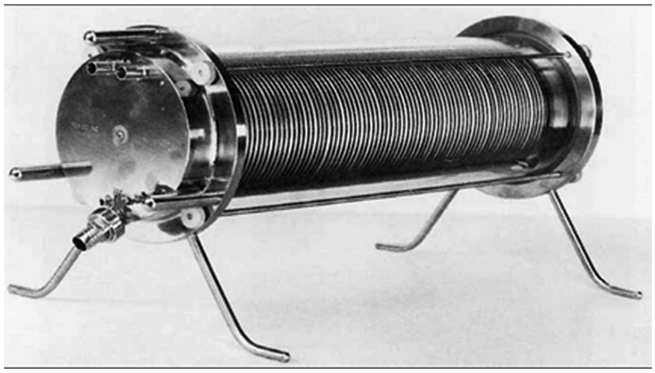

Fig. 3 - Disc oxygenator, 1956. Source: Souza & Elias, 2006.

risks they pose, during the arterialization process. In these oxygenators, venous blood is exposed to an oxygen stream at the reservoir inlet, forming a cascade of bubbles of varying sizes that arterialized the deoxygenated blood. In 1950 and 1952, Clark[30] designed and built bubble oxygenators that incorporated a dispersion chamber, facilitating control of oxygenation. In 1956, DeWall developed a helical bubble oxygenator based on concepts learned from other surgeons that was innovative both for its simplicity and for a disposable version that was developed soon thereafter[31,32]. A smaller, more compact oxygenator with a bolder design – which also contributed to ease of assembly – had been developed by Gollan[33] in 1952.

In 1955, Kolff[34] constructed the first prototype of a membrane oxygenator, using polyethylene tubing wrapped around a central axis, which gave the oxygenator a coil-like appearance. In 1958, Clowes and Neville[35] developed a flat Teflon membrane oxygenator specifically for use in cardiac surgery, and published a series of case reports describing the use of their apparatus. Other oxygenators later entered clinical use, such as that designed by Bramsen, Peirce, and Landè-Edwards and known as the "sandwich-type" oxygenator, which was quite similar to the Clowes and Neville model[36-38]. In 1965, Kolobow[39] modified the Kolff oxygenator by adding long silicone strips with spacers that prevented membrane collapse. The continued development of new technologies contributed to the production of capillary membranes, ushering in the latest generation of modern membrane oxygenators with increased efficiency and safety, which remain in use to this day.

BLOOD PUMPS FOR CARDIOPULMONARY BYPASS

The search for pumps capable of displacing large volumes of blood deserves its own chapter in the history of CPB, as it demonstrates investigators' constant concern with obtaining safe ways to accomplish artificial blood circulation.

The pumps used by early physiologists displaced small volumes of blood; however, the trauma they inflicted on blood components was already apparent. Flow velocity was the main culprit implicated in hemolysis.

The search for better CPB pumps led to a discussion that persists to this day: pulsatile or continuous flow? Since no consensus emerged, studies focused on the occluding mechanism, as output could be maintained during blood pumping.

Overall, pumps are classified according to the mechanism that transfers energy to the fluid. Using this criterion, pumps can be classified into two categories: displacement (roller) pumps and kinetic (centrifugal) pumps.

Displacement pumps impel the fluid progressively forward. One example is the well-known Sigmamotor® finger pump, which Lillehei used from 1954 before replacing it with a roller pump (Figure 4). This pump was traumatic to blood components and was intolerably loud while in operation[40,41].

The roller pump design, introduced in 1955, remains in

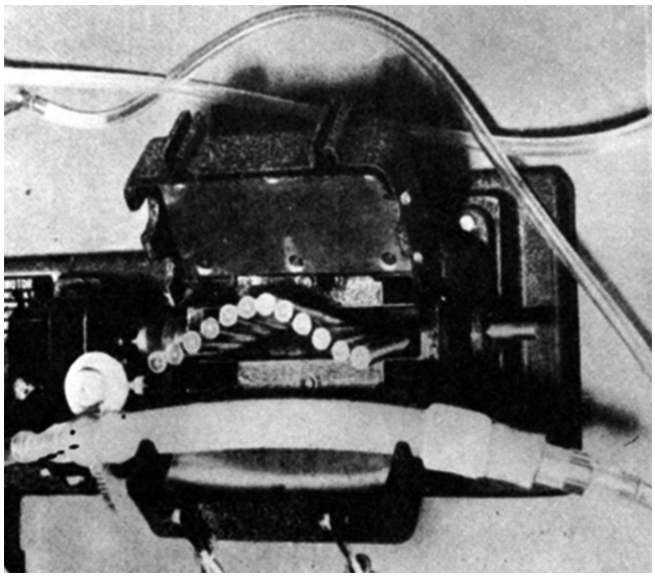

Fig.4 - Sigmamotor® pump. Source: Correa Neto, 1988.

Fig. 5 - Modern roller pump. BEC Heart Lung Machine. Source: Braile Biomédica®.

use for all types of cardiovascular surgical procedures. Briefly, on the horseshoe-shaped rigid console of the pump, a segment of silicone tubing is bent into a semicircle within which two cylinders (rollers) are placed opposite to each other, equidistant from the central axis. As the axis rotates, the rollers compress this segment of tubing and impel the blood forward[42].

The first roller pump was patented in 1855 by Porter and Bradley[43]. In 1934, DeBakey made some modifications that enabled its use for blood transfusion. The two-roller DeBakey design was further modified before being applied to CPB (Figure 5).

Kinetic pumps impart energy generated by the rotation of an element known as an impeller. The first centrifugal pump was developed in the late 17th century, when Denis Papin built a centrifugal fan with straight vanes, which he named the Hessian bellows in honor of his patron, the Landgrave of Hesse. However, only in the 19th century were centrifugal pumps first manufactured and used in the United States. The rotary vane design was developed in England by John Appold, in 1851.

Although the operating principle of centrifugal pumps dates back to the early days of fluid engineering, it was not until the 1970s that the first such pumps were designed specifically for use in CPB circuits. In these pumps, forward movement of the blood was accomplished by imparting kinetic energy produced by a rotating element.

Fig. 6 - Modern centrifugal pump module. Centripump. Source: Braile Biomédica®.

The most common type, the vortex pump, featured a set of concentric cones, with the outermost cone containing a central inlet and a lateral outlet. The innermost cone was magnetically coupled to the outer rotor, which made it spin at a high RPM, causing rotation of the other cones and thus creating a centrifugal force that drove blood flow through the circuit (Figure 6).

Despite the advantages and disadvantages of both major pump types for CPB in cardiovascular surgery, the optimal design in terms of minimizing patient complications remains unclear[44,45].

COMPLICATIONS OF CARDIOPULMONARY BYPASS

Due to its mechanical components and their interaction with blood, CPB can produce significant changes in the body. All organs were affected by CPB systems, due to factors such as contact between blood and artificial materials, continuous flow, hemodilution, hypothermia, and anticoagulation. These complications could arise immediately after surgery or later in the intensive care unit. Despite improvements in equipment, it was clear that longer durations of CPB were associated with increased risk and severity of complications[46].

Other issues were identified as contributing factors for the development of CPB-related complications, including age, the presence of multiple or complex injuries, the presence of comorbidities, and reoperation.

The main complications of CPB are hemorrhage, low cardiac output, arrhythmias, respiratory failure, renal failure, neurological or neuropsychiatric changes, fluid and electrolyte imbalances, abdominal changes, hemolysis, and inflammation.

MARKERS OF HEMOLYSIS

Markers of hemolysis are capable of demonstrating acute tissue injury during its acute phase. These markers were measured at centers that had the laboratory capacity to do so using specific kits for the marker of interest, thus enabling diagnosis of hemolysis and investigation of its etiology (hemolytic anemia, CPB, prosthetic valve dysfunction, acute myocardial infarction, etc.).

One acute phase marker specific to hemolysis (detectable even in surgical trauma) is the serum concentration of haptoglobin, a protein that binds hemoglobin to form a complex that prevents renal loss of hemoglobin, thus decreasing its levels in the bloodstream[47,48]. A reduction in haptoglobin levels is indicative of hemolysis.

Lactate dehydrogenase (LDH) in an enzyme that catalyzes the conversion of pyruvate to lactate in the Krebs cycle. It can also be measured as a nonspecific marker of hemolysis: when cell lysis occurs, LDH is released from within the ruptured cells and remains in the bloodstream at high concentrations[49].

Reticulocyte counts are also used as a nonspecific marker of hemolysis, but infrequently so, as their levels increase not only in hemolysis but in the presence of hypoxia as well[50]. As reticulocytes are larger than erythrocytes, when the reticulocyte count increases, so does the mean corpuscular volume (MCV), including in hemolysis.

Bilirubin can also be used as a marker of hemolysis. Jaundice develops when bilirubin levels are elevated, and it may be a consequence of liver disease or hemolysis.

MARKERS OF INFLAMMATION

Markers of inflammation are chemicals released by certain cells that act on tissue injury in the acute or chronic phases of the inflammatory process. Specific kits can be used to measure the concentration of inflammatory mediators. However, the high cost of some of these kits precludes their routine use.

The human body maintains constitutive cytokine production, whereby specialized cells contain a baseline level

Table 1. Comparative analyses of roller vs. centrifugal pumps for cardiopulmonary bypass, using markers of hemolysis as outcome measures.

Author	Marker of hemolysis	Statistical analysis		*P* value
		CP	RP	
		Mean		
Pêgo-Fernandes et al. [57]	Haptoglobin (g/dL)	1.2	1.3	>0.05
	Platelet count (10^3/mm^3)	99000	121846	>0.05
	Hemoglobin (mg/dL)	67.9	45.5	>0.05
		Mean ± standard deviation		
Berki et al. [58]	Platelet count (10^3/mm^3)	13.02±6.8	9.66±3.4	<0.01 RP
	Hematocrit (%)	36±4.8	23.14±4.2	<0.05 RP & CP
		Mean ± standard deviation		
Yoshikai et al. [59]	LDH (U/L)	1475.9±490.5	3814.2±1125.0	>0.05
	Platelet count (10^3/mm^3)	15.8±55	14.4±4.1	>0.05
		Mean ± standard deviation		
Morgan et al. [60]	Hematocrit (%)	31±0.05	32±0.06	>0.05
	*Haptoglobin (g/dL)	-	-	-
		Mean ± standard deviation		
Andersen et al. [61]	Platelet count (10^3/mm^3)	221±13	222±12	>0.05
	Hemoglobin (mg/dL)	11.1±0.3	11.2±0.4	>0.05
	Hematocrit (%)	32±0.01	33±0.01	>0.05
		Mean		
Keyser et al. [62]	Platelet count (10^3/mm^3)	150000	170000	>0.05
	Hematocrit (%)	32	34	>0.05
	LDH (U/L)	160	180	>0.05
	Bilirubin (mg/dL)	1.2	0.9	>0.05
		Meta-analysis		
Saczkowski et al. [63]	Platelet count (10^3/mm^3)			>0.05
	Hemoglobin (mg/dL)			>0.05

CP=centrifugal pump; RP=roller pump.

**Haptoglobin: after the start of CPB, the haptoglobin levels in nearly all samples exceeded the limit of quantitation (0.1g/L) and could not be measured.*

of these substances in normal situations. Cytokines must bind to specific cell membrane receptors to exert their effects. In most cases, the action of one or more cytokines is required for an immune response to mount; therefore, these substances form a complex network in which production of one cytokine influences the production or response of others.

Levels of interleukin (IL)-1β are usually increased after CPB[47]. However, this cytokine is often undetectable due to the hemodilution inherent to CPB[47]. IL-1β is also responsible for inducing synthesis of IL-6, and acts synergistically with tumor necrosis factor-alpha (TNFα) in a feedback loop that ensures continuity of the inflammatory process. Alongside TNFα, these are the first interleukins to play a role in the inflammatory response to CPB.

Another widely studied interleukin is IL-6, levels of which increase 2 to 4 hours after any surgical incision. The intensity of the IL-6 response correlates with the duration of the surgical procedure, which makes this factor extremely important in the inflammatory process[47]. The IL-6 response pattern is consistent with the role of a major mediator of the acute-phase reaction to CPB; therefore, IL-6 may be a more precise indicator of the progression of inflammatory states[19].

IL-8 is a potent chemotactic agent involved in the homing of neutrophils and leukocytes to sites of infection[47,48-54]. It may be present in any tissue, and its effects may occur during infection, ischemia, trauma, and other disorders of homeostasis[54].

TNFα is implicated in several systemic complications and severe infections, inducing a febrile state that is often detectable in the immediate postoperative period of CPB. High concentrations of TNFα in plasma may induce low cardiac output, decrease vascular smooth muscle tone, and cause intravascular thrombosis[55]. High levels of this cytokine after acute myocardial infarction have been associated with increased risk of recurrent infarction[56].

The most important determinant of the erythrocyte sedimentation rate (ESR) is fibrinogen, an acute-phase protein, levels of which increase two- to fourfold in the presence of acute inflammation. Fibrinogen is also a known risk factor for coronary artery disease, peripheral artery disease, and stroke.

Immunoglobulins are also implicated in this phenomenon, and play an important role in chronic inflammatory processes.

Comparative studies of the hemolytic response to cardiopulmonary bypass

Table 1 lists studies that have compared roller vs. centrifugal pumps for CPB, using markers of hemolysis as the measures of interest.

In these comparative analyses of roller vs. centrifugal pumps, with the exception of one study[62] that reported significant differences in platelet count and hematocrit respectively, the remaining studies found no significant differences in the most reliable markers of hemolysis between the two pump types. This corroborates a meta-analysis by Saczkowski et al.[63] that also failed to find any difference between roller and centrifugal pumps in terms of hemolysis. Quite a wide variety of markers were used, which favored this result.

Comparative studies of the inflammatory response to cardiopulmonary bypass

Table 2 lists studies that have compared roller vs. centrifugal pumps for CPB, using markers of hemolysis as the measures of interest.

In these comparative analyses of roller vs. centrifugal pumps, with the exception of two studies[59,62] that found no significant differences, the remaining studies reported significant differences between the two pump types in terms of inflammatory response, as assessed by measurement of markers of inflammation. However, results were variable and sometimes controversial, and the evidence remains inconclusive.

CONCLUSION

Steady progress has been made in CPB techniques in the years since modern extracorporeal circulation was first conceived of by Gibbon. Over essentially seven decades, many changes were made, not only to CPB apparatuses and circuits but also to protocols and standards of work. The patient population has also changed: patients undergoing CPB are now in much more severe condition, due to such factors as comorbidities, advanced age, adverse lifestyles, and, many times, limited access to healthcare services.

The constant evolution of CPB and attempts to minimize its complications notwithstanding, it is essential that clinicians respect the particularities of each patient's physiological function. Patients undergoing CPB require constant care and attention, as the complications of this procedure still pose a very severe threat.

Hemolysis and inflammation were cited in the majority of studies addressing the complications of CPB with roller and centrifugal pumps, but these two phenomena were generally studied separately. Some investigators found no significant differences between these two types of pumps in terms of hemolysis. Nevertheless, it has been suggested empirically that centrifugal pumps be used in prolonged bypass to mitigate hemolysis. In practice, however, this decision should rest with the perfusion team.

Only one of seven studies reviewed reported significant changes (in platelet count and hematocrit) with roller pumps. Conversely, regarding inflammation, five of the seven studies reviewed reported significant differences between roller and centrifugal pumps. IL-6 was the marker of inflammation most commonly cited in these studies, particularly when centrifugal pumps were used.

Table 2. Comparative analyses of roller vs. centrifugal pumps for cardiopulmonary bypass, using markers of inflammatory response as outcome measures.

Author	Marker of inflammation	Statistical analysis		*P* value
		CP	RP	
		Mean ± standard deviation		
Berki et al. [58]	Fibrinogen (mg/dL)	258±160	216±148	<0.01 RP
		Mean ± standard deviation		
Yoshikai et al. [59]	C3 (mg/dL)	36.4±10.4	41.1±7.3	>0.05
	C4 (mg/dL)	13.7±3.0	19.3±2.3	>0.05
	IgA (mg/dL)	172.8	191.95	>0.05
	IgG (mg/dL)	1011.4	836.81	>0.05
	IgM (mg/dL)	126.7	78.0	>0.05
		Mean ± standard deviation		
Morgan et al. [60]	IL-6 (pg/dL)	329±59	392±57	<0.05 CP
		Mean		
Ashraf et al. [64]	IL-1β (pg/dL)	-	-	-
	IL-6 (pg/dL)	341	260	<0.05 CP
	IL-8 (pg/dL)	143	150	>0.05
	TNFα (pg/dL)	-	-	-
	C5b-9 (ng/mL)	765	509	<0.05 CP
	ANC(x109)	8.15	6.2	<0.05 CP
		Mean		
Baufreton et al. [65]	IL-6 (pg/dL)	770	600	<0.01 CP
	IL-8 (pg/dL)	115	122	<0.05 CP
	TNFα (pg/dL)	160	130	<0.01 CP
		Mean		
Braulio [66]	IL-6 (pg/dL)	904.4	393.2	<0.05 RP
	TNFα (pg/dL)	1648.0	1255.8	<0.05 RP
		Mean		
Keyser et al. [62]	Fibrinogen (mg/dL)	250	230	>0.05

ANC=absolute neutrophil count; CP=centrifugal pump; RP=roller pump.

Although the complications of CPB have many postoperative repercussions, including a direct influence on the duration of mechanical ventilation and length of intensive care unit stay, pump designs meant to mitigate these complications are not yet based on scientific evidence. Further studies are required to compare roller and centrifugal CPB pumps and their association with hemolysis and inflammatory response.

Authors' roles & responsibilities

ACP	Analysis and/or interpretation of data; final approval of the manuscript; writing of the manuscript and critical review of its content
MAMS	Final approval of the manuscript; conception and design; Manuscript writing and critical review of its content
WBY	Final approval of the manuscript; conception and design; manuscript writing and critical review of its content

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