Progress in the Study of Cardiovascular Physiology During the Italian Renaissance

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Abstract: This short report underlines the importance of collaboration and communication among scientists. The ideals of progress in medicine and in the care of suffering people have represented continuous stimuli allowing to overcome prejudices, religious and political differences. The modern concepts of blood circulation have been established through a close collaboration and exchanges of ideas among scientists coming from different countries, different religious and political backgrounds. In those days Europe was theater of continuous wars based on political and religious contrasts. There were continuous outbreaks of Plague in several countries. Religious contrasts occurred inside the Christianity and between the Christianity and Islam; contrasts which were based on theological disputes associated with economic and expansionist ambitions, resulting in extreme and rigid religious orthodoxy. Despite these difficulties, medical scientists collaborated overcoming the close boundaries of everyday general confrontations. The ambition for advancement in science and for progress with the potential consequent common good inspired a general sense of community and drove to overcome the boundaries based on contrasts. Science, scientific thinking,

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dedication to research and to improve knowledge represented yesterday and continue to represent today the common ambition to break down cultural, religious and economic walls. The generosity of science is superior to the superstition of contrasts and arrogance. A message we can bring from the past back to the future and back to today (Curr Probl Cardiol 2024;49:102045.)

Introduction

The Renaissance (French term for rebirth) was a cultural movement that characterized the Italian and European life from the 14th to the 17th century.

During this period Italy experienced an unexpected economic growth and rich families supported the most gifted artists and scientists.

In this brief review we analyze the progresses of cardiovascular research in Italy during the Renaissance comparing those situations to the present.

Methods

A literature search was performed by the authors to identify the most important studies on the cardiovascular physiology during the Italian and European Renaissance.

Results

Leonardo Da Vinci (1492-1519)

Leonardo started to perform studies in humans, including postmortem dissections, at the age of 19 when he obtained a degree of "Painter."[1-5] In Florence artists had a special permission to perform human dissections. In Pavia (near Milan-1509), Leonardo met Marcantonio Della Torre, Professor of Theoretical Medicine, who asked for a collaboration regarding a textbook on anatomy. They planned to write a new textbook entitled *De humanis corpore* with many illustrations.

In those days Marcantonio Della Torre moved from the University of Padua to the University of Pavia. Padua was devastated by attacks from the Austrian-German army and the university was closed.

Marcantonio Della Torre died 1 year later at the age of 31 years taking care of people who had contracted the Plague. The textbook

was not published and the drawings and annotations by Leonardo were bought around 1670 by King Charles II and since then they have been well preserved in Windsor Castle. The drawings were made public almost 300 years later. Leonardo analyzed the anatomy of fresh specimen; he also performed in vivo studies on pigs, to analyze the movement of the blood in the beating heart through small metallic tracers. He made several wax casts of the bull heart, and from these casts, he constructed glass models to study the hydraulic characteristics of the blood flowing through the heart and its valves, an in vitro circulation model to mimic the human circulation. Seeds were used to visualize turbulences and blood flow.

Leonardo moved slowly from the accepted theories to new ideas, describing in detail the arterial circulation. He writes, "the heart is a muscle which contracts spontaneously." He examined in detail the bronchi up to their smaller ramifications, noting that each of them is accompanied by a small branch of the pulmonary artery (Fig 1). He hypothesized that the bronchial arteries receive freshness from the bronchi, full of air, and that the venous blood receives freshness in the lung, before returning to the heart. He studied in detail the anatomy of the coronary artery and veins, coming to the conclusion that the heart feeds itself.

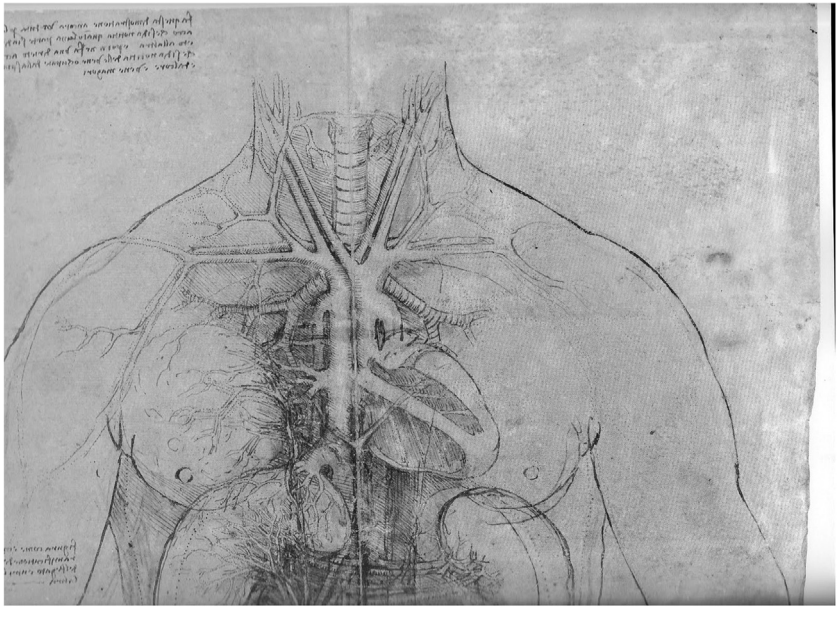

FIG 1. Drawing of the heart, the bronchi, and the superior vena cava by Leonardo. Royal Collection Trust/_ Her Majesty Queen Elizabeth II 2015 (1510).

He noted that atria contract when the ventricles dilate, explaining the movement of blood from the atria to the ventricles. The right atrium and ventricle are larger than those on the left. Having a special interest in hydraulic engineering, Leonardo studied the anatomy of the cardiac valves. He concluded that all 4 valves should open and close completely, otherwise the heart will not function adequately, with regurgitation of blood in the atria from the ventricles. Looking at nature he described the venous system like a plant: the large veins divide in smaller veins.[6] However, in one of his annotations about the heart he wrote "I could tell more if I was allowed to so. . .."

Andrea Alpago (1450-1522) and Ibn Al-Nafis (1213-1288)

Alpago obtained a degree in Medicine and Philosophy in 1470; in 1487 he was appointed as physician of the Venetian Consulate in Damascus (Syria).[7-10] He learned Arabic. He became fascinated by Arabic Medicine spending almost 30 years in looking for Arabic Medical textbooks all over the Middle East and North Africa. In 1520 he returned to the University of Padua where he presented the results of his researches. He published revisions of the previous translations of Avicenna and of Serapione. Costantine the African (1080), Gerardo da Cremona (114-1187) and Gerardo da Sabionetta (c 1250) had already translated in Latin the most important Arabic scientific textbooks including the Book of Healing and the Canon of Medicine by Avicenna.

Ibn al-Nafis (1213-1288) was born near Damascus. He was an excellent surgeon and had special interest in anatomy and physiology. Probably was one of the few Arabic anatomists who performed animal and human dissections. Ibn al-Nafis lived most of his life in Egypt, and witnessed several wars with the rise of the Mamluks dynasty. He became an authority in medicine in the Arabic world.

In 1242 he published "Commentary on Anatomy in Books I and II of Ibn Sina's Kitab al-Qanun (Avicenna)" underlying the importance of the anatomical knowledge for the physician, and the vital relationship between anatomy and physiology. His textbooks were well known in the Arabic world and Andrea Alpago was able to read them. Alpago translated in Latin some of Ibn Al-Nafis work concerning the use of medical treatments. Even if there is no official report, it is conceivable that Alpago reported some of the theories on the cardiovascular system expressed in the "Commentary" to the scientists of the University of Padua. Several historians deny the

possibility that the theories on blood circulation by Ibn al-Nafis were introduced by Alpago in Padua.

Ibn Al-Nafis wrote "...The heart has only 2 ventricles...and between these 2 there is absolutely no opening...The benefit of this blood (that is in the right cavity) is to go up to the lungs, mix with what air is in the lungs, then pass through the arteria venosa to the left cavity of the 2 cavities of the heart; and of that mixture is created the animal spirit..." For this reason the arterious vein has solid substance with 2 layers, in order to make more refined that (the blood) which transudes from it. The venous artery, on the other hand, has thin substance in order to facilitate the reception of the transuded [blood] from the vein in question. And for the same reason there exists perceptible passages (or pores) between the 2 [blood vessels].

The Commentary on Anatomy in Avicenna's Canon by Ibn al-Nafis was made known to the Western world only about 100 years ago. A young Egyptian physician Muhyo Al-Deen el Tatawi came across the manuscript in the Prussian State Library in Berlin. Max Meyerhof, an eminent medical orientalist in Cairo published German, French, and English translations of the relevant parts of the Commentary written by Ibn al-Nafis.

Michael Servetus (1511-1553)

Born and educated in Spain, he traveled and studied all over Europe.[10-12] He was interested in mathematics, astronomy and meteorology, human anatomy, medicine and pharmacology, showing a fertile imagination, continuously introducing new hypotheses.

Servetus was condemned by the Church for his criticism of the concept of the Trinity (De Trinitatis Erroribus and Dialogorum de Trinitate 1531). Servetus moved to Paris to study medicine in 1536 where he assisted in human dissections together with another brilliant student Vesalio. In 1553 Michael Servetus published another religious work with further antitrinitarian views entitled Christianismi Restitutio. He entered in an open and contrasting correspondence with Calvin. After being condemned by Catholic authorities in France for his book, he decided to move to Italy. He stopped in the Calvinist Geneva where he was denounced by John Calvin himself and burned for heresy by order of the city's governing council. In the same Christianismi Restitutio he described, first for those days, the idea of the pulmonary circulation. He wrote "However, this communication is made not through the middle wall of the heart, as is commonly believed, but by a very ingenious

arrangement. . . the refined blood is urged forward from the right ventricle of the heart over a long course through the lungs; it is treated by the lungs, becomes reddish-yellow and is poured from the pulmonary artery into the pulmonary vein."

Historians debate if Servetus developed the concept of pulmonary circulation on the basis of the new ideas circulating in the University of Padua, where in the meantime his old student-colleague Vesalius was Professor of Anatomy and few years later were described with similar words by Realdo Colombo, who took the chair left by Vesalio. The description of the pulmonary transit by Servetus seems to be a translation of the writing by Ibn al-Nafis. Servetus execution was condemned by many authorities giving birth to the concept of the importance of religious tolerance in Europe.

Andreas Van Wesel (Vesalius in Latin) (1514-1564)

Van Wesel was born to a rich family with a close relationship with the Emperor Charles V.[7,8,11,12] He was educated in Leuven and Paris, and in 1538 (very young at the age of 24) he became Professor of Surgical Anatomy in the prestigious University of Padua. In 1543 (at the age of 29), he published the textbook "De Humani Corporis Fabrica," which was a revolution in the concept of Anatomy of Galen. He asked the Bottega of Tiziano to make the drawings for his textbook. Vesalius described the venous and the arterial system in detail but he did not enter in the field of physiology and accepted almost all theories by Galen on the blood circulation.

Realdo Colombo (1516-1559)

Realdo Colombo trained and worked as surgeon in Venice with Lonigo, a famous and experienced surgeon.[11-14] He desired to have an academic education and in1538 he started to study medicine in Padua. Colombo became a close collaborator of Vesalius assisting him in many dissections. He succeeded Vesalius as Professor of Anatomy and Surgery in Padua; soon he moved to the University of Pisa and then to the Sapienza University in Rome. He published in 1572 the textbook "De Re Anatomica." Despite the revolutionary and modern concepts on the arterial and venous circulation, the textbook by Realdo Colombo had limited diffusion: there were no illustrations. Realdo Colombo asked Michelnagelo Buonarotti to illustrate his book, but the artist did not accept the task because of his advanced age.

Andrea Cisalpino (1524-1603)

He studied medicine at the University of Pisa, following the lectures of Realdo Colombo.[11-14] Adrea Cisalpino was appointed Professor, being interested in Botanic, Surgery and Anatomy. In 1592 was appointed Professor of Medicine at the University of Rome Sapienza and personal doctor of the Pope. He continued the research of Realdo Colombo. In 1569 he published "Quaestionum peripateticarum Libre quinque." He described in detail the anatomy of the heart and the pulmonary circulation. In contrast to the hypotheses by Cerveto who described the air mixing with the blood in the lungs, he believed that the purification of the blood in the lungs needed only a simple contact with the air. He also supported the concept that arterial and venous circulation were connected in their smaller ramifications. His textbooks are a mixture of philosophy and anatomy. Despite the revolutionary concepts on the arterial and venous circulation, the textbooks by Andrea Cisalpino had limited diffusion due to the continuous search for connections between anatomic observations and philosophical dissertations and for the lack of illustrations.

Girolamo Fabrizio D'Acquapendente (1533-1619)

He graduated from the University of Padua where he become Professor of Surgery and Anatomy.[15,16] He was considered an excellent clinician and made fundamental discoveries in anatomy and embryology. Probably venous valves were already noted, but Fabrizio analyzed in detail the valves in all the venous system. The textbook "De Venarum Ostiolis" (1603) had a large scientific diffusion because it was characterized by clear annotations and artistic color illustrations. The basic physiological role played by the venous valves for Fabrizio was to avoid that too much blood could stagnate in the extremities, with resulting reduced perfusion of the more proximal organs. Fabrizio misinterpreted the physiological role of the venous valves trying to conciliate the anatomic findings with the traditional concept of Galen in which the veins originate in the heart and liver bringing blood to the periphery (Figs 2-4).

William Harvey (1578-1657)

After graduating from Cambridge, he decided to study in Padua as assistant to Fabrizio D'Acquapendente.[17-19] In 1602 William Harvey

FIG 2. The venous valves of the cephalic and basilic veins (Tabula I - De Venarum Ostiolis Fabrizio D'Acquapendente 1603). It is evident the different orientation of the valve of the opened jugular vein. A detail noted by William Harvey to support his hypothesis of the centripetal direction of the venous blood flow. (Color version of figure is available online.)

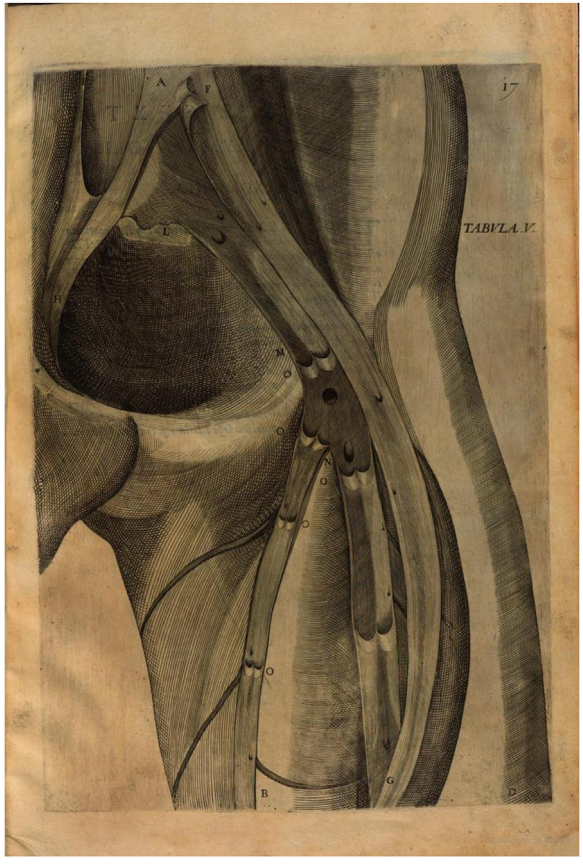

FIG 3. The venous valves of the saphenous vein (Tabula V - De Venarum Ostiolis Fabrizio D'Acquapendente 1603). (Color version of figure is available online.)

obtained his degree in Medicine and Philosophy and returned to England. He continued and perfected some experiments in animals after they were killed during hunting trips by the King and his court. Harvey had a close relationship with the English Royal Family, because he married Elisabeth Browne, daughter of Lancelot Browne, personal physician of both Queen Elisabeth I and King James I. In 1628, Harvey published the book "Exercitatio Anatomica de Motu Cordis and Sangunis in Animalibus," in which he described the blood circulation in detail (Fig 5). This book began a revolution in the ideas of how the blood circulated and in the function of the heart. The only unanswered question in Harvey theories concerned the mechanisms which allowed the oxygenated blood to move from the venous to the arterial pulmonary system.

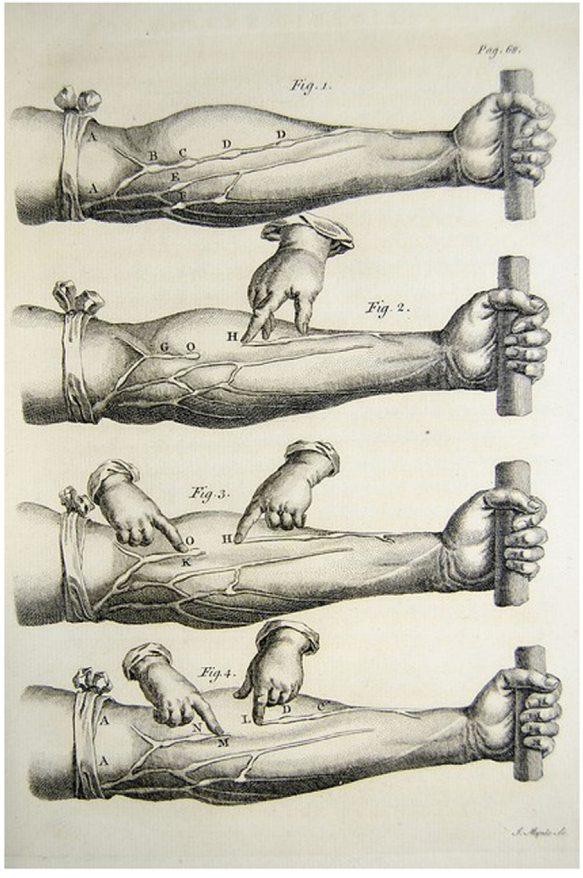

FIG 4. The veins of the forearm (Tabula II - De Venarum Ostiolis Fabrizio D'Acquapendente 1603). It is evident that the author followed Galen theories about the centrifugal direction of the venous blood flow. For the author the veins originate from the heart like a plant, which becomes thinner toward the periphery, after the origin of their branches. (Color version of figure is available online.)

Marcello Malpighi (1628-1694)

Marcello Malpighi was professor of Theoretical Medicine at the University of Bologna and was elected member of the London Royal Society of Medicine.[20] He introduced in Anatomy the use of the microscope. In 1661, he published the textbook "De Pulmonibus Observationes Anatomicae" in which he observed and described the pulmonary capillaries explaining the oxygenation of the venous blood in the lungs and how the oxygenated blood returns to the heart, completing the theories by Harvey.

FIG 5. The classic experiments by William Harvey (Exercitatio Anatomica de Motu Cordis and Sangunis in Animalibus - 1628) to demonstrate the centripetal direction of the venous blood flow. (Color version of figure is available online.)

Comments

This short report underlines the importance of collaboration and communication among scientists. The ideals of progress in medicine and in the care of suffering people have represented continuous stimuli allowing to overcome prejudices, religious and political differences. The modern concepts of blood circulation have been established through a close collaboration and exchanges of ideas among scientists coming from different countries, different religious and political backgrounds. In those days Italy was divided in smaller states characterized by a basic tendency to prevaricate each other. Padua, Bologna, Milan, Rome, Pisa belonged to different states with different laws and traditions. Italy was involved by a devastating war, in which the most powerful armies in Europe (League of Cambrai; 1508-1511; League Santa 1511-1512; League of Cognac 1526) moved initially against the Venetian Republic and later against the French Army to limit their expansion in Italy. The city of Padua was besieged by the Austrian Army for several months and the University was closed for a long time. The French army invaded and conquered Milan. In 1527 the Austrian-German army invaded and looted Rome. Europe was theater of continuous wars based on political and religious contrasts. There were continuous outbreaks of Plague in several

countries. Religious contrasts occurred inside the Christianity and between the Christianity and Islam; contrasts which were based on theological disputes associated with economic and expansionist ambitions, resulting in extreme and rigid religious orthodoxy. Despite these difficulties, medical scientists collaborated overcoming the close boundaries of everyday general confrontations. The ambition for advancement in science and for progress with the potential consequent common good inspired a general sense of community and drove to overcome the boundaries based on contrasts. Science, scientific thinking, dedication to research and to improve knowledge represented yesterday and continue to represent today the common ambition to break down cultural, religious and economic walls.

The generosity of science is superior to the superstition of contrasts and arrogance.

A message we can bring from the past back to the future and back to today.

Authors' Contribution

Patrizia Fughelli: Conceived the Idea, Collected Data, Revised the Manuscript and Gave Suggestions.

Antonio Sterpetti: Conceived the Idea, Collected Data and Wrote the Original Draft.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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