The Impact of Personalized Medicine in the Treatment of Ventricular Septal Defects to Evaluate the Accuracy of Surgery Using 3D Printed Hearts

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ABSTRACT

Ventricular septal defect (VSD) is a well-known anomaly among congenital heart diseases typically diagnosed in infancy. Defects in the ventricular septum cause an interventricular shunt. The excess amount of mixed blood passes through the pulmonary circuit and overfills the lungs, leading to pulmonary hypertension. Approximately 0.3% of infants are born with congenital heart defects, and approximately 20%-30% of them are VSD related. Studies show that mutations in genes, such as *NKX2-5* and *TBX5*, have significant effects on the etiology of VSD. In this study, we suggest a unique perspective. To cure the disease and avoid complications, a personalized approach would be more efficient in surgical operations. Here, we focus on the importance of three-dimensional printing of the patient's heart in critical cases. Inspired from the quote "treat the patient not the disease," we believe that each defect emerges with different outcomes. Using the specific three-dimensional (3D) printed heart model, a thorough preoperative planning of the operation can be achieved. We believe that 3D printers open to medical use will allow the widespread use of this method in the future.

Key Words: Personalized therapy; ventricular septal defect; 3D printers

Kişiselleştirilmiş Tıbbın 3 Boyutlu Yazıcı ile Basılmış Kalp Yoluyla Ventriküler Septal Defekt Tedavisinde Uygun Cerrahi Değerlendirmenin Yapılmasında Önemi

ÖZET

Ventriküler septal defekt (VSD) çoğunlukla bebeklikte tanı konan doğumsal kalp anomalileri arasında en iyi bilinenlerden biridir. Ventriküler açıklık üzerinde yer alan kusurlar, interventriküler şanta neden olur. Aşırı miktarda karışık kan pulmoner devreden geçerek akciğerleri aşırı doldurur ve pulmoner hipertansiyona yol açar. Bebeklerin yaklaşık %0.3'ü konjenital kalp rahatsızlıkları ile doğar. Bunun yaklaşık %20-30'u sebebi VSD bağlantılıdır. Çalışmalar *NKX2-5* ve *TBX5* gibi genlerdeki mutasyonların VSD etyolojisi üzerinde önemli etkileri olduğunu göstermektedir. Biz bu çalışmada farklı bir perspektif önermekteyiz. Hastalığı tedavi etmek ve komplikasyonları önlemek için kişiselleştirilmiş bir yaklaşım cerrahi operasyonlarda daha etkin olacaktır. Bu nedenle, bu yazıda, kritik olgularda hastanın kalbinin üç boyutlu baskısının önemine odaklanılacaktır. Hastalığı değil hastayı tedavi mantığı ile baktığımızda herbir kusurun farklı sonuçlar ortaya çıkardığını söyleyebiliriz. Böyle özel hastalar için 3 boyutlu basılı kalp modeli ile ameliyat öncesinde kapsamlı bir ameliyat planlaması yapılabilir. 3 boyutlu yazıcıların tıbbi kullanıma açıldığına, bu yöntemin gelecekte yaygın olarak kullanılabileceğine inanıyoruz.

Anahtar Kelimeler: Kişiselleştirilmiş tedavi; ventriküler septal defekt; 3 boyutlu yazıcılar

INTRODUCTION

To understand the importance of personalized medicine, we need to go back in time. The history of a personalized approach starts with Hippocrates. A thousand years ago, he stated that "It's far more important to know what person the disease has than what disease the person has." Later, in the 19th century, Sir William Osler emphasized, "If it were not for the great variability among individuals, medicine might well have been a science and not an art," about personalized medicine(1). Toward the end of 1990s the expression "Personalized

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Medicine" was coined that meant "tailoring of medical treatment to the individual characteristics of each patient." It does not literally mean the creation of drugs or medical devices that are unique to a patient, but rather the ability to classify individuals into subpopulations that differ in their susceptibility to a particular disease or their response to a specific treatment. Prevention or therapeutic interventions can then be focused on those who will benefit, sparing the cost and side effects for those who will not[2]. Currently, personalized medicine is an ever-evolving field for medical researchers, medical doctors, and physicians. There is a remarkable growth in scientific researches on personalized medicine within the past decades, particularly in the cardiovascular-related researches[3,4].

Ventricular Septal Defects

Ventricular septal defects (VSDs) are the most common anomalies among congenital heart diseases (CHD). Defects related to both the aortic and the pulmonary valves are known as subarterial infundibular type (type I). Approximately 70% of VSD cases are located in the area of the membranous septum, with several extensions to the outlet septum or to the trabecular septum; therefore, they are known as perimembranous VSD[5]. In addition to this, these defects are very close to the aortic valve so, they are also known as subaortic or infracristal VSDs (type II). Some perimembranous defects extend beneath the septal leaflet of the tricuspid valve toward the inlet septum; they are known as atrioventricular canal type (type III). The first VSD repair was performed by Lillehei et al. in 1954[6]. Surgery has been operated for many years and has been the gold standard for the treatment of VSD. However, it is associated with morbidity and mortality, patient discomfort, sternotomy, and skin scar. These risks are increased in patients with complex CHDs, particularly in patients with redo surgical phases[7]. Complex CHDs associated with VSD cases occur when certain factors are existed such as patients' age and size, location of defects, some defects, along with other anatomical morphological variations, previous surgical procedures[5]. In such complex cases, surgical closing all of the shunts is not easy as it seems in mapping materials (such as MRI, CT, and ECO), thereby necessitating, more data. This raises the following question: How to cope up with this situation? Considering the aforementioned information, personalized medicine is a unique way to cure complex CHDs associated with VSD.

Three-Dimensional (3D) Printers in Medical Use

Initial steps of this technology were developed at the Massachusetts Institute of Technology. Three-Dimensional Printing (3DP) fabricate 3D structures by injecting printing liquid binder solution onto a powder bed[8-10]. Various materials have been used in biomaterial printings[11]. Thus, 3D-printable biomaterials have a huge potential in medical use. Those 3D models can be used in personalized treatments that take into account patient-specific anatomical variations[12]. In our study, flexible resin was used as a biomaterial for the 3D heart modeling (Figure 1). In this way, personalized treatment in complex CHDs associated with VSDs has become a reality using 3D printers at preoperative planning phase. The essential materials required for the 3D printed heart model are the mapping systems, such as CT, MRI, and ECO. CT or MRI scans of patients reveal the 2D/3D digital data. Digital data format (DICOM) data can be exported and processed into stereo lithography (STL) data files, such as stereo lithography, or other 3D file formats by using segmentation, surface extraction, and 3D model post-processing[12]. After segmentation, a surface model is generated[13-15]. For medical visualization, these types of shaded surface display techniques are well developed due to topological correction, decimation, laplacian smoothing, and local smoothing[16-19]. These methods are used to create a 3D model for 3DP. In addition, virtual simulation is performed for patient-specific preoperative planning. Based on such planning, surgical guides is designed using computer-aided design software. After adjusting the 3D heart model, and according to the application, the most suitable 3D printer is selected. The 3D heart model file is uploaded into the 3D printer. The 3D printer uses layer-by-layer stereo lithographic accumulation to fabricate the 3D physical model. In general, the accuracy of the 3DP object depends on the following aspects: the accuracy of the medical reputation the proper imaging process for 3D modelling, and the 3DP accuracy of the system[12].

CONCLUSION

This study is performed with the collaboration of University of Health Sciences' students and academic members. The researchers received aid from the Division of Pediatric Cardiovascular Surgery of Kartal Kosuyolu SAUM. After studying the diseases and methods for long, literature has been compiled the article. In conclusion, thoughts and pathways were made in this case. Studies in 3D modeled biomaterials show that risk of surgeries in cases that are similar will visibly decrease if our asserted method is implemented. In addition, the development of inexpensive 3D printers as well as the application of 3D printing has drawn attention. Concerning patient's health, manufactured 3D models allow us to mimic the real heart. The development and optimization of the entire procedure, from digital images to 3DP fabrication, require personalized approach. In addition, it is important to select the right case to use this method. Almost all research on this subject suggests the use of our asserted pathway only in complex CHD cases due to fact that the additional cost of 3D printing is as expensive as the surgery itself. However, patients with complex CHDs along with the VSDs are at the highest risk during surgery,

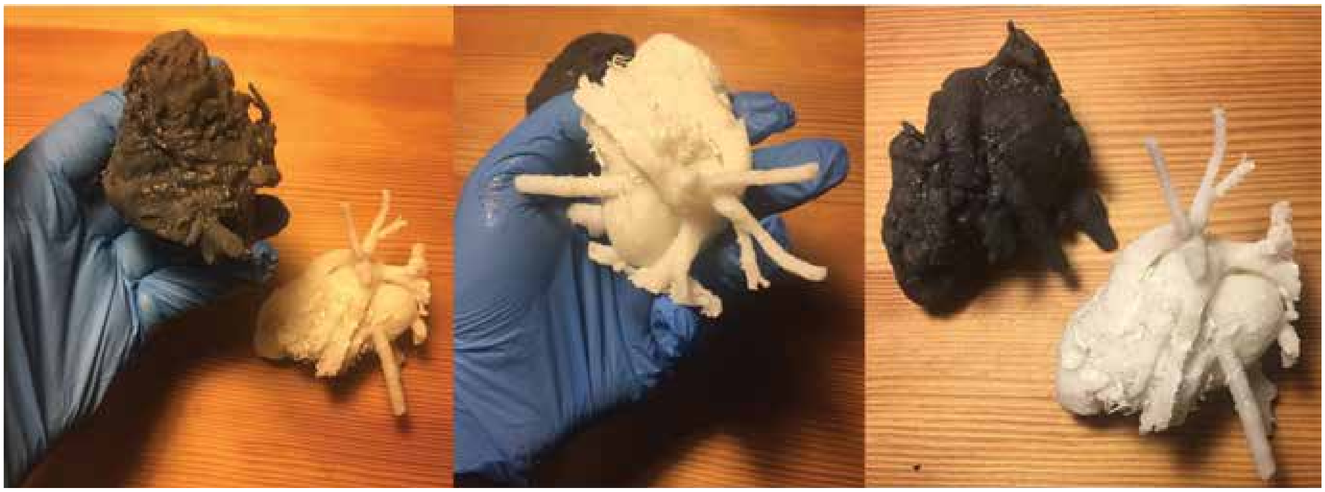

Figure 1. Comparative display of three-dimensional printed heart models.

thereby making our method most essential. We have previously mentioned that the use of 3D printers is essential in evaluating the accuracy of complex VSD surgeries. In the early 2000s, 3D printers have been used mainly for hard tissue applications[12]. Our pathway against complex VSDs are to get an accurate preoperative planning phase. Therefore, 3D printed heart model of a patient is required by the surgeon before surgery. Although some may argue that the expense to manufacture patient's 3D printed heart model in VSD surgery would not be productive. However, in complex CHD cases along with the VSDs, preoperative planning of the operation is still difficult due to the technical problems. Therefore, we believe that this evolving personalized method will be a milestone in surgeries of CHDs in the future.

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