The Impact of Personalized Medicine in the Treatment of VSDs To Evaluate the Accuracy of Surgery Via 3 D Printed Hearts

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ABSTRACT

Ventricular Septal Defect (VSD) is one of the most-known anomalies among congenital heart diseases mostly diagnosed in infancy. Defects located on the ventricular septum cause an interventricular shunt. Excess amount of mixed blood goes through pulmonary circuit and overfills the lungs leading to pulmonary hypertension. Approximately %0.3 of infants are born with congenital heart defects. About %20-30 of the cases 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. In order to cure the disease and avoid complications, a personalized approach would be more efficient in surgical operations. Therefore, this paper will focus on the importance of three-dimensional printing of patient's heart in critical cases. As we inspired from the "treat the patient not the disease" wise saying, each defect emerges with different outcomes. According to that specific patient's 3D printed heart model a thorough preoperative planning of the operation can be realized. We believe that 3D printers open to medical use, give rise to the thought that this method will be used widespread in the future.

Keywords: Personalized therapy; Ventricular septal defect; 3D printers.

Kişiselleştirilmiş Tıbbın 3 Boyutlu Yazıcı ile Basılmış Kalp Yoluyla VSD Tedavisinde Uygun Cerrahi Değerlendirmenin Yapılmasında Önemi

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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 etiyolojisi 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 vakalarda 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 açıklık; 3 boyutlu yazıcılar.

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Introduction

To understand the importance of personalized medicine, we need to go back in time. History of personalized approach starts with Hippocrates. He stated that "It's far more important to know what person the disease has than what disease the person has" thousand years ago. Later on, 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 in the 19th century [1]. Towards the end of 1990s the expression "Personalized Medicine" announced as "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. Preventive or therapeutic interventions can then be concentrated on those who will benefit, sparing expense and side effects for those who will not." by the Council of Advisors on Science and Technology of USA [2]. At the present time, personalized medicine became 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, especially in the cardiovascular related researches [3,4].

Ventricular Septal Defects

Ventricular septal defects (VSDs) are the most common anomalies among congenital heart diseases (CHD). Around 70% of the VSD cases are located in the area of the membranous septum with several extensions to the outlet septum or to the trabecular septum [5]. These defects are defined as perimembranous VSD. These defects are very close to the aortic valve and are also defined as subaortic or infracristal VSDs (type II). Some perimembranous defects extend beneath the septal leaflet of the

tricuspid valve towards the inlet septum and are defined atrioventricular canal type (type III). Defects related to both the aortic and the pulmonary valves are defined as subarterial infundibular type (type I). 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 has associated with morbidity and mortality, patient discomfort, sternotomy and skin scar. These risks are increased in patients with complex CHDs and in particular in subjects 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, number of defects, along with other anatomical morphological variations, previous surgical procedures [5]. In these complex cases, closing all of the shunts surgically is not easy as it seems in mapping materials (MRI, CT, ECO etc.). Because of that, risk of mortality or morbidity is increased. Hereafter, one question appears in our minds. How to cope up with this situation? In the light of this information's, personalized medicine highlights a unique pathway to cure complex CHDs associated with VSD.

Three-Dimensional (3D) Printers in Medical Use

First steps of this technology were developed at the Massachusetts Institute of Technology. Three-Dimensional Printing (3DP) fabricates 3D structures by inkjet printing liquid binder solution onto a powder bed [8-10]. A diversified amount of materials has been utilized in biomaterial printings [11]. Hereby, 3D-printable biomaterials became a huge potential in medical use. Those biomaterials 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 become reality in the use of 3D printers at preoperative planning phase. 3D printers' essential material for the 3D printed heart model is the Mapping systems such

as CT, MRI, ECO, etc. Patient's scans by CT or MRI reveal us the 2D / 3D digital data. The DICOM (digital data format) 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 should be generated [13-15]. For medical visualization, these types of shaded surface display techniques are well developed because of the topological correction [16], decimation [17], laplacian smoothing [18], and local smoothing [19]. These are methods that to create a 3D model for 3DP. In addition, virtual simulation is performed for patient-specific surgical planning. Based on such planning, surgical guides is designed using computer-aided design (CAD) software. After adjusting a 3D heart model, the most suitable 3D printer for the application should be 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 combination of the accuracy of the medical image, which should be as thin as possible, the appropriate imaging process for 3D modeling, and the 3DP accuracy of the system [12].

Conclusion

This study is performed by the assistance of University of Health Sciences' students and academic members. For the researches, aids of Division of Pediatric Cardiovascular Surgery of Kartal Kosuyolu SAUM were received. After a long period of studying the diseases and methods, literature research has been made for the article. In conclusion, thoughts and pathways were made for this case. Studies in 3D modeled biomaterials show that risks of surgeries in related cases are discernibly going down if our asserted pathway would be implemented. In addition, the developments of inexpensive 3D printers and 3D printing applications have drawn attention. Concerning patient's

health, manufacturable 3D models allow us to mimic the real heart itself. Development and optimization of the entire procedure, from digital images to 3DP fabrication, are required personalized approach. In addition, it is important to select the right case to use this method. Almost all of the researches in this subject suggest 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 nowadays. Yet the patients with complex CHDs along with the VSDs are at the highest risk during surgery. This is why our personalized method becomes most essential. From the very beginning of this article we said, use of 3D printers becomes essential in order to evaluate the accuracy of complex VSD surgeries. In the early 2000s, 3D printers have been used mainly for hard tissue applications due to the hardness of most 3D printable materials [12]. But, our pathway against complex VSDs are to get an accurate preoperative planning phase. Because of that 3D printed heart model of patient is needed in the hands of surgeon before surgery. Some will say, that kind of expense in such surgery (VSD surgery) to manufacture patient's 3D printed heart model wouldn't be productive. But in complex CHD cases along with the VSDs are hard to make an accurate preoperative planning in today's world mapping systems. Therefore, we believe that our personalized pathway will be a keystone in surgeries of CHDs at the future.

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Figure 1. Comparative display of 3D printed heart models that we produced by formlabs form2 in our laboratory