# Transcatheter device closure of atrial septal defects guided completely by transthoracic echocardiography: A single cardiac center experience with 152 cases

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# **ABSTRACT**

**Objective:** This study aimed to assess the safety and feasibility of transcatheter device closure of atrial septal defects (ASDs) guided completely by transthoracic echocardiography (TTE).

Methods: A total of 152 patients underwent transcatheter device closure of ASDs guided completely by TTE in our center from September 2014 to June 2017. We used routine delivery sheaths during the procedure and then closed the ASDs by releasing a domestic occluder.

Results: The closure was successful in 150 patients, and surgical repair was required in two patients. The size of the deployed occluder ranged from 10 mm to 38 mm (21.4±8.5 mm), and the procedure duration ranged from 30 to 90 min (38.2±21.4 min). No fatal complications were observed. Minor complications included transient arrhythmias (n=12) during the process of device deployment. The follow-up period was 3 months to 2 years, with no occluder dislodgment, residual fistula, or thrombus-related complications. In our comparative studies, no statistically significant differences were observed in success rates and complications.

Conclusion: Transcatheter device closure of ASDs guided completely by TTE may be safe and effective and can be an alternative to traditional methods. (Anatol J Cardiol 2018; 20: 330-5)

Keywords: congenital heart disease, septal defect, cardiac intervention

#### Introduction

Atrial septal defect (ASD) is a common congenital heart disease. Its principal treatment involves open-heart repair under cardiopulmonary bypass and transcatheter device closure guided by echocardiography and fluoroscopy. According to literature, both treatments can give satisfactory clinical results but have various shortcomings. For patients undergoing surgical repair, unpleasant surgical scars and inevitable damage from cardiopulmonary bypass are the main complications. For most selected cases, transcatheter device closure is often the first choice as it does not require surgical incision (1-4). However, the biggest drawback of this procedure is X-ray radiation exposure. To overcome the shortcomings of the two methods, our approach was to use a transcatheter technique to close the ASD. This resulted in better cosmetic results than those by surgical

repair. Moreover, our technique was completely guided by transthoracic echocardiography (TTE), thus avoiding X-ray exposure. This study aimed to evaluate the safety and efficacy of our procedure, and the results were found to be encouraging.

## **Methods**

This study was approved by the Ethics Committee of Fujian Medical University, China, and adhered to the tenets of the Declaration of Helsinki. In addition, written informed consent was obtained from the patients or parents of the patients.

All patients who enrolled at our cardiac center between September 2014 and June 2017 were included in the study. They were divided into two groups based on the therapeutic method chosen. Group I included 152 patients (62 males and 90 females) undergoing transcatheter device closure guided completely by

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TTE. Their age ranged from 3 to 75 years (mean±standard deviation, 17.6±16.7 years). The body weights ranged from 15 to 72 (35.6±18.5) kg. Group II included 125 patients (43 males and 62 females) who underwent transcatheter device closure guided by fluoroscopy and echocardiography. The ages ranged from 4 to 60 (18.2±15.1) years, and the body weights ranged from 18 to 76 (34.1±16.2) kg. No differences in age and body weight distribution were found between the groups.

All patients were diagnosed with secundum ASDs by preoperative TTE. Inclusion criteria for both groups were secundum ASD with the presence of adequate rims (distance from the edge of the defect to the adjacent anatomic structures of ≥5 mm) and the maximum diameter of the ASD of 36 mm. Other indications included hemodynamically significant left-to-right shunts, significant chamber enlargement, and/or mild-to-moderate pulmonary hypertension, with the presence of clinical symptoms. The exclusion criteria included association with other congenital heart disease (such as partial pulmonary venous anomaly), severe pulmonary hypertension (pulmonary vascular resistance >4 Woods units), multiple ASDs, congestive heart failure, and an inability to provide informed consent. Obese patients with vague TTE acoustic window were also excluded from this study.

Routine examinations included a standard electrocardiogram, chest X-ray, and blood tests. In both groups, 65 patients had mild-to-moderate pulmonary hypertension that was assessed by TTE with pulmonary artery systolic pressures of 30-60 mm Hg. Forty-three patients had symptoms, including recurrent pulmonary infection, chest tightness, palpitations, shortness of breath, exercise intolerance, and insignificant chest pain. The chest X-rays showed pulmonary congestion, and echocardiography showed hemodynamically significant left-to-right shunts and/or significant chamber enlargement.

The domestic ASD occluder (Shan Dong Visee Medical Apparatus Co. Ltd., China) used in this study was similar to the Amplatzer ASD occlude but less expensive. A fenestrated occluder was not used. The routine catheter was purchased from Beijing Huayi Shengjie Technology Co. Ltd.

In group I, endotracheal intubation and combined intravenous-inhalation anesthesia were used in juvenile patients, whereas local anesthesia or local anesthesia with intravenous sedatives was used in adult patients. The patients were placed supine and were draped for exposure of the entire chest with the probe placed below the xiphoid and at the apex and parasternal side to guide the entire procedure. Heparin was intravenously administered, and the activated clotting time was monitored to be maintained at >250 s. The right femoral vein was punctured, and a venous sheath was inserted. A mark on a multifunctional catheter was set to measure the distance from the puncture point to the heart, which allowed for effective manipulation of the catheter depth into the veins. Subsequently, a multifunctional catheter and a guide wire were advanced into the venous sheath. Under the guidance of real-time TTE, the multifunctional catheter and guide wire were advanced into the right atrium via

the inferior vena cava. By adjusting the angle, the direction, and the depth of the tip, the multifunctional catheter and guide wire were advanced into the left atrium through the ASD (Fig. 1), and then, the multifunctional catheter was withdrawn (Fig. 2). A delivery sheath was inserted along the guide wire into the left atrium, and the inner core and the guide wire were withdrawn (Fig. 3). The tip of the sheath was confirmed in the left atrium. Next, an occluder was delivered carefully through the sheath by pushing a rod. The left atrial disc of the occluder was opened and pulled back parallel to the atrial septum (Fig. 4), and the right disc was sequentially opened to close the ASD (Fig. 5). After checking the occluder's immobility and the possible presence of a residual shunt, the occluder was released, and the delivery sheath was withdrawn. In group II, the standard method of transcatheter device closure of ASDs guided by echocardiography and fluoroscopy was used as previously reported (5).

# Statistical analysis

The Statistical Package for Social Sciences software version 19.0 was used for statistical analysis. Continuous data are presented as the mean±standard deviation and range. The data



Figure 1. A multifunctional catheter was advanced into the left atrium under echocardiographic guidance



Figure 2. A guide wire was inserted into the left atrium



Figure 3. A delivery sheath was inserted into the left atrium



Figure 4. The left atrial disc was opened



Figure 5. The right atrial disc was opened

were tested using normality test (the Shapiro-Wilk test) had normal distribution. The clinical parameters between the two groups were compared using the independent samples t-test. A p value of <0.05 was considered as statistically significant.

Table 1. Comparison of clinical data between the two groups			
	Group I	Group II	<i>P</i> value
Number of patients	152	125	
Male/Female	62/90	43/62	
Age (years)	17.6±16.7	18.2±15.1	0.894
Body weight (kg)	35.6±18.5	34.1±16.2	0.861
ASD size (mm)	21.4±8.5	22.5±7.9	0.923
Operative time (min)	38.2±21.4	35.5±19.8	0.918
Hospital stay (days)	3.1±1.2	3.2±1.1	0.908
Follow-up (years)	2.1±1.1	1.8±1.2	0.910
Successful occlusion rate	98.7%	98.4%	0.844
Fluoroscopy time (min)	0	2.1±1.5	
ASD - atrial septal defect			

## Results

In group I, successful occlusion was achieved in 150 patients. The other two patients were converted to surgical closure because of device dislodgment into the right atrium during the perioperative period. Among the successful 150 cases, the operative time ranged from 30 to 90 (38.2±21.4) min, the size of the occluder ranged from 10 to 38 (21.4±8.5) mm, and the hospital stay was 2-5 (3.1±1.2) days. The overall immediate complete closure rate was 90.7%. A tiny residual flow through the device or the junction of the occluder and the rims of the ASD was observed in the intraoperative period in 14 patients, all of which had disappeared at follow up. Minor complications were encountered in a small number of patients, including transient arrhythmia (n=12) in the course of device deployment, which spontaneously recovered or were easily treated by drugs. Puncture site hematoma occurred in two patients, requiring no medical treatment. During the perioperative period, no complications related to embolism, residual fistula, complete atrioventricular block, hemolysis, infection, or thrombosis-related conditions were noted. During the follow-up period of 3 months to 2 years, functional assessment, TTE, and ECG were performed. Symptoms had resolved totally or had improved significantly. The complete closure rate was 100%. No episodes of endocarditis, thromboembolism, device disruption, heart valve distortion, or permanent rhythm disturbances were noted.

Table 1 displays the comparison of the clinical data of all patients in both groups. No statistically significant differences were observed in the success rates or complications. The only difference was that fluoroscopy was not performed in group I.

#### **Discussion**

According to the literature, the treatment of ASDs began with traditional surgical thoracotomy patch repair and advanced to

a minimally invasive surgical repair. Today, transcatheter device closure guided by echocardiography and fluoroscopy is widely used worldwide (1-4). All treatments give satisfactory clinical results. However, cardiopulmonary bypass leads to some adverse outcomes, including systemic inflammatory responses, multiple organ dysfunction, and various disfiguring scars. To improve this situation, Mills et al. (6) introduced transcatheter device closure of an ASD in 1978. Thereafter, this technology has gained popularity worldwide. With the invention and application of various new occluders, it has become another standard treatment for the closure of ASD in most patients. In addition to the satisfactory treatment result, its advantages are obvious, including absence of scar, no pain, and very short hospital stays. However, the greatest risk is that both doctors and patients are exposed to Xrays, which may lead to radioactive damage. In recent years, many Chinese cardiac centers have started performing transthoracic minimally invasive device closure of ASD, combining the advantages of transcatheter and surgical procedures (7, 8). Although the procedure is cost-effective, with no X-ray exposure and relatively good cosmetic outcomes, it still involves a 3-4 cm incision. In this study, we performed transcatheter device closure of ASD guided completely by TTE and reported our experience.

TTE played an important role and was used as only a guiding tool during the complete procedure in this study. It should be performed by an experienced sonologist. Many reports have suggested that the effectiveness and accuracy of TTE is lower than that of transesophageal echocardiography (TEE) (9-11). According to our experience, TTE can be sufficient to measure the diameter of an ASD and guide device closure of the ASD, consistent with the reports by other scholars. We concluded that this procedure can be accomplished considering the patient's clear acoustic window by TTE, especially in the Chinese population. Bartakian et al. (12) reported that the use of TTE is as efficacious and safe as TEE for assessing and guiding ASD occlusion in selected pediatric patients. TTE may also offer the additional benefit of reduced X-ray exposure. Azhar (13) concluded that TTE has the same efficacy as TEE in device closure of ASDs but with superior safety features, including significantly reduced procedural time and fluoroscopy times and less use of general anesthesia. Ding et al.'s (14) study showed that TTE guidance alone may be considered as efficacious and safe as TEE during transcatheter device closure of ASDs in selected adults. Oto et al. (15) demonstrated the efficacy and safety of TTE guidance during percutaneous device closure of patent foramen ovale, demonstrating a shortened procedural time without the need for general anesthesia or endotracheal intubation. We also used TTE to guide transthoracic device closure of ASDs and transcatheter device closure of patent ductus arteriosus with satisfactory results (16, 17). Increasing the number of investigators confirmed that TTE can be used as a reliable tool for guidance during device closure by skilled hands.

The most difficult part of this procedure was the measurement of the diameter of the ASD and the evaluation of the circumferential margin. With our previous experience, we gained the insight that TTE guidance could provide an accurate measurement of these parameters from the apical four chamber view, the parasternal long-axis view, and the subxiphoid acoustic window, enabling completion of the procedure and determination of the maximum diameter of the defect. In the traditional procedure, fluoroscopy with the waist of a compliant balloon is used to determine the appropriate size of the occluder, which is the most important step in the entire procedure. Chien et al. (18) developed a noninvasive sizing method for transcatheter closure of ASDs under TTE without balloon sizing that does not require fluoroscopy. Li et al. (19) also evaluated the ability to determine the ASD size by TTE and the efficacy and safety of TTE guidance prior to, during, and after transcatheter device closure of the ASD. Sah et al. (20) concluded that the preprocedural TTE assessment of the ASD size using a scaling formula in patients with adequate TTE windows can accurately predict the occluder size. All studies supported the notion that TTE can be used as the only guiding tool to precisely measure the ASD diameter. However, for the ASDs with deficient rims, using TTE presents some risk. O'Byrne et al. (21) reported the accuracy of TTE in assessing retro-aortic rims prior to the device closure of ASDs. Li et al. (22) reported the efficacy and safety of TTE-guided transcatheter closure of ASDs with deficient superior-anterior rims. We also used TTE as the only tool to guide transthoracic device closure of ASDs with inferior vena cava rim deficiency and obtained satisfactory clinical results (23).

Many studies have reported their experience regarding the safety and efficacy of transcatheter device closure of ASDs guided by TTE, but it should be used in combination with fluoroscopy to reduce the fluoroscopic times. Other researchers used TTE as the only tool, similar to our preliminary report. Pan et al. (24) also reported their experience of transcatheter device closure of ASDs using TTE guidance as the only imaging tool. Their method avoided fluoroscopy, endotracheal intubation, and probe insertion and was associated with a satisfactory procedural success rate and low costs (24). Yang et al. (25) used a modified delivery system and a re-established procedure. They showed that transcatheter closure of ASDs without fluoroscopy is a safe technique in selected children (25). Similar results were also reported by Sadiq et al. (26) and Zaqout et al. (27). They concluded that TTE can be effective and safe as the only tool for measuring ASDs and for guidance during device deployment in young children by skilled and professional hands (26, 27).

Our approach was similar to that in the above mentioned study, in that we also proved that the procedure can be completed with successful results without fluoroscopic guidance. A critical first step was to build a delivery track. Without X-ray positioning, the surgeon's spatial thinking and constant communication with the sonologist were especially important during guide wire placement in the left atrium. In general, the tip of the catheter is not clearly displayed by TTE; therefore, we set a mark in a multifunctional catheter to ensure preliminary estimation of

the distance between the puncture point and the heart, thereby effectively preventing cardiac rupture by the catheter. Meanwhile, the process of catheter and sheath insertion should be careful and slow, usually requiring various echocardiography views (apical four-chamber and parasternal long-axis or sub-xiphoid views) to detect the location of the catheter and the sheath. The catheter could be rotated to make the tip appear clear in the view, and repeated views should be taken to confirm its position. This step was different from that in the routine method. All other steps were similar to those in the routine method.

In our series, device closure was successful in 98.7% patients, and the closure rate was very impressive. The clinical result obtained using our procedure were similar to those obtained using the routine procedure. Moreover, another advantage of our procedure was that it did not require radiation, making it a more attractive option for adolescents and children. The use of computed tomography and cardioangiography for diagnosis and therapy has increased dramatically in recent years. Although the dose of radiation is very low, increasing number of clinical studies have focused on radiation-related side effects, especially in pediatric patients. Many experts have found that these procedures may increase the risk of leukemia, brain tumors, and other types of cancer in children (28, 29). Furthermore, this technique can simplify the procedure and is easy to implement. The average operative time was ≤1 h, which is acceptable by most operators. However, this process requires a learning curve on the part of operators. The operator should be familiar with openheart surgery and transcatheter device occlusion, especially the spatial structure of cardiac anatomy.

#### Study limitations

Our study has some limitations. First, the number of cases was small, and there may have been selection bias. In addition, some cardiac centers are already using this procedure, as we mentioned above; future studies with a larger sample size and more multicenter trials with long-term follow-up are needed to better assess the efficacy and safety of this procedure. Finally, we do not want to claim that this procedure can replace the traditional method. However, it can be used as an alternative for the patients who are unable or unwilling to be exposed to radiation.

# Conclusion

In conclusion, we believe that transcatheter device closure of ASDs guided completely by TTE is safe and effective. It can avoid surgical scars, cardiopulmonary bypass, and X-ray exposure, and it provides good clinical results and esthetically favorable outcomes. Although the short- and mid-term follow-up results were encouraging, further long-term follow-up is still needed to evaluate the long-term outcomes of this procedure.

**Funding:** This research was sponsored by Chinese National and Fujian Provincial Key Clinical Specialty Construction Programs.

**Acknowledgments:** We highly acknowledge the contribution by the participating doctors: Xu-dong Sun, Feng Lin, Qi-min Wang, Zhong-yao Huang, Han-fan Qiu, Xiao-fu Dai, Xi-jie Wu, Xue-Shan Huang, Hui Zhang, and Zeng-chun Wang. In addition, we wish to extend our gratitude to Xiu-jun Wang and her colleagues.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

**Authorship contributions:** Concept - H.C.; Design - Q.C., H.C.; Supervision - H.C.; Fundings - L.C.; Materials - Q.C., H.C.; Data collection &/or processing - Q.C., G.Z., H.L., L.Y.; Analysis &/or interpretation - Q.C.; Literature search - Q.C.; Writing - Q.C.; Critical review - H.C., L.C.

### References

- Luo H, Wang J, Qiao C, Zhang X, Zhang W, Song L. Evaluation of different minimally invasive techniques in the surgical treatment of atrial septal defect. J Thorac Cardiovasc Surg 2014; 148: 188-93.
- Vida VL, Tessari C, Fabozzo A, Padalino MA, Barzon E, Zucchetta F, et al. The evolution of the right anterolateral thoracotomy technique for correction of atrial septaldefects: cosmetic and functional results in prepubescent patients. Ann Thorac Surg 2013; 95: 242-7. [CrossRef]
- 3. Hoashi T, Yazaki S, Kagisaki K, Kitano M, Kubota SM, Shiraishi I, et al. Management of ostium secundum atrial septal defect in the era of percutaneous trans-catheter device closure: 7-Year experience at a single institution. J Cardiol 2015; 65: 418-22. [CrossRef]
- Aytemir K, Oto A, Özkutlu S, Canpolat U, Kaya EB, Yorgun H, Şahiner L, et al. Transcatheter interatrial septal defect closure in a large cohort: midterm follow-up results. Congenit Heart Dis 2013; 8: 418-27.
- Cao H, Chen Q, Zhang GC, Chen LW, Qiu ZH, Lu H. Percutaneous device closure of atrial septal defect with totally transthoracic echocardiography guide, without x-ray machine. Medicine (Baltimore) 2016; 95: e5256. [CrossRef]
- Mills NL, King TD, Thompson SL. Umbrella catheter for nonoperative closure of atrial septal defects. Med Instrum 1978; 12: 65-9.
- Liang T, XiangJun Z, XiaoJing M, Yun L, Leng CY. New minimally invasivetechnique to occlude secundum atrial septal defect in 53 patients. Ann Thorac Surg 2006; 81: 1417-9. [CrossRef]
- Hongxin L, Wenbin G, Lijun S, Zhengjun W, Hao L, Chengwei Z, et al. Intraoperative device closure of secundum atrial septal defect using a right anterior minithoracotomy in 100 patients. J Thorac Cardiovasc Surg 2007; 134: 946-51. [CrossRef]
- Taniguchi M, Akagi T, Kijima Y, Sano S. Clinical advantage of realtime three-dimensional transesophageal echocardiography for transcatheter closure of multiple atrial septal defects. Int J Cardiovasc Imaging 2013; 29: 1273-80. [CrossRef]
- Mazic U, Gavora P, Masura J. The role of transesophageal echocardiography in transcatheter closure of secundum atrial septal defects by the Amplatzer septal occluder. Am Heart J 2001; 142: 482-8.
- Kobayashi T. Monitoring tool of transcatheter atrial septal defect: transesophageal echocardiography or transthoracic echocardiography? J Cardiol 2015; 65: 1. [CrossRef]

- Bartakian S, El-Said HG, Printz B, Moore JW. Prospective randomized trial of transthoracic echocardiography versus transesophageal echocardiography for assessment and guidance of transcatheter closure of atrial septal defects in children using the Amplatzer septal occluder. JACC Cardiovasc Interv 2013; 6: 974-80. [CrossRef]
- Azhar AS. Safety and efficacy of transthoracic versus transesophageal echocardiography in transcatheter closure of atrial septal defects. Reporting a single center experience from Saudi Arabia. Saudi Med J 2016; 37: 1196-205. [CrossRef]
- Ding C, Chang JK, Lin CC, Wu YJ, Hsieh KS. Efficacy and Safety of Transthoracic Echocardiography Alone in Transcatheter Closure of Secundum-Type Atrial Septal Defects in Adults. Echocardiography 2016; 33: 579-85. [CrossRef]
- Oto A, Aytemir K, Ozkutlu S, Kaya EB, Yorgun H, Canpolat U, et al. Transthoracic echocardiography guidance during percutaneous closure of patent foramen ovale. Echocardiography 2011; 28: 1074-80. [CrossRef]
- Chen Q, Cao H, Zhang GC, Chen LW, Chen DZ. Safety and feasibility
  of intra-operative device closure of atrial septal defect with transthoracic minimal invasion. Eur J Cardiothorac Surg 2012; 41: 121-5.
- 17. Cao H, Chen Q, Zhang GC, Chen LW, Xu F, Zhang JX. Clinical study of stand-alone transthoracic echocardiography-guided percutaneous occlusion of patent ductus arteriosus. Anatol J Cardiol 2018; 20: 30-4. [CrossRef]
- Chien KJ, Lee CL, Huang TC, Lin CC, Weng KP, Huang SH, et al. A noninvasive sizing method to choose fitted Amplatzer septal occluder by transthoracic echocardiography in patients with secundum atrial septal defects. Heart Vessels 2007; 22: 245-50. [CrossRef]
- Li GS, Kong GM, Ji QS, Li JF, Chen YG, You BA, et al. Reliability of transthoracic echocardiography in estimating the size of Amplatzer septal occluder and guiding percutaneous closure of atrial septal defects. Chin Med J (Engl) 2008; 121: 973-6.
- Sah SP, Bartakian S, El-Said H, Molkara DP, Printz B, Moore JW. Preprocedural Transthoracic Echocardiography Can Predict Amplatzer Septal Occluder Device Size for Transcatheter Atrial Septal Defect Closure. Congenit Heart Dis 2016; 11: 656-62. [CrossRef]

- 21. O'Byrne ML, Glatz AC, Goldberg DJ, Shinohara R, Dori Y, Rome JJ, et al. Accuracy of Transthoracic Echocardiography in Assessing Retro-aortic Rim prior to Device Closure of Atrial Septal Defects. Congenit Heart Dis 2015; 10: E146-54. [CrossRef]
- 22. Li GS, Li HD, Yang J, Zhang WQ, Hou ZS, Li QC, et al. Feasibility and safety of transthoracic echocardiography-guided transcatheter closure of atrial septal defects with deficient superior-anterior rims. PLoS One 2012; 7: e51117. [CrossRef]
- Chen Q, Chen LW, Cao H, Zhang GC, Chen DZ, Zhang H. Intraoperative device closure of atrial septal defects with inferior vena cava rim deficiency: a safe alternative to surgical repair. J Thorac Cardiovasc Surg 2011; 141: 631-6. [CrossRef]
- 24. Pan XB, Ou-Yang WB, Pang KJ, Zhang FW, Wang SZ, Liu Y, et al. Percutaneous Closure of Atrial Septal Defects Under Transthoracic Echocardiography Guidance Without Fluoroscopy or Intubation in Children. J Interv Cardiol 2015; 28: 390-5. [CrossRef]
- Yang Y, Zhang W, Wu Q, Gao L, Jin W, Zhao T. Transcatheter closure of atrial septal defects without fluoroscopy: a well-established procedure for alternative use in children. EuroIntervention 2016; 12: e652-7. [CrossRef]
- Sadiq N, Ullah M, Sultan M, Akhtar K. Transthoracic echocardiography as a measuring and guiding tool for transcatheter device closure of secundum atrial septal defect in young children. J Invasive Cardiol 2014; 26: 245-8.
- 27. Zaqout M, Suys B, De Wilde H, De Wolf D. Transthoracic echocardiography guidance of transcatheter atrial septal defect closure in children. Pediatr Cardiol 2009; 30: 992-4. [CrossRef]
- Pearce MS, Salotti JA, Little MP, McHugh K, Lee C, Kim KP, et al. Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: a retrospective cohort study. Lancet 2012; 380: 499-505. [CrossRef]
- 29. Miglioretti DL, Johnson E, Williams A, Greenlee RT, Weinmann S, Solberg Ll, et al. The use of computed tomography in pediatrics and the associated radiation exposure and estimated cancer risk. JAMA Pediatr 2013; 167: 700-7. [CrossRef]