ISSN 2220-3168 (online)

World Journal of *Hypertension*

World J Hypertens 2015 August 23; 5(3): 104-114

Published by Baishideng Publishing Group Inc

WJH

World Journal of Hypertension

A peer-reviewed, online, open-access journal of hypertension

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2011-2015

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World Journal of
Hypertension

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INDEXING/ABSTRACTING

World Journal of Hypertension is now indexed in Digital Object Identifier.

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I-III Editorial Board

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NAME OF JOURNAL
World Journal of Hypertension

ISSN
ISSN 2220-3168 (online)

LAUNCH DATE
December 23, 2011

FREQUENCY
Quarterly

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PUBLISHER
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8226 Regency Drive,
Pleasanton, CA 94588, USA
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PUBLICATION DATE
August 23, 2015

INSTRUCTIONS TO AUTHORS
Full instructions are available online at http://www.wjgnet.com/2220-3168/g_info_20100722180909.htm.

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DOI: 10.5494/wjh.v5.i3.104

World J Hypertens 2015 August 23; 5(3): 104-106
ISSN 2220-3168 (online)

EDITORIAL

Dairy: A lower percent investment in the volatile hypertensive environment

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Author contributions: Pearman ME and Tanaka H wrote the paper.

Conflict-of-interest statement: There are no conflicts of interest to report.

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Received: March 26, 2015
Peer-review started: March 28, 2015
First decision: May 13, 2015
Revised: June 1, 2015
Accepted: July 7, 2015
Article in press: July 8, 2015
Published online: August 23, 2015

Abstract

In cross-sectional and intervention studies, low-fat dairy has proven to be effective in lowering blood pressure in a hypertensive population. Contributing mechanisms include the angiotensin-converting enzyme-inhibiting effects of peptides and possible interplay between calcium and vitamin D. Easily added to the diet, low-fat dairy is an attractive addition to nutritional, lifestyle, and pharmacological interventions to treat hypertension.

Key words: Dairy; Blood pressure; Hypertension; Milk; Cardiovascular

Core tip: Low-fat dairy has shown to be effective in lowering blood pressure in a hypertensive population. Contributing mechanisms include the angiotensin-converting enzyme-inhibiting effects of peptides and possible interplay between calcium and vitamin D. Easily added to the diet, low-fat dairy is an attractive addition to nutritional, lifestyle, and pharmacological interventions to treat hypertension.

Pearman ME, Tanaka H. Dairy: A lower percent investment in the volatile hypertensive environment. *World J Hypertens* 2015; 5(3): 104-106 Available from: URL: http://www.wjgnet.com/2220-3168/full/v5/i3/104.htm DOI: http://dx.doi.org/10.5494/wjh.v5.i3.104

BRIEF REVIEW: LOW-FAT DAIRY AND HYPERTENSION

Hypertension affects nearly 1/3 of Americans over the age of 20 and 3/4 of those over 65 years of age[1]. Hypertension can be treated with pharmacological interventions, but the drug therapies are often accompanied by unwanted side effects including reduced functional capacity and orthostatic hypotension[2]. Accordingly, non-pharmacological lifestyle modifications that can help resolve hypertension without the associated side effects of medication are increasingly emphasized. Indeed, recommendations by the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure indicate that lifestyle-based interventions can elicit hypotensive effects and should be incorporated into any treatment plan for high blood pressure[3]. Some interventions require a lot of effort (*e.g.*, regular exercise) or drastic changes (*e.g.,* hypocaloric diet) that compliance and adherence rates may be substantially low. In this context, an idea of simply adding milk into the routine diet is attractive as it is easy and simple to implement. Does that help lower blood pressure?

Cross-sectional studies have found higher intakes of low-fat dairy are associated with lower risk of hypertension[4]. Consuming 2 or more servings a day of low fat dairy products decreased the relative risk of incident hypertension by 11%[5]. The results of the dietary intervention studies are consistent with the cross-sectional or observational findings. The Dietary Approaches to Stop Hypertension (DASH) diet is low in total fat, saturated fat, and sodium, but high in fruit and vegetables. In a hypertensive population, consuming the DASH diet combined with low-fat dairy products decreased blood pressure more than a diet high in fruits and vegetables alone[6]. The hypotensive effects seen from the inclusion of low-fat dairy in the DASH diet are preserved by adding 4 servings/d of low-fat dairy without further adjustments to a typical diet[7]. Yet this effect is not seen with the addition of a single serving of low-fat dairy[8] suggesting that there is minimum dose required for the hypotensive effects of low fat dairy. Further, beneficial effects of dairy on retinal vascular structures offer promise for improved microcirculation and end-organ vascular health potentially achieved with chronic dairy consumption[9,10].

Physiological mechanisms underlying the hypotensive effects of dairy are unknown but multiple mechanisms are likely involved. Increasing serum calcium through dietary intake would decrease serum 1,25-OH_2-vitamin D concentrations and decrease the calcium ion flux into cells thereby preventing the intracellular calcium-mediated vasoconstriction of smooth muscle cells in the muscularis externa of the arterial wall[11]. In fact, the DASH diet with low-fat dairy included lowered 1,25-OH_2-vitamin D and intracellular calcium more than the DASH diet alone; the decreased intracellular calcium correlated with a fall in blood pressure[12]. Additionally, an independent association between the isoform of vitamin D and increased blood pressure has been established further reinforcing the link between calcium, vitamin D, and blood pressure[13].

Bovine milk is comprised of 31%-33% protein of which 80% is casein and 20% is whey. Both forms of proteins have been implicated in eliciting the hypotensive effects of dairy[14-17]. These effects are likely due to the ACE-inhibiting properties of peptides, specifically casein and whey derived lactotripeptides, casokinins and lactokinins, respectively[11,18]. Both require enzymatic hydrolysis to release the functional peptides, which is accomplished through the fermentation process of digestion by lactic acid-producing bacteria. Proline-proline dipeptides, including Ile-Pro-Pro and Val-Pro-Pro, have shown to resist degradation during digestion and may be more effective at lowering blood pressure than other peptides[11,18]. Twelve weeks of casein and whey supplementation in overweight men and women decreased blood pressure with no difference between the two forms of proteins[19]. These hypotensive effects may require regular consumption of proteins as acute ingestion of whey and casein do not exert an effect on blood pressure[15]. Certain milk peptides may inhibit endothelin-1 release by endothelium cells, reduce chronic vasoconstrictor tone, and exert the hypotensive effects[20]. Interestingly, fermented strains of Lactobacillus helveticus (naturally high in ACE inhibitory tripeptides) have also been shown to reduce blood pressure, suggesting the bacteria responsible for fermentation may also play a role[17,21].

Is there any benefit of consuming whole milk and full-fat dairy products? In the 1970s, the link between saturated fat intake and cardiovascular disease (CVD) was identified, but it wasn't until the early 1990s when recommendations to reduce saturated fat intake led to the emergence and popularity of low fat diets. As a result, the notion that whole milk/dairy would exert unfavorable effects on blood cholesterol and thus cardiovascular health became wide spread among the public. Recent reviews and meta-analyses on dairy and blood pressure have found no such link between full-fat dairy and CVD[14,22]. In regards to blood pressure, while low fat dairy has consistently demonstrated hypotensive effects, full-fat dairy showed no such association[4,23]. Interestingly, if peptides and calcium are the primary contributors to the hypotensive effects of dairy, it seems reasonable that full-fat dairy products would also elicit the hypotensive effects seen from low-fat dairy as these components are still present at similar quantities. Future dietary interventions using whole milk and full-fat dairy are needed to answer this important and relevant question.

Clearly, simply adding milk and dairy to the routine diet does not elicit unwanted side effects and is an easy lifestyle modification to make. It is much easier than performing strenuous exercise or undergoing hypocaloric diet. Obviously, this dietary intervention is not suitable for those with lactose intolerance but is highly generalizable to most individuals with high blood pressure. However, there are a lot of unanswered questions regarding the relation between dairy products and hypertension. Is whole milk and full-fat dairy effective in lowering blood pressure? What is the dominant physiological mechanisms underlying the hypotensive effects of dairy? What dairy products (*e.g.,* milk, yogurt, cheese) are most effective in reducing blood pressure? Is there any additive hypotensive effects of dairy when they were combined with other lifestyle modifications[24]? Regardless, for those diagnosed with hypertension, adding low-fat dairy to a treatment plan of nutritional, lifestyle, and pharmacological interventions could be a small investment that yields a lifetime of returns.

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P- Reviewer: Salles GF, Tan XR, Turgut O, Xiao DL
S- Editor: Tian YL **L- Editor**: A **E- Editor**: Wu HL

World Journal of Hypertension

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Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
DOI: 10.5494/wjh.v5.i3.107

World J Hypertens 2015 August 23; 5(3): 107-114
ISSN 2220-3168 (online)

MINIREVIEWS

Multi-slice computerized tomography critical role in transcatheter aortic valve implantation plan: Review of current literature

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Author contributions: All authors contributed to the writing, editing and reviewing of the manuscript.

Conflict-of-interest statement: None.

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Received: December 4, 2014
Peer-review started: December 4, 2014
First decision: February 7, 2015
Revised: April 29, 2015
Accepted: May 16, 2015
Article in press: May 18, 2015
Published online: August 23, 2015

Abstract

Transcatheter aortic valve implantation (TAVI) has been shown in improve outcome of severe aortic stenosis (AS) patients, deemed surgical high-risk or inoperable, and has grown popular in the past decade. The procedure requires accurate prior planning, and demands an integration of a "Heart Team" consisted from cardiac surgeons, interventional cardiologists, and imaging experts. The role of cardiac imaging and especially multi-slice computerized tomography (MSCT) has been a mainstay of pre-evaluation of severe AS patients that allows to accurately depict and size the cardiac and vascular structures, and has become the primary tool for procedural planning. This article is aimed to evaluate current uses of MSCT in severe AS patients undergoing TAVI, delineate the various measurements derived from this modality and review current literature regarding it's advantages over other techniques.

Key words: Transcatheter aortic valve implantation; Multi-slice computerized tomography; Aortic annular sizing; Vascular access

Core tip: Transcatheter aortic valve implantation (TAVI) has been shown in improve outcome of severe aortic stenosis patients, deemed surgical high-risk or inoperable, and has grown popular in the past decade. The procedure requires accurate prior planning, and demands an integration of a "Heart Team" approach consisted from cardiac surgeons, interventional cardiologists, and imaging experts. The role of cardiac imaging and especially multi-slice computerized tomography (MSCT) has been a mainstay of TAVI evaluation, and allows accurate depiction and sizing of the cardiac and vascular structures. This article is aimed to review current use of MSCT in TAVI patients.

Koifman E, Hamdan A. Multi-slice computerized tomography critical role in transcatheter aortic valve implantation plan: Review of current literature. *World J Hypertens* 2015; 5(3): 107-114 Available from: URL: http://www.wjgnet.com/2220-3168/full/v5/i3/107.htm DOI: http://dx.doi.org/10.5494/wjh.v5.i3.107

INTRODUCTION

Transcatheter aortic valve implantation (TAVI) has been shown to improve outcome of severe aortic stenosis patients deemed inoperable[1] or high risk[2], with mortality rates lower than surgical aortic valve replacement[3]. However, this procedure incurs complications such as paravalvular leak, vascular access complications, stroke, conduction defects requiring pacemaker implantation, and less commonly, annular rupture[4,5].

A "heart team" approach is recommended in any patient considered for TAVI[6,7]. This team is comprised of a multidisciplinary team including general cardiologists, cardiac surgeons, interventional cardiologists, anesthesiologists and imaging cardiologists. The assessment of each patient requires evaluation of symptoms, cardiac and valvular function[8] to determine the severity of aortic stenosis and appropriateness of intervention. Once a patient is considered for intervention, the risk of surgery should be determined according to comorbidities, patient function and frailty and technical aspects such as porcelain aorta and prior cardiac surgery[9,10]. In case of inoperability or high surgical risk, additional imaging should be performed for the evaluation of suitability for TAVI in order to determine annular size, distance between annulus and coronary artery ostium, implantation angle, and vascular access. This can be done by various methods, most commonly by multi-slice computerized tomography (MSCT). This review aim is to describe MSCT for evaluation of patients referred for TAVI.

MSCT DATA

Unlike surgery, where direct visualization and sizing of the valve is done, TAVI is performed with a 2-dimentional fluoroscopy guidance, where it is difficult to asses proper valvular size and access routes. MSCT enables extracting a large amount of data from a 3-dimentional image which include access options by measuring the diameters of the arteries and aorta in the perpendicular plane, establishing the presence of protruding atherosclerotic plaques, assessing the calcification of the arteries and aortic annulus and evaluating annular dimensions and its proximity to important anatomical landmarks such as the coronary arteries ostium (Table 1). These measurements require an accurate alignment of images in the appropriate plane done by an imaging expert and reviewed by the interventional cardiologist.

MSCT DATA ACQUISITION

The acquisition of the CT data should be performed during an inspiratory breathhold while the electrocardiogram (ECG) should be recorded simultaneously to allow retrospective or prospective gating of the data. Imaging of the annulus in systole, when the aortic annulus size increases[11], may be preferable over the diastole; however, analysis of the aorta and peripheral arteries can be performed without ECG synchrony.

Table 1 Data derived from multi-slice computerized tomography imaging

Assessment of the aortic annulus
Annular shape
Calcification
Annular diameters, area and perimeter coronary artery ostia and additional
Aortic root dimensions
Coronary ostium height
Sinus of valsava diameter and height
Sinutubular junction diameter
Ascending aorta diameter
Aortic annulus plane for fluoroscopy
Degree of aortic angulation in relation to the annulus
Optimal projection angle
Access route evaluation
Pelvic and aortic minimal diameters
Vascular calcification
Vascular tortuosity
Presence of protruding atherosclerotic plaques and thrombi

ASSESSMENT OF THE AORTIC ANNULUS

The aortic root is a complex anatomic structure comprised from a tri-leaflet valve inserted in a semi-lunar mode into the left ventricle and aortic root, which creates the sinuses of valsava that accommodate the coronaries origin. It lies in a close proximity to the atrioventricular node and the left bundle of the cardiac conduction system[12].

Accurate measurement of the aortic annulus is a critical step in the planning of TAVI, since it enables proper valve sizing, grades calcification of aortic annulus and measure the distance to the coronaries origin. These parameters point to possible complications including paravalvular leaks[13,14], annular rupture[15,16] and coronary arteries obstruction[17,18], all of which have adverse impact on patients outcome[19,20].

The aortic annulus has an oval shape, thus measuring its diameter in a single plane is inaccurate and misleads the operators when sizing the valve[21]. Therefore measuring annular diameter by 2D echocardiography usually provides the shorter diameter and consequently undersizes annular dimensions[22]. Precise measurement of annular dimensions requires alignment of the image in a perpendicular plane to the basal part of leaflets insertion (Figure 1). The parameters derived from annular measurements include short and long diameters, mean diameter, perimeter and area. The aortic annulus, generally elliptic, assumes a more round shape in systole, thus increasing cross sectional area without substantial change in perimeter. Perimeter changes are negligible in patients with calcified valves, because tissue properties allow very little expansion. Aortic annulus perimeter appears therefore ideally

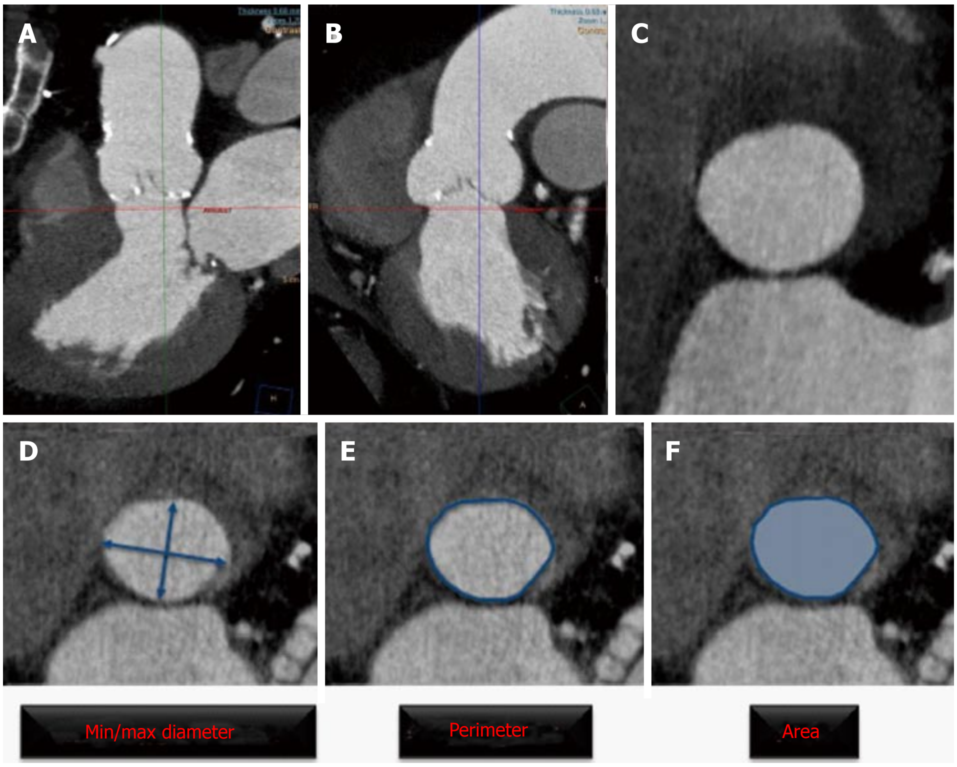

Figure 1 Aortic annulus dimensions.

suited for accurate sizing in TAVI[11]. Inter- and Intra-observer variability of these measurement by MSCT is small and highly reproducible as shown in a recent study[23] and studies comparing different modalities for prosthesis sizing have shown reduction in paravalvular leak with MSCT measurement compared with 2D echocardiography[24,25] and therefore MSCT is currently regarded as an essential tool for accurate prosthesis sizing.

CORONARY ARTERY OSTIA AND ADDITIONAL AORTIC ROOT DIMENSIONS

Besides aortic annular dimension, other considerations should be taken into account upon deciding valve type and size. Coronary ostia height and sinus of valsalva diameter should be measured (Figures 2 and 3), and coronary obstruction risk must be assessed since the native valve leaflets are displaced and could potentially obstruct the coronary flow. In a multicenter registry, coronary obstruction was reported in less than 1% of TAVI patients[17]. Predictors of coronary obstruction were low coronary ostia height and small sinus of valsalva diameter along with female gender, valve-in-valve procedure and balloon expandable valve[17]. The outcome of this complication is catastrophic with a 30-d mortality rate of more than 40%. Therefore, it is crucial to measure coronary ostia height, ensure adequate sinus of valsalva diameter and height according to the device requirements, as published by the manufacturer.

Sinotubular junction diameter (Figure 4) should also be considered since a smaller diameter than the valve implanted could pose a risk of aortic injury upon balloon inflation in balloon expandable valves. In self-expandable valves the ascending aorta (Figure 5) acts as an anchorage point, hence, large diameters as in aortic aneurysm are a contraindication for the use of this type of valve.

AORTIC ANNULUS PLANE FOR FLUOROSCOPY

Positioning of the valve is a critical step in TAVI procedure, which is usually performed under angiography guidance. Since, angiography is a 2D image, precise planar projection is required for accurate centered implantation of the valve in a perpendicular angle to the native valve plane. Assessment of the proper implantation plane can be located by angiography, however, this methods has some caveats such as, additional contrast injection and radiation exposure along with the inherent requirement for interpreting a 2D image in a 3 dimensional manner. Moreover, certain anatomic features can complicate this task, like severe calcification of the aortic valve and root, which can obscure the leaflet insertion, and chest deformation, which can require extreme angles for implantation. MSCT allows a 3D image reconstruction without the need for additional contrast or radiation, and has been shown to accurately predict the valve deployment

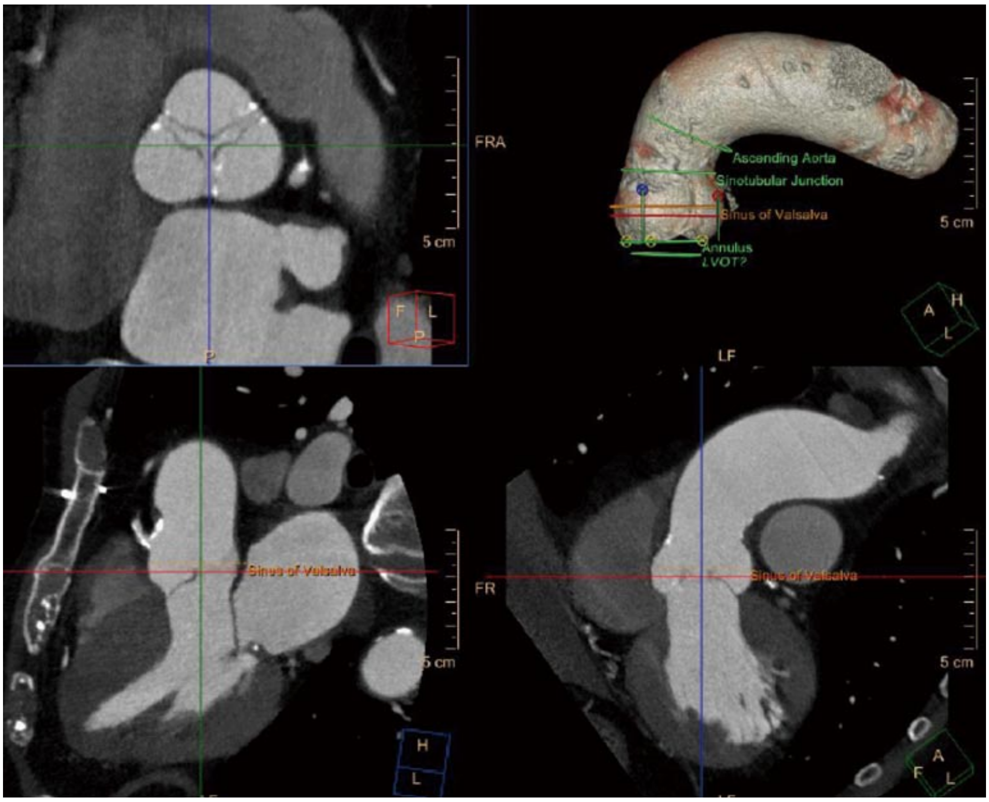

Figure 2 Sinus of valsalva dimensions.

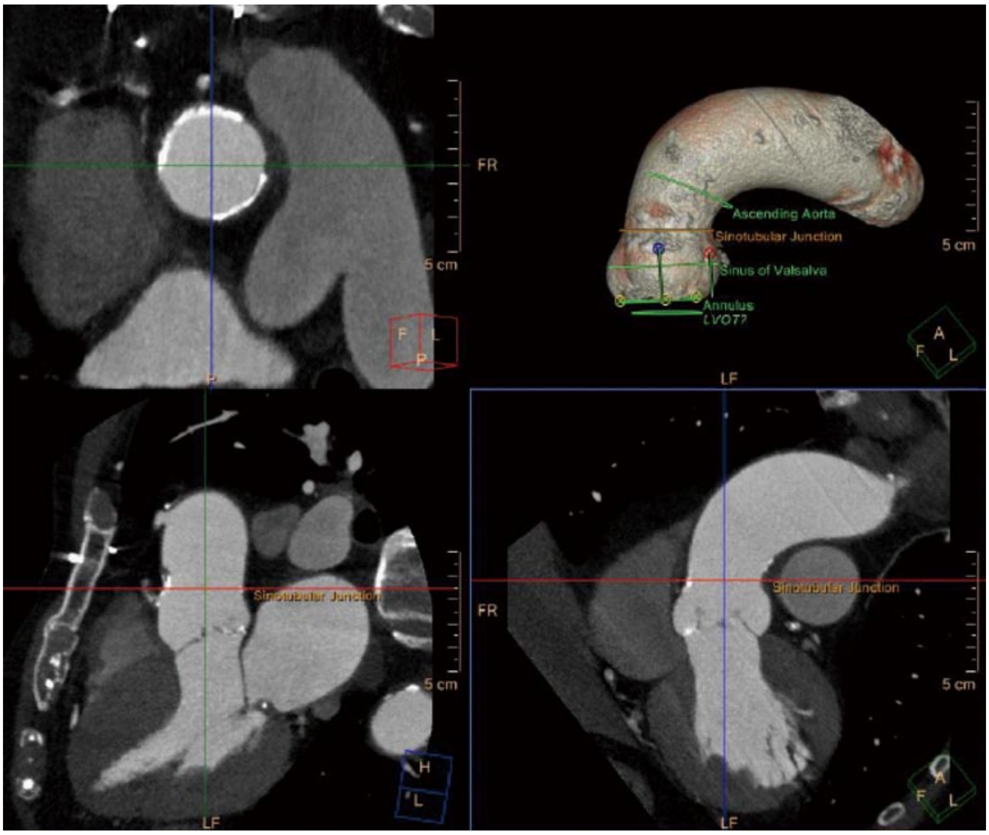

Figure 3 Sinotubular junction dimensions

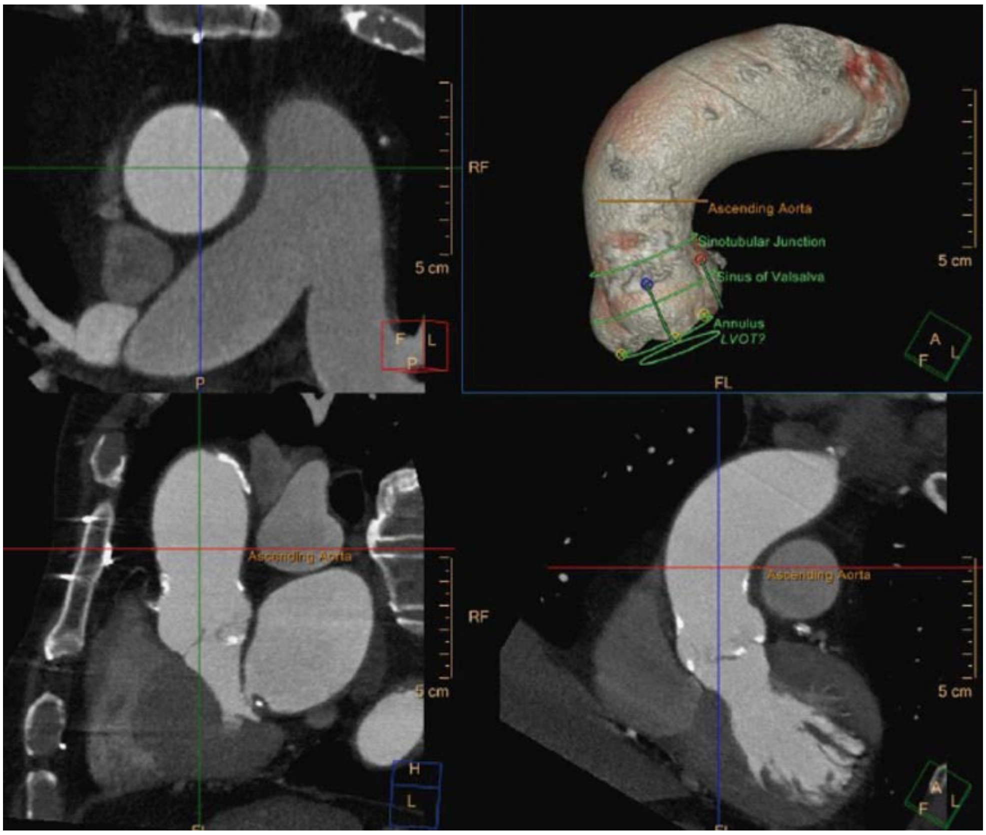

Figure 4 Sinotubular junction dimensions.

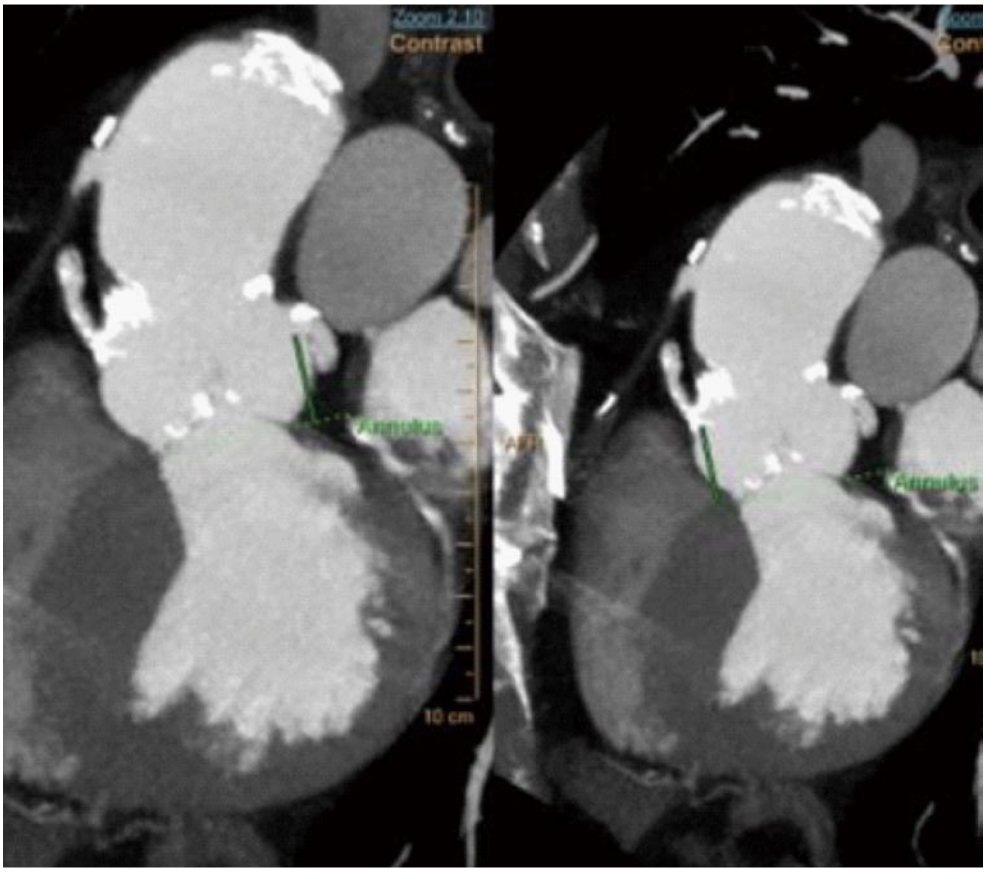

Figure 5 Coronary height for the left main (right image) and right coronary artery (left image).

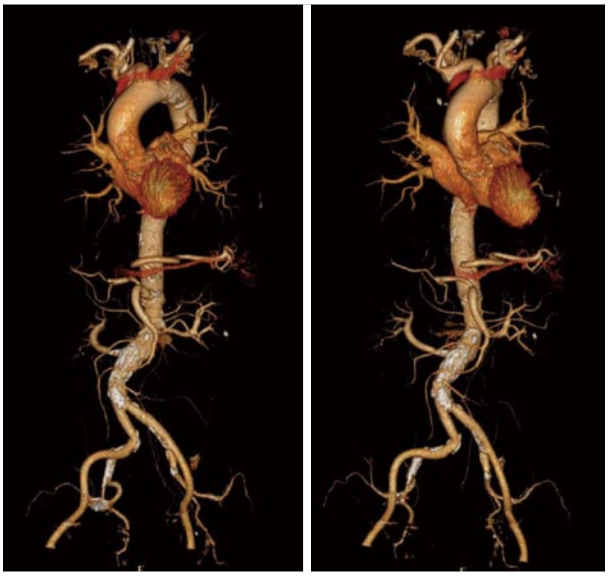

Figure 6 Aorta and iliac arteries 3D reconstruction.

projection[26], by creating a "line of perpendicularity" which denotes the projections that can be used in order to implant the valve in an orthogonal plane to the native valve[26].

ACCESS ROUTE EVALUATION

The transfemoral route is currently the default approach for TAVI procedure. The femoral arteries can accommodate a sheath with slightly higher diameter if it is not calcified; however, circumferential calcification and tortuosity especially with involvement of bifurcations are predictors of vascular complication. Thus, utilization of transfemoral approach requires precise evaluation of vascular diameters, calcification and tortuosity (Figure 6). This can be achieved by MSCT, which accurately depicts the vascular anatomy in a 3D imaging. Vascular complications have been shown to impact outcome of TAVI patients, and its incidence was above 30% in the PARTNER trial[1], where route assessment was performed by angiography. The utilization of MSCT have reduced major vascular complications rate from 8% to 1% and minor vascular complications from 24% to 8% over the 2-year study period. The vessel minimal luminal diameter being smaller than the sheath external diameter (23% *vs* 5%) and the presence of calcified vessels (29% *vs* 9%) were strong predictors for vascular complications[27].

Measurements of minimal vessel diameters should be performed after a multi-planar reconstruction along the entire course of the vessels in order to attain a perpendicular image. Vessel calcifications should be assessed according to circumferential involvement due to its limitations in accommodating the sheath, and prohibiting the safe passage of the delivery system. Vessel calcification can falsely cause underestimation of its diameter due to the "blooming" effect, in which the calcified segment appears larger than it true dimension thus reducing the size of the true lumen. Tortuosity can be evaluated after 3D reconstruction the aorta and iliofemoral vessels[28], and although severe tortuosity can be straightened. Assessment of alternative routes can be performed by reconstructing images depicting the subclavian artery diameter, calcification and course for this route, and aortic calcification for a transaortic route.

CONCLUSION

TAVI frequency is growing worldwide, and accordingly the experience with regard to planning the procedure, avoiding complications, and treating them when they occur. The utilization of advanced imaging techniques such as MSCT, with sophisticated data acquisition protocols have significantly improved our ability to assess the access site, accurately size the aortic root dimension and select the appropriate device size, and importantly estimate and avoid fatal complications. Accordingly, most of TAVI programs include an imaging specialist in the heart team. We expect that the use and experience of MSCT will grow and enhanced techniques and algorithms will allow us to further improve the outcome of patients undergoing TAVI in light of the large number of new devices that are currently available or on trial.

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P- Reviewer: Castillo R, Li JD **S- Editor**: Ji FF **L- Editor**: A
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