Comparison of 64-Slice EKG-Gated Computed Tomographic Angiography, Transthoracic Echocardiography, and Transesophageal Echocardiography for Detection and Complete Characterization of Anomalous Coronary Arteries in Infants with Comorbid Congenital Cardiac Malformations

A thesis submitted to the University of Arizona College of Medicine – Phoenix
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Dedication

I would like to dedicate this work to my family members
who have supported me in the pursuit of my dreams
and have made this work possible.

Acknowledgement

I would like to take this opportunity to acknowledge Dr. Randy Richardson for providing mentorship and guidance throughout the duration of this study.

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Abstract

Background and Objective: Computed tomographic angiography (CTA) offers several benefits over echocardiography in the detection of CAAs (coronary artery anomalies). These include higher spatial resolution, operator independency, non-invasiveness, and the availability of reconstructive techniques to track the entire arterial course.[1,4,9] Accordingly, standard clinical practice (per ACC/AHA guidelines for adults with CAAs) for adults with suspected CAAs includes use of CTA as a first-line imaging modality.[6] Currently, there is no evidence favoring either CTA, transthoracic echocardiography (TTE), or transesophageal echocardiography (TEE) for initial imaging of infants with suspected CAAs. Therefore, the aims of this retrospective study include investigating the efficacy of CTA, TTE, and TEE in the detection and complete characterization of CAAs.

Methods: Imaging and surgical data for 27 patients who presented for evaluation of congenital heart disease between 2006 and 2011 were evaluated. Patients had a mean age of 2.2 ± 0.7 months at initial evaluation and had undergone EKG-gated 64-slice cardiac CTA with 3D reconstruction in addition to multiple TTE and TEE studies. Performance metrics (including sensitivity, specificity, positive predictive value, negative predictive value, and accuracy) of each modality in CAA detection were computed. Concordance between each modality and surgical/conventional angiographic diagnosis in the characterization of anatomy along the origin, course, and termination of anomalous coronary arteries was evaluated. The rate of limitations of each modality in the imaging and interpretation of coronary anatomy was also reported.

Results: Using surgical/angiographic diagnosis as the gold standard, CTA produced a sensitivity, specificity, and accuracy of 80%, 50%, and 74%, respectively. TTE produced a sensitivity, specificity, and accuracy of 20%, 50%, and 26%, respectively. TEE produced a sensitivity, specificity, and accuracy of 27%, 100%, and 42%, respectively. CTA outperformed TTE and TEE at characterizing anatomy at the origin and course of an anomalous coronary artery. At characterizing anatomy at the termination of an anomalous coronary artery, CTA outperformed

TEE but did not significantly outperform TTE. CTA had a higher rate of documented limitations to imaging/interpretation compared to TTE and TEE but a lower rate when compared to conventional angiography.

Conclusion and Impact: CTA is a rapid, non-invasive, operator-independent imaging modality that offers high resolution, 3-dimensional imaging of CAAs in infants. The results of this study indicate that CTA is the most sensitive and accurate modality for detection of CAAs in infants and is optimal for characterizing anatomy along the entire length of an anomalous coronary artery. As such, CTA may be the optimal modality for first-line coronary artery imaging in infants with suspected anomalous coronary artery anatomy who have a high pretest probability for having a CAA.

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Introduction

Coronary artery anomalies (CAAs) are present in approximately 1% of the general population and in as much as 15.11% of patients with comorbid congenital cardiac malformations.[1,2] In children with CAAs and comorbid cardiac malformations, the rate of mortality due to sudden death is as high as 59%.[3] For this reason, efficient and highly accurate detection and characterization of anomalous coronary artery anatomy, especially in patients with comorbid congenital cardiac malformations, is imperative. Identification of malignant (or potentially malignant) anomalies, which constitute about 20% of all CAAs,[4] can help avoid poor outcomes and guide interventional planning. As such, early detection of potentially life-threatening anomalies is desirable.

Typically, CAAs are detected later in life (childhood or adulthood) in the symptomatic individual presenting with dyspnea, syncope, cardiomyopathies, angina, myocardial ischemia, myocardial infarction, and sudden death.[1,5] For such cases in which a CAA may be suspected, the recommended imaging modality is computed tomographic angiography (CTA).[6,7] Though the efficacy of imaging modalities in the detection of CAAs has been studied in children and adults, it has been studied to a lesser degree in infants.

In infants, the decision to perform CTA is more complex. Part of this complexity stems from the concern over radiation exposure at such an early age and from the risk of contrast reactions in patients who may be less able to tolerate hemodynamic instability due to cardiovascular dysfunction. As such, in symptomatic infants suspected of having a CAA, transthoracic echocardiography (TTE) is often the initial imaging modality of choice. Transesophageal echocardiography (TEE) has also been documented as having been used in the diagnosis of CAAs in infants,[8] though it is less favorable due to the possibility that these patients may have difficulty tolerating or recovering from an invasive procedure or its complications. Although echocardiography offers a radiation-free method to image coronary arteries, its low spatial resolution can lead to misdiagnosis or lack of diagnosis of CAAs. Inconclusive echocardiograms are often supplemented with CTA, which is more robust and offers higher spatial resolution and reproducibility.[1,4,9]

Imaging of CAAs in the infant population has not been extensively studied. One study reported a sensitivity of 100% and specificity of 100% for dual source CTA in the preoperative detection of coronary artery anomalies in infants with tetralogy of Fallot using surgical diagnosis as the gold standard.[10] However, there are no comparative studies that formally evaluate the relative efficacy of CTA, TTE, and TEE in the diagnosis and management of infants with CAAs. Also, to the best of our knowledge, there is no information on the relative efficacy of CTA, TTE, and TEE in the complete characterization of anatomic features along the entire length of an anomalous coronary artery, from origin to course to termination.

Understanding the diagnostic capabilities of CTA, TTE, and TEE in detecting and characterizing CAAs in infants can serve helpful in guiding ordering of appropriate imaging to minimize the number of misdiagnosed or undiagnosed cases of CAAs. In turn, this can help minimize the number of imaging studies to reach a diagnosis and shorten the time to diagnosis, ultimately helping reduce cost of care. In this study, we evaluate the ability of CTA, TTE, and TEE to detect and completely characterize coronary artery anomalies in infants 0-24 months of age with comorbid congenital cardiac malformations.

Materials and Methods

This is a retrospective study that was approved by the St. Joseph's Hospital and Medical Center (SJHMC) Institutional Review Board.

Patient Population

Data was collected from the PACS system imaging reports and medical records of patients who underwent conventional angiography and/or open cardiac surgery and were imaged using CTA, TTE, and TEE. The target patient population for the study consisted of infants with congenital heart disease aged 0-24 months of age at the time of evaluation.

Imaging

Each patient included in the study had undergone multi-detector EKG-gated CTA using a GE Lightspeed™ 64-slice CT scanner (GE Healthcare, Wauwatosa, WI, USA) for evaluation of cardiac morphology. Axial, coronal, sagittal images, and a 3-D reconstruction were produced. CTAs had been read by subspecialty-trained pediatric radiologists. Patients had also undergone TTE and TEE, which had been performed by several operators and interpreted by several cardiologists.

Case Selection

A total of 292 congenital heart disease patient cases were recorded on a case list at the SJHMC Department of Radiology. This case list contained a brief description of the final diagnosis rendered on each case based on the preponderance of medical evidence. The keyword "coronary" was used to mine this list for cases that discussed coronary artery anatomy (regardless of final diagnosis). Those cases that did not discuss coronary arteries or that described post-reconstructive coronary artery surgery findings were excluded. Cases in which the patient was older than 24 months at initial evaluation were excluded.

CTA, TTE, and TEE reports associated with each case were acquired. Cases without CTAs or available CTA reports were excluded. Cases without available TTE and TEE reports were excluded.

Associated surgery and conventional angiography reports were acquired. Cases without at least one surgery or conventional angiography report were excluded. Cases in which there was failure to comment on coronary artery anatomy in both surgery and conventional angiography reports were excluded.

This search yielded a total of 27 cases of infants with a mean age of 2.2 ± 0.7 months who had presented to SJHMC between 2006 and 2011 with congenital heart disease. For each case, the following information was collected: dates of surgery and imaging studies, details regarding the type of surgery or imaging study, and the diagnoses of each surgery and imaging study.

CTA Study Selection

For each case evaluated, only those CTA studies specifically aimed at evaluating cardiac anatomy were considered.

Echocardiography Study Selection

For each case evaluated, echocardiography reports (whether TTE or TEE) that had a limited scope and did not include evaluation of the coronary artery anatomy were excluded. For certain cases that contained coronary artery reconstructive surgeries done after initial diagnosis, only echocardiography reports done prior to the reconstructive surgery were considered. Only those TTE and TEE studies which were designated for evaluation of complete cardiac morphology or coronary artery morphology were included.

Detection of Coronary Artery Anomalies

The ability of CTA, TTE, and TEE to detect anomalous coronary artery anatomy was assessed by computing sensitivity, specificity, and diagnostic accuracy.

The diagnostic result of each imaging study for a particular patient case was compared to the "gold standard diagnosis" for that case, which included diagnoses that were made either with conventional angiography or direct observation during surgery. Each imaging study was treated as an independent event and assigned the designation of either "true positive," "false positive," "true negative," or "false negative" based on whether the main diagnostic result (regarding the coronary anatomy) of each imaging study matched that of the gold standard for that case.

Since inclusion criteria for CTA, TTE, and TEE studies included those studies designated for evaluation of cardiac or specifically coronary artery morphology, those studies in which there was no comment on coronary artery anatomy were considered to be negative (and assigned the designation of either true negative or false negative based on the gold standard diagnosis for that particular case).

For each patient case, diagnostic results from CTA and the initial TTE and TEE studies performed were included in the calculation of the aforementioned performance metrics. Cases without at least one study of each modality were excluded from the calculation. This approach allowed assessment of the statistical significance of the difference between the sensitivities, specificities, and accuracies of each modality at initial use. An alpha level of 0.05 was used. Differences in performance metrics that yielded p-values between 0 and 0.05 were deemed significant. Differences that yielded p-values between 0.5 and 0.1 were deemed marginally significant. Differences that yielded p-values greater than 0.1 were deemed insignificant. To determine whether the sensitivity, specificity, and accuracy were reproducible in a larger sample size, all documented imaging studies (CTA, TTE, and TEE) performed for each patient were included in the calculation of sensitivity, specificity, and accuracy of each modality.

Complete Characterization of Anomalous Coronary Arteries

The ability of CTA, TTE, and TEE to fully describe the anatomy of an anomalous coronary artery, addressing features of coronary artery origin, course, and termination, was assessed. Anomalies of origin were defined as those that occurred at the level of the coronary cusps and usually involved ectopic origin of the coronary artery in question. Anomalies of course were defined as those that occurred along the length of the coronary artery and usually involved abnormal or malignant paths, accessory arteries, or ectopic distal branches. Anomalies of termination were defined as fistulous connections to any cardiac chamber, outflow tract, or great vessel.

The total number of features reported by either angiography or surgery regarding origin, course, and termination were collected for each case. Then, the number of features reported by CTA, TTE, and TEE regarding the origin, course and termination that were concordant with those reported by the gold standard were collected for each case. Percent feature concordance was then computed for each case by dividing the number of concordant features reported by CTA, TTE, or TEE regarding either the origin, course, or termination of the anomalous coronary artery by the corresponding number of features reported by the gold standard. Evaluation of feature concordance in this manner (as opposed to using contingency analysis to calculate sensitivity, specificity, and accuracy of each modality at the origin, course, or termination of an anomalous coronary artery) allowed assessment of CTA, TTE, and TEE in the characterization of anomalous coronary arteries even in cases where certain features of coronary anatomy (i.e. origin, course, or termination), when normal, were not commented upon. APFC (average percent feature concordance) was computed by taking the average of all percent feature concordance values for a particular modality at a particular anatomic point along a coronary artery across all patient cases. It is to be noted that individual percent feature concordance values which were equivalent to a number divided by zero (i.e. in the case that the gold standard did not report any features regarding one portion (origin, course, or termination) of a certain anomalous coronary artery) were not included in the calculation of the APFC. This resulted in possibly different sample sizes for each dataset associated with the percent feature concordance between a particular imaging modality and the gold standard at a particular site along the coronary artery.

This produced nine APFC values that described the ability of CTA, TTE, and TEE to characterize the anatomy at the origin, course, and termination of the anomalous artery of interest. The test of differing proportions was performed on this data to determine whether there was a significant difference between CTA, TTE, and TEE in the characterization of anatomic features at the origin, course, and termination of an anomalous coronary artery. μ_0 held that there was no significant difference between the APFC with the gold standard between one modality and another regarding the origin, course, and termination of an anomalous coronary artery. An alpha level of 0.05 was used. Comparisons between two modalities that generated p-values under 0.05 were considered significant. Comparisons that yielded p-values between 0.05 and 0.1 were considered marginally significant. Comparisons that yielded p-values higher than 0.1 were considered insignificant.

Rates of Documented Limitations to Imaging

The number of imaging studies of each modality (conventional angiography, CTA, TTE, TEE) with noted limitations that prevented proper imaging and interpretation of coronary artery anatomy was collected across all patient cases. This was then divided by the total number of imaging studies of each modality (conventional angiography, CTA, TTE, TEE) across all patient cases to produce the limitation rate.

The test of differing proportions was then conducted to determine whether there was a significant difference between the limitation rates of the modalities mentioned above when they were compared one on one to each other. μ_0 held that there was no significant difference between the limitation rate of one modality and another. An alpha level of 0.05 was used.

Results

Detection of Coronary Artery Anomalies

The following performance metrics including SN (sensitivity), SP (specificity), PPV (positive predictive value), NPV (negative predictive value), and ACC (accuracy) were generated from 19 cases in which the results of the initial CTA, TTE, and TEE were considered. CTA yielded a SN of 0.80±0.20, a SP of 0.50±0.49, a PPV of 0.86±0.18, a NPV of 0.40±0.43 and an ACC of 0.74±0.20. TTE yielded a SN of 0.20±0.20, a SP of 0.50±0.49, a PPV of 0.60±0.43, a NPV of 0.14±0.18 and an ACC of 0.26±0.20. TEE yielded a SN of 0.27±0.22, a SP of 1.00±0.00, a PPV of 1.00±0.00, a NPV of 0.13±0.23 and an ACC of 0.22±0.27. These data are shown in **Table 1** and graphically represented in **Figure 1**.

Paired t-tests between one modality and another were conducted to determine if there was a significant difference in each performance metric between the two modalities. Comparisons generating a p-value ≤0.05 were considered significant. Comparisons generating a p-value >0.05 and ≤0.1 were considered marginally significant. Comparisons generating a p-value >0.1 were considered insignificant. The sensitivity of CTA was significantly greater than that of TTE or TEE. The specificity of TEE was significantly greater than that of CTA or TTE. The accuracy of CTA was significantly greater than that of TTE and marginally significantly greater than that of TEE. The results of this analysis are shown in **Table 2**.

Detection of Anomalous Coronary Artery Anatomy – Initial Imaging Studies

Modality	SN	SP	PPV	NPV	ACC	N
CTA	0.80	0.50	0.86	0.40	0.74	19
TTE	0.20	0.50	0.60	0.14	0.26	19
TEE	0.27	1.00	1.00	0.27	0.42	19

Table 1: The numerical values for sensitivity (SN), specificity (SP), positive predictive value (PPV), negative predictive value (NPV), and accuracy (ACC) produced from the analysis of the diagnostic outcomes of CTA, initial TTE, and initial TEE studies across 19 qualifying patient cases are shown.

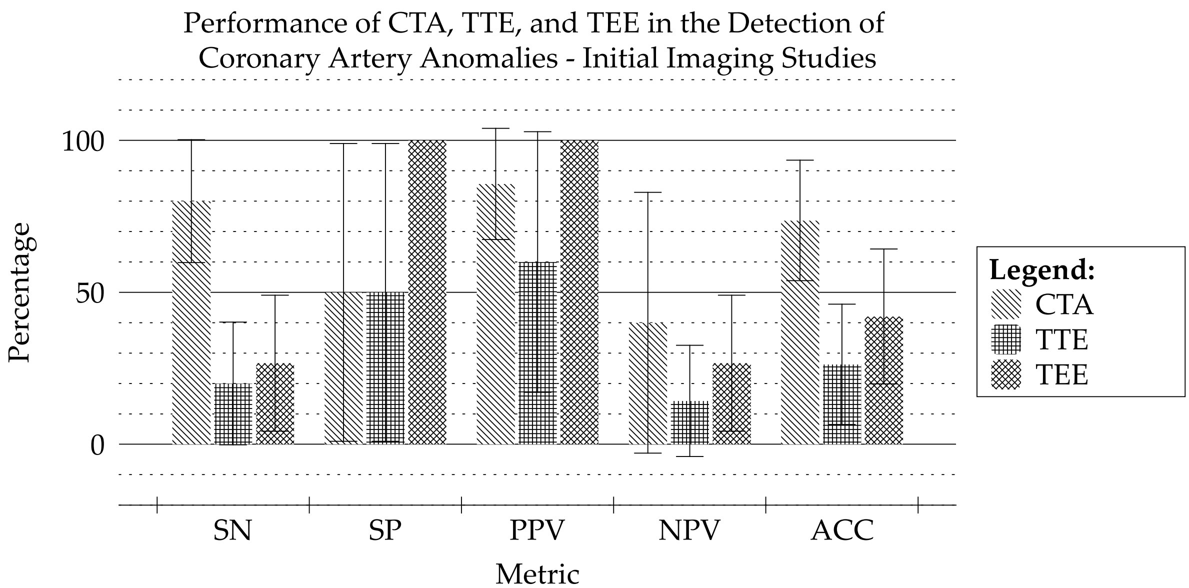

Figure 1: The sensitivity (SN), specificity (SP), positive predictive value (PPV), negative predictive value (NPV), and accuracy (ACC) produced from the analysis of the diagnostic outcomes of CTA, initial TTE, and initial TEE studies across 19 qualifying patient cases are represented graphically with 95% confidence interval bars.

Comparison of Performance Metrics Using Paired t-Testing

Comparison	SN	SP	PPV	NPV	ACC
CTA vs. TTE	0.00	0.99	0.19	0.19	0.02
CTA vs. TEE	0.01	0.02	0.47	0.50	0.10
TTE vs. TEE	0.77	0.02	0.15	0.50	0.41

Table 2: P-values generated with paired t-tests between each modality of interest are shown above for the following performance metrics: sensitivity (SN), specificity (SP), positive predictive value (PPV), negative predictive value (NPV), and accuracy (ACC). The metrics used to make these comparisons are based on diagnostic outcomes of CTA, initial TTE, and initial TEE studies across 19 qualifying patient cases. Using an alpha level of 0.05, comparisons generating a p-value ≤0.05 were considered significant (*green*). Comparisons generating a p-value >0.05 and ≤0.1 were considered marginally significant (*orange*). Comparisons generating a p-value >0.1 were considered insignificant (*red*).

When these performance metrics were reassessed using all imaging studies from all 27 cases that fit original criteria, the following performance metrics were produced. CTA yielded SN of 0.81±0.17, SP of 0.67±0.38, PPV of 0.90±0.14, NPV of 0.50±0.35 and ACC of 0.78±0.16. TTE yielded SN of 0.11±0.05, SP of 0.96±0.04, PPV of 0.87±0.14, NPV of 0.33±0.06 and ACC of 0.38±0.06. TEE yielded SN of 0.18±0.13, SP of 1.00±0.00, PPV of 1.00±0.00, NPV of 0.30±0.14 and an ACC of 0.39±0.14. These data are shown in **Table 3** and graphically represented in **Figure 2**.

Detection of Anomalous Coronary Artery Anatomy – All Imaging Studies

Modality	SN	SP	PPV	NPV	ACC	N
CTA	0.81	0.67	0.89	0.50	0.78	27
TTE	0.11	0.96	0.87	0.33	0.38	255
TEE	0.18	1.00	1.00	0.30	0.39	46

Table 3: Sensitivity (SN), specificity (SP), positive predictive value (PPV), negative predictive value (NPV), accuracy (ACC), and sample size (N) of each modality are displayed. These performance metrics are based on diagnostic outcomes of all CTA, TTE, and TEE studies completed across all 27 patient cases that met original inclusion criteria.

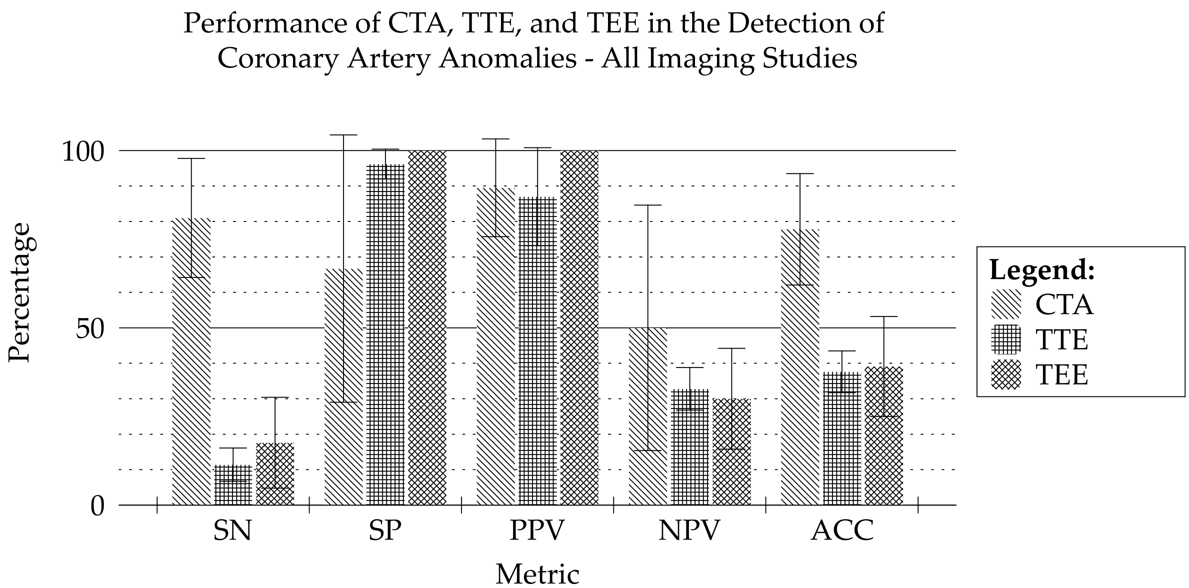

Figure 2: The sensitivity (SN), specificity (SP), positive predictive value (PPV), negative predictive value (NPV), and accuracy (ACC) produced from the analysis of the diagnostic outcomes of all CTA, TTE, and TEE studies across all 27 patient cases that met original inclusion criteria are represented graphically with 95% confidence interval bars.

Complete Characterization of Anomalous Coronary Arteries

The ability of CTA, TTE, and TEE to completely characterize anomalous coronary artery anatomy was assessed by computing the APFC between CTA, TTE, and TEE and the gold standard at the origin, course, and termination of the anomalous coronary artery across all 27 patient cases. This data is shown in **Figure 3**. When assessing the anatomy of the origin of an anomalous coronary artery, CTA, TTE, and TEE demonstrated APFCs of 72.7±17.5% (N=25), 41.3±20.1% (N=23), and 29.8±27.0% (N=11), respectively. When assessing the anatomy of the course of an anomalous coronary artery, CTA, TTE, and TEE demonstrated APFCs of 68.8±18.2% (N=25), 30.4±18.8% (N=23), and 29.2±26.9% (N=11), respectively. When assessing the anatomy of the termination of an anomalous coronary artery, CTA, TTE, and TEE demonstrated APFCs of 90.9±12.9% (N=19), 72.7±21.8% (N=16), and 57.1±36.7% (N=7), respectively. The test of differing proportions was used to determine whether there was a significant difference between the APFC of one modality compared to another in the characterization of features of origin, course, and termination of the anomalous coronary artery in question and across the entire anomalous coronary artery.

CTA demonstrated a significantly higher APFC than TEE in the characterization of anomalous coronary artery origin (p-value of 0.03) and termination (p-value of 0.02). Also, CTA demonstrated a marginally higher APFC than TTE (p-value of 0.07) and TEE (p-value of 0.06) in the characterization of anomalous coronary artery course. The difference in APFC between TTE and TEE in the characterization of any site of an anomalous coronary artery was found to be insignificant (p-value > 0.1). Additionally, the difference in APFC between CTA and TTE in the characterization of anomalous coronary artery termination was found to be insignificant. When APFC was averaged across all portions of an anomalous coronary artery (origin, course, and termination) for each modality (CTA, TTE, and TEE), it was found that CTA demonstrated a significantly higher APFC compared to TEE (p-value of 0.03) and a marginally higher APFC compared to TTE (p-value of 0.08). However, by the same measure, the difference between the APFC between TTE and TEE was found to be insignificant (p-value > 0.1). These p-values are shown in **Table 4**.

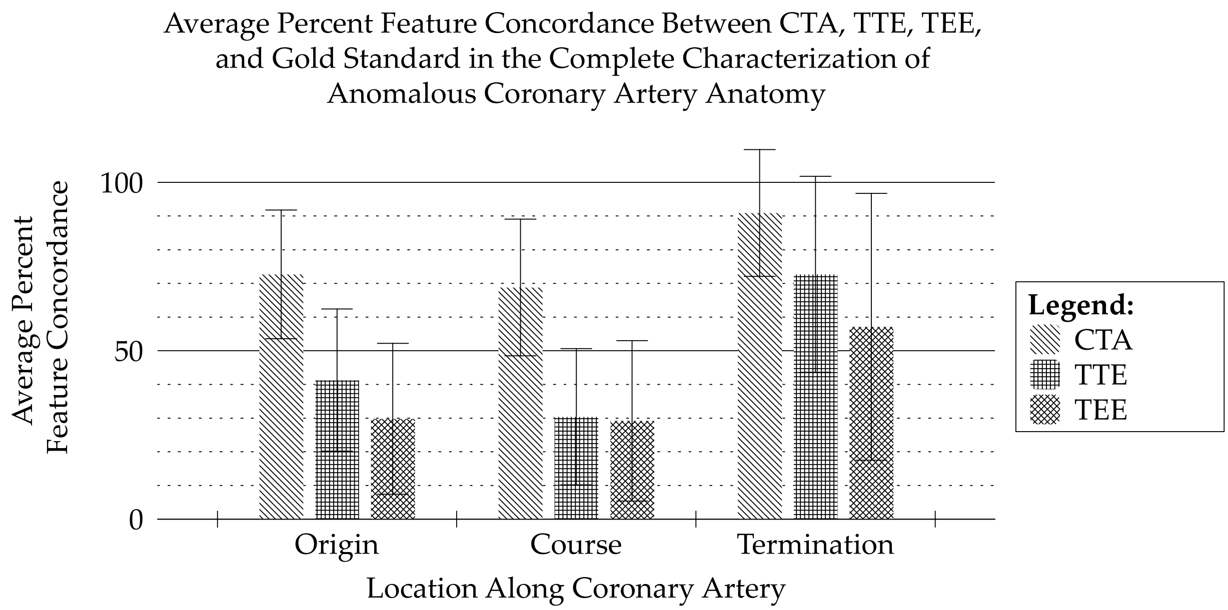

Figure 3: Average percent feature concordance between CTA, TTE, and TEE, and the gold standard with standard error of the mean error bars are shown. Proceeding from left to right,

Comparison of Average Percent Feature Concordance with Gold Standard Using Test of Differing Proportions

Anatomical Distribution	Comparison Made	p-value
Origin	CTA vs. TTE	0.09
	CTA vs. TEE	0.03
	TTE vs. TEE	0.60
Course	CTA vs. TTE	0.07
	CTA vs. TEE	0.06
	TTE vs. TEE	0.95
Termination	CTA vs. TTE	0.11
	CTA vs. TEE	0.02
	TTE vs. TEE	0.38
Total	CTA vs. TTE	0.08
	CTA vs. TEE	0.03
	TTE vs. TEE	0.64

TABLE 4: The p-values for each of the comparisons between CTA, TTE, and TEE in the characterization of the anatomy of the origin, course, and termination of anomalous coronary arteries are shown. Using an alpha level of 0.05, comparisons with p-values ≤0.05 were considered significant (*green*). Comparisons with p-values >0.05 and ≤0.1 were considered marginally significant (*orange*). Comparisons with p-values >0.1 were considered insignificant (*red*).

Rates of Documented Limitations to Imaging

The percentage of studies with noted limitations that prevented proper imaging and interpretation of the coronary arteries was calculated for each imaging. Among the modalities of interest, CTA had the highest number of noted limitations per study, at 7.4% (N = 27), TTE had the lowest number of noted limitations per study, at 5.1% (N = 255), and TEE had an intermediate number of noted limitations per study, at 6.5% (N = 46). This is compared to CA (conventional angiography), which had a higher number of noted limitations per study, at 11.8% (N = 17), which is higher than those of CTA, TTE, and TEE. These data are shown in **Table 5**. The test of differing proportions was used to determine whether there was a significant difference in the rates of limitations between any of the modalities. The p-values associated with these comparisons are shown in **Table 6**.

Rates of Limitations Across All Imaging Studies

	Angiography	CTA	TTE	TEE
%	11.8	7.4	5.1	6.5
N	17	27	255	46

Table 5: The percentage of studies that contained documented limitations to imaging among all studies performed for each patient case was calculated for angiography, CTA, TTE, and TEE and the results are shown. N represents the sample size for each modality, which was calculated as the total number of imaging studies of a particular type (angiography, CTA, TTE, or TEE) across all 27 qualifying patient cases that met inclusion criteria.

Comparison of Limitation Rate Using Test of Differing Proportions

Comparison Made	p-value
CA vs. CTA	0.98
CA vs. TTE	0.85
CA vs. TEE	0.83
CTA vs. TTE	0.85
CTA vs. TEE	0.84
TTE vs. TEE	0.99

Table 6: P-values generated by the test of differing proportions used to compare the rates of documented limitations among conventional angiography (CA), computed tomographic angiography (CTA), transthoracic echocardiography (TTE), and transesophageal echocardiography (TEE) studies are shown. All comparisons produced p-values over 0.1 and were therefore considered insignificant (*red*).

Discussion

Detection of Coronary Artery Anomalies

Detection of CAAs, especially in infants presenting with comorbid cardiac malformations is important and allows appropriate interventional planning and implementation to prevent adverse health outcomes for the patient later in life.

When attempting to detect the presence of a dangerous and potentially lethal pathological condition such as certain CAAs, the sensitivity of the diagnostic test is of great importance. A test with a higher sensitivity confers the ability to rule out suspected pathology with a greater degree of confidence if negative. Our results show that among the three modalities of interest, CTA is the most sensitive for detection of the presence of anomalous coronary arteries in infants aged 0-24 months. Furthermore, the sensitivity of CTA (80%) was found to be significantly different from those of TTE (20%, p=0.004) and TEE (27%, p=0.010). However, the sensitivity of TTE was not significantly different from that of TEE (p=0.770).

The specificity of a diagnostic test used to detect CAAs is also of importance, as a test with a higher specificity confers the ability to better differentiate between anomalies that may and may not require intervention. Our results show that among the three modalities of interest, TEE is the most specific for detection of the presence of any anomalous coronary arteries. The specificity of TEE (100%) was found to be significantly different from that of CTA (50%, p=0.015) and TTE (50%, p=0.015). The specificity of CTA was not significantly different from that of TTE (p=0.990).

The accuracy of each imaging modality describes its ability to enable correct diagnosis, whether positive or negative for a CAA. Higher accuracy reduces the rate of diagnostic error, which in turn, reduces unnecessary and potentially harmful tests and interventions as well as failure to diagnose and manage clinically significant CAAs. Our results show that CTA is the most accurate modality in the detection of any anomalous coronary arteries. The accuracy of CTA was not significantly different but perhaps marginally significantly different from that of TEE (42%, p=0.100). It is possible that the accuracy of CTA is significantly different from that of TEE and that this difference may have been significant (p<0.05) in a larger sample size. The accuracy of TTE was not statistically significant from TEE (p=0.410).

It is important to note that these results are based on a sample size of 19 (as there were 19 cases which met all criteria and were associated with at least one CTA, one TTE, and one TEE). Given this small sample size, it is possible that the results described above are not necessarily representative of CTA, TTE, and TEE when used for detection of coronary artery anomalies. However, when the scope of the data was broadened to include all imaging studies that were completed for each patient (27 CTA, 255 TTE, and 46 TEE studies), the aforementioned trends in results were reproduced. CTA exhibited the highest sensitivity at 81% (N=27) and highest accuracy at 78% (N=27) while TEE exhibited the highest specificity at 100% (N=46). However, the difference in sample sizes between different modalities in this secondary analysis is noted.

Complete Characterization of Anomalous Coronary Arteries

Proper assessment of a CAA requires proper documentation of features of origin, course, and termination of the anomalous coronary artery in question. In this study, the concordance between the features of origin, course, and termination reported using CTA, TTE, and TEE and those reported as part of the gold standard diagnosis was examined.

Feature concordance analysis demonstrated that CTA significantly outperformed TEE in properly characterizing the origin and termination of anomalous coronary arteries. CTA also marginally outperformed TEE in properly characterizing the course of anomalous coronary arteries. When the performance of both modalities was examined across all anatomic sites (origin, course, and termination combined), CTA significantly outperformed TEE.

CTA marginally outperformed TTE in the characterization of the anatomy of the origin and course of anomalous coronary arteries and was no better than TTE at characterization of the anatomy of the termination of anomalous coronary arteries. CTA marginally outperformed TTE in the characterization of features at all anatomic sites combined.

This analysis also revealed that there was no significant difference between the ability of TTE and TEE to characterize anatomic features of anomalous coronary arteries at the origin, course, termination, and at all anatomic sites combined.

These outcomes point to CTA as the modality of choice for the complete characterization of coronary artery anomalies. In cases where CTA is contraindicated, TTE may be preferred to TEE, as the results of our study suggest that there is no significant difference in the ability of these two modalities to characterize anatomy at the origin, course, and termination of anomalous coronary arteries.

Rates of Documented Limitations to Imaging

The rate of limitations that prevented proper imaging of coronary artery anatomy was assessed. All imaging studies documented for each patient were included in this analysis. 7.4% of CTA studies (2 of 27 studies) documented limitations. In one CTA study, the limitation was attributed to the small size of the coronary anatomy and in another CTA study, the limitation was noted without a specified cause. 5.1% of TTE studies (13 of 255) documented limitations that were attributed to various causes including poor image quality, suboptimal acoustic windows, and diagnostic ambiguity. 3 of these TTE studies documented recommendations for additional imaging. 6.5% of TEE studies (3 of 46 studies) documented limitations. Attributed causes included poor identification of coronary arteries, suboptimal window, and difficulty identifying coronary arteries. It is of note that one TEE study was aborted after the patient became unstable and developed hypotension and tachycardia. Angiography demonstrated a limitation rate of 11.8% (2 of 17 studies). The difference between the limitation rates of angiography and CTA, angiography and TTE, and angiography and TEE were found to be insignificant using the test of differing proportions. In addition, it was found that the differences between the limitation rates of CTA and TTE, CTA and TEE, and TTE and TEE were insignificant.

Study Limitations

The study population included infants with various types of comorbid congenital heart disease. The inclusion of patients with same comorbid pathologies may have helped limit the variability in anatomic complexity which may have impacted the ability to properly image coronary anatomy. The results of this study may not be generalizable to infants without congenital heart disease for this reason. However, it is not possible to conduct this study in infants without comorbid congenital heart disease, as coronary artery imaging is not indicated in asymptomatic infants who are perfectly healthy.

As this study was retrospective in nature, it was not possible to control the training or number of operators who acquired TTE or TEE studies. Interpretations of imaging studies were rendered by multiple individuals. Observer bias may have influenced image acquisition and interpretation, as knowledge of previously diagnosed conditions or comorbidities may have affected the search patterns used during image acquisition and interpretation.

Coronary anatomy was not addressed in all surgery and conventional angiography reports. For this reason, the gold standard diagnosis was constructed using findings from both surgery and conventional angiography.

Coronary anatomy was not always addressed in certain imaging reports (particularly TTE and TEE reports). In such cases, it was assumed that coronary anatomy was normal. This assumption was made based on the fact that the studies included in our analysis were those that evaluated complete cardiac morphology and should have therefore commented on any abnormalities in coronary anatomy.

Though some of the results of this study, such as the sensitivity of CTA, were shown to be significantly different from those of the other two modalities evaluated, this was done using a fairly small sample size of 19 (analyzing only one CTA, one TTe, and one TEE study for each of the 19 cases that were eligible for statistical analysis). As such, the findings of this study may not be generalizable. To address this issue, the analysis was repeated using all imaging studies that were completed for all 27 patients. Though only 27 patient cases met all inclusion criteria, varying numbers of TTEs and TEEs were completed for each patient. The sensitivity, specificity, and accuracy were recalculated using the results of 27 CTAs, 255 TTEs, and 46 TEEs. Though the CTA sample size was still relatively small, the sensitivity and accuracy were within a few percentage points (within 10%) from those produced by the initial analysis. However, there was an increase in specificity by 17%.

The sensitivity, specificity, and accuracy of each modality in the characterization of anomalous coronary artery anatomy at each point of the coronary artery (origin, course, and termination) could not be calculated due to the fact that only findings positive for anomalous anatomy were reported in the majority of imaging studies. As such, the concordance between findings reported using CTA, TTE, or TEE and those from the gold standard diagnosis was measured.

Future Work

As discussed, one of the main limitations of this study was sample size. Future iterations of this study would involve a larger number of qualifying cases of infants with coronary artery anomalies presenting for congenital cardiac morphology evaluation. With enough cases of several types of coronary anomalies, it would be helpful to separate these cases based on type of coronary anomaly and calculate performance metrics of each modality in the detection and characterization of each type of anomaly. A prospective approach to data collection controlling the number of image interpreters, echocardiography operators, and surgeons would help improve the quality of data collected. Using multiple image interpreters for each imaging study would help remove subjectivity of interpretations. With a larger sample size and appropriate quality control, it would be possible to measure sensitivity, specificity, and accuracy of each modality of interest in the characterization of anatomic features along the origin, course, and termination of the anomalous coronary artery of interest. Information regarding the outcome of imaging and intervention was not addressed in this study. In the future, analysis of this data would be helpful in determining which coronary anomalies truly went on to cause clinical problems and whether the outcome was in any way influenced by the result of diagnoses made on imaging. Also, assessment of the relative efficacy of magnetic resonance angiography, an up and coming modality in coronary artery imaging, in the detection and characterization of CAAs would also be of benefit.

Conclusion

The use of an imaging modality that is highly sensitive, specific, and accurate for the detection of coronary artery anomalies is desired. In our study, CTA demonstrated the highest sensitivity and accuracy of the three imaging modalities evaluated. As such, this suggests that CTA is the imaging modality of choice in the detection of anomalous coronary artery anatomy. CTA was also better than TTE and TEE in the characterization of the anatomic features along the entire length of an anomalous coronary artery and therefore is also the preferred modality for this use.

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