UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, D.C. 20301-4000

PERSONNEL AND READINESS

MAR 2 5 2021

The Honorable Adam Smith
Chairman
Committee on Armed Services
U.S. House of Representatives
Washington, DC 20515

Dear Mr. Chairman:

The enclosed report is in response to House Report 116-442, page 151, accompanying H.R. 6395, the William (Mac) Thornberry National Defense Authorization Act for Fiscal Year 2021, Cardiac Arterial Disease Diagnostic Improvements.

The report summarizes current pathways for diagnosis of Cardiac Arterial Disease in the Military Health System (MHS), cost analysis of Fractional Flow Reserve Derived from Computed Tomography (FFR_{CT}), an analysis of cost savings for Cardiac Arterial Disease evaluation and diagnosis pathways, and implications on use of FFR_{CT} in theater. Findings of the report show that it is not currently practical to conclude cost savings to the MHS directly related to the addition of FFR_{CT} due to several factors, including lack of widespread use currently within the MHS. Additionally, due to cybersecurity concerns, as well as the degree of technological demand and high level of expertise required to perform and interpret FFR_{CT}, its use is currently not feasible in theater.

Thank you for your continued strong support for the health and well-being of our Service members, veterans, and their families.

Sincerely,

//SIGNED//

Virginia S. Penrod
Acting

Enclosure:
As stated

cc:
The Honorable Mike D. Rogers
Ranking Member

Report to House Armed Services Committee

Report on Cardiac Arterial Disease Diagnostic Improvements
Requested by: House Report 116-442, page 151, to Accompany H.R. 6395, the William M. (Mac) Thornberry National Defense Authorization Act for Fiscal Year 2021

March 2021

The estimated cost of this report or study for the Department of Defense (DoD) is approximately $6,570 in Fiscal Years 2018-2019. This includes $0 in expenses and $6,570 in DoD labor.
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EXECUTIVE SUMMARY

This report is in response to House Report 116-442, page 151, to accompany H.R. 6395, the Willaim M. (Mac) Thornberry National Defense Authorization Act (NDAA) for Fiscal Year (FY) 2021, which requests a report analyzing the cost savings (including avoidance of transport from the theater of operations) of an anatomy-guided pathway for the diagnosis of coronary artery disease (CAD), as contrasted with the functional or ischemia-guided approach followed by invasive coronary angiography (ICA).

This report contains data on recent utilization of non-invasive and invasive procedures for evaluating CAD in patients without a previous diagnosis of CAD. It also contains a limited analysis on cost difference between an anatomy-first approach (coronary computed tomography angiography [cCTA]) versus a functional or ischemia-guided approach (traditional pathway) within the Military Health System (MHS), and outside of the MHS.

Key findings of this report include:

- A functional or ischemia guided pathway with non-invasive cardiac stress tests (graded exercise treadmill testing [GXT], single-photon emission computer tomography [SPECT], stress echocardiogram [SE], and stress cardiac magnetic resonance imaging [CMR]) is the most used method to diagnose possible obstructive CAD in patients with stable chest pain.
- Transitioning from a functional imaging to an anatomic strategy is currently endorsed by international guidelines; however, U.S. guidelines do not support this approach at the time of this writing.
- Results from studies within the MHS found that CAD identified by cCTA is associated with improved risk stratification, lower rates of subsequent evaluations for chest pain and repeat testing, and improved use of preventive cardiovascular medications in the low to intermediate-risk population served by the MHS.
- To date, there is no large scale prospective randomized trial evaluating the impact of Fractional Flow Reserve Computed Tomography (FFR_{CT}) on cost, and it remains questionable that a broad application of FFR_{CT} would be cost-effective.
- Data on use of FFR_{CT} is very limited to date in the MHS, as it was only approved as a benefit in network provided care (NPC) in November 2019. It is currently not practical to evaluate cost savings to the MHS directly related to the addition of FFR_{CT}.
- A pilot on use of FFR_{CT} in the Direct Care system is ongoing, with eight sites currently participating. Although the main objective of the pilot is to validate the information technology pathway connections, further cost data will be collected from these pilot sites.
- Due to limitations on equipment available in theater, cybersecurity concerns, as well as the level of dedicated expertise from nurses, physicians, and radiologists required to administer and evaluate cCTA and FFR_{CT}, it is not currently a practical solution for diagnosis of CAD in theater.
- There are several factors to consider for the transition to an anatomical pathway of care, including current widespread availability of other types of non-invasive testing within the MHS. In order to provide cCTA and meet access to care standards throughout the MHS, cardiovascular and radiology training programs would need to ensure increased scanner

availability and that their graduates are qualified and trained to perform high-quality cCTA.

- With an increase in the use of cCTA, the role of FFR_{CT} may increase in patients considered for ICA after an abnormal cCTA.

PURPOSE

As requested by the House Armed Services Committee, this report analyzes the cost savings (including avoidance of transport from the theater of operations) of an anatomy-guided pathway for the diagnosis of CAD through cCTA with the adjunct of fractional flow reserve computed tomography (FFR_{CT}) followed by invasive coronary angiography (ICA), as contrasted with a functional or ischemia-guided approach followed by invasive coronary angiography. The Committee also requested that the report outline necessary steps to move to the anatomical pathway and a plan of action for accomplishing that move.

This report analyzes the recent utilization of non-invasive and invasive procedures for evaluating CAD in patients without a diagnosis of previous CAD. In addition, it contains a limited potential cost difference analysis between an anatomy first approach (cCTA approach) versus a functional or ischemia-guided approach (traditional pathway) within the MHS. Due to data limitations, this report also describes research on cost savings to date outside of the MHS.

BACKGROUND

A functional or ischemia guided pathway with non-invasive cardiac stress tests (graded exercise treadmill testing [GXT], single-photon emission computer tomography [SPECT], stress echocardiogram [SE], and stress cardiac magnetic resonance imaging [CMR]) is the most used method to diagnose possible obstructive CAD in patients with stable chest pain. This approach is supported by the current United States (U.S.) and International guidelines. [1–3] Recently, cCTA use has seen an increase in the U,S., and recent International guidelines have recommended using cCTA as an initial test for diagnosing CAD in symptomatic patients with the same level of evidence and class recommendation as functional or ischemia guided imaging. [3,4] When the clinical evaluation yields a high likelihood of obstructive CAD, with a high event risk, with symptoms of chest pain not responding to medical therapy or chest pain with low levels of exercise, the current guidelines recommend further risk evaluation with ICA, which remains the gold standard in assessment of coronary anatomy and risk. [1–3] Decisions to pursue revascularization (placement of a coronary artery stent or referral for coronary artery bypass surgery) were based on ICA disease severity. Still, recent evidence supports that these decisions require both anatomical and functional information. To date, ICA combined with invasive fractional flow reserve (FFR) is the most validated form of testing for CAD. [5–7] However, recent evidence from national registries and new trials demonstrate a significant discrepancy between non-invasive test findings and ICA, revealing that non-invasive stress imaging only partially succeeds in its intended role as a gatekeeper to ICA. [8–12]

More recently, evidence from randomized clinical trials advocates for a new paradigm of imaging that can detect coronary atherosclerosis, not only stenosis, by using cCTA as a first test strategy. [10,13,14] Studies have shown that cCTA has the strong ability to rule out CAD with a high degree of accuracy, is a better predictor of obstructive CAD, is associated with a reduced incidence of myocardial infarction (MI), and increased prescriptions for aspirin and cholesterol medications. These capabilities are due to its ability to assess for the presence of coronary artery atherosclerotic plaque and identifying patients at risk at an earlier stage of the disease.[14–16] cCTA findings of normal coronary arteries are associated with an excellent prognosis and low risk of future events beyond five years. [17–20] Recent evaluations have examined the relationship between the atherosclerotic plaque characteristics identified by cCTA to identify myocardial ischemia with good correlation. [21–23] Despite this ability, cCTA has a lower specificity for identifying obstructive CAD. The overestimation of disease severity leads to an increased number of ICA in clinical trials. [15,23–25] Noninvasive fractional flow reserve (FFR_{CT}) is a currently available technology designed to address and predict the physiologic consequences of CAD detected by cCTA. This technology creates patient-specific blood flow models from cCTA images using deep learning algorithms based on computational fluid dynamic analysis to create a blood flow solution analysis of a blood vessel. [26] The only vendor currently authorized by the Food and Drug Administration (FDA) to perform FFR_{CT} in the U.S. is Heartflow®. By improving the specificity of cCTA, a cCTA/FFR_{CT} approach to evaluating chest pain has been more effective at identifying patients with obstructive CAD considered for referral for ICA.

In a recent clinical trial in the study's interventional arm, a cCTA/FFR_{CT} approach resulted in 61 percent of ICA safely canceled without an event at one year of follow-up. [27,28] Various centers and post-hoc analyses have demonstrated a higher burden of obstructive CAD at the time of ICA utilizing this approach. [29,30] Furthermore, a post-hoc analysis of a large contemporary U.S.-based clinical trial identified that a combined cCTA/FFR_{CT} approach reduced the rate of cCTA studies with obstructive disease while also reducing the incidence of non-obstructive disease by ICA (52 percent vs. 12 percent) when compared to a functional or ischemia based pathway. [31] The performance of cCTA/FFR_{CT} when compared to other functional noninvasive tests, has revealed a similar specificity but higher sensitivity for obstructive CAD. [24,32–35] Despite its FDA approval and its increase in clinical use, there is limited knowledge about its impact on clinical decision making, patient outcomes, and cost in the absence of a large-scale prospective randomized clinical trial. There are additional concerns regarding its precise clinical definition of abnormal value, its upfront cost, and the rejection rate due to inadequate image quality.

USE OF cCTA IN THE MHS

Service members with symptoms of chest pain warrant further evaluation before these Service members can return to duty. The challenge remains in identifying high-risk findings among a generally low-risk population, where the system requires the means to accurately and expeditiously exclude the presence of CAD. [36–39]

A military tertiary center retrospective analysis evaluating the performance of SPECT imaging and cCTA (without FFR_{CT}) for the evaluation of obstructive CAD after an equivocal or moderate risk stress electrocardiogram (ECG) demonstrated a false positive rate of nearly 15 percent among SPECT evaluated patients that translated into 93 percent of those Service members having no evidence of obstructive CAD on ICA. [40] In comparison, cCTA effectively ruled out obstructive CAD in nearly 98 percent of patients, with only 16.5 percent having non-obstructive coronary atherosclerosis. In this analysis, the incidence of referral to ICA was 2.4 percent, further solidifying the negative predictive value of cCTA amongst MHS beneficiaries. [40] Furthermore, radiation doses received by MHS beneficiaries undergoing SPECT imaging remains similar to observed contemporary amounts compared to a nearly 70 percent reduction in radiation doses over the years in cCTA. [41,42]

cCTA in the MHS informs on cardiovascular prognosis[43,44], lowers rates of subsequent evaluations for chest pain and repeat testing [45,46], increases use of preventive cardiovascular medications[47], and safely dispositions patients presenting to the emergency department with chest pain.[48] cCTA has demonstrated that, among MHS beneficiaries with obstructive CAD and non-obstructive coronary atherosclerosis, there was a significant increase in the initiation and intensification of statin therapies, aspirin therapy, and blood pressure medications. These medication changes resulted in significant improvements in total cholesterol, low-density lipoprotein cholesterol, and blood pressure, similar to observed medication changes in contemporary cohorts. [15,16,47] The results from these studies support that CAD identified by cCTA is associated with improved risk stratification, lower rates of subsequent evaluations for chest pain and repeat testing, and improved use of preventive cardiovascular medications in the low to intermediate-risk population served by the MHS.

USE OF FFR_{CT} IN THE MHS

In June 2019, the Department of Defense (DoD) submitted a Report to Congress detailing benefits and limitations on the use of FFR_{CT} as compared to more invasively measured FFR and non-invasive tests such as stress testing, stress echocardiography, and nuclear myocardial perfusion. Following the publication of that report, the Director, DHA issued a Medical Benefit Determination on October 2, 2019, and the use of FFR_{CT} was added as a covered service in the TRICARE Policy Manual on November 12, 2019 (Change 55). Since approval, data shows that roughly 85 percent of FFR_{CT} performed in network provided care (NPC) have been for beneficiaries enrolled in TRICARE for Life (TFL).

Table 1: FFR_{CT} Performed in NPC, November 2019 - June 2020

Month	Non-TFL	TFL	Total
Nov 2019	1	13	14
Dec 2019	2	26	28
Jan 2020	2	22	24
Feb 2020	5	28	33
Mar 2020	7	17	24
Apr 2020	4	10	14
May 2020	2	12	14
Jun 2020	4	20	24
Total	27	148	175

The process of using Heartflow® requires sending the patient's cCTA images to Heartflow's® headquarters in Redwood City, California, where their software creates the models to estimate FFR in the coronary arteries. Until recently, cybersecurity concerns prevented military Medical Treatment Facilities (MTFs) from sharing data through this mechanism, so there is little to no volume in Direct Care. However, following DHA directed 8582b approval, Heartflow® will be approved to connect to the Medical Community of Interest (MedCOI) servers, DoD electronic medical record, and imaging Picture and Archiving Communication Systems through an approved Business2Business connection. Once approved, MTFs will not need to apply separately for the 8582b connection.

The use of FFR_{CT} in the Direct Care system via Heartflow® is being piloted at eight sites within the MHS Direct Care system. The primary objectives are validating the information technology pathway connections, cybersecurity, its use, and impact in the downstream utilization of resources, cost-effectiveness, and ICA rates. There are two MTFs actively submitting data as of the publication of this report, with a total of 10 cases as of September 2020: Lackland Air Force Base and Brooke Army Medical Center. Additional pilot sites will include Walter Reed National Military Medical Center, Madigan Army Medical Center, Tripler Army Medical Center, Travis Air Force Base, Wright Patterson Air Force Base, and Portsmouth Naval Medical Center.

COST ANALYSIS OF FFR_{CT}

CIVILIAN SECTOR

To date, there is no large scale prospective randomized trial evaluating the impact of FFR_{CT} on cost. Several initial studies and registries have estimated the economic value of FFR_{CT} with limited outcomes and cost-effectiveness data, particularly compared to cCTA alone or cCTA followed by a functional test. [28,49–51] While studies have demonstrated decreased costs with FFR_{CT}, cost reduction reduces with the number of patients referred for ICA. [28] With an improved prediction of obstructive CAD by cCTA/FFR_{CT}, including the additional cost and potentially higher catheterization and revascularization costs, it remains questionable that a broad application of FFR_{CT} could be cost-effective. [52] It is important to note that recent studies have found the use of cCTA without FFRct to be cost-effective before ICA. [53,54]

MILITARY HEALTH SYSTEM

To calculate the total cost of FFR_{CT}, the four Current Procedural Terminology (CPT) codes for FFR_{CT} were used to analyze administrative data from NPC (0501T-0504T). Table 2 shows the volume and average allowed amounts for each of these four CPT codes. The volumes presented are not additive because some claims use more than one of these CPT codes; however, volumes are presented to show the relative frequency of different codes.

Table 2: Average Allowed Amounts of FFR_{CT}, November 2019 - June 2020

CPT Code	No. of Records	Average Allowed Amount
0501T	6	$507

0502T	8	$133
0503T	130	$990
0504T	113	$94

*Includes only NPC.

To calculate cost of an FFR_{CT} claim, values were summed across all CPT codes for a given person and day. The average prices are shown in Table 3. The average amount paid for TFL is lower, as Medicare pays approximately 80 percent of the cost primarily, followed by TRICARE paying the remainder. Due to this reason, the average amount paid for the total population is skewed, and the average allowed amount may be a more appropriate measure of the expected cost of FFR_{CT}.

Table 3: Average Cost of FFR_{CT} Performed in NPC, November 2019 - June 2020

	No. of FFR_{CT}	Total Allowed Amount	Average Allowed Amount	Total Amount Paid	Average Amount Paid
Non-TFL	27	$21,208	$785	$19,453	$720
TFL	150	$122,210	$815	$24,521	$163
Total	177	$143,418	$810	$43,974	$248

Given that FFR_{CT} was very recently approved, the low utilization of FFR_{CT} in MHS NPC and Direct Care, and less than a year of complete data in the MHS, it is not practical to conclude cost savings in the MHS directly related to the addition of this technology.

FFR_{CT} utilization rates for the evaluation of chest pain in the military may be low because the impact of adding FFR_{CT} for evaluating stable chest pain depends on the utilization of cCTA.

PLANNED MHS COST SAVINGS ANALYSIS FOR CAD EVALUATION AND DIAGNOSIS PATHWAYS

To explore the potential utilization and financial impact FFR_{CT} may have in the MHS, we are performing an analysis of the diagnostic evaluations for CAD over the past five fiscal years. The investigation thus far has revealed that functional stress tests account for nearly 95 percent of the diagnostic tests (80 percent SPECT, 15 percent SE, 0.2 percent CMR) obtained over the past five years. Trends in utilization for the past five years reveal a small decline in functional tests, while cCTA utilization increased by 12 percent (3.5 percent in FY16 to 5.75 percent FY20). 95 percent of SPECT and 71 percent of cCTA tests are performed in NPC, while Direct Care performs 5 percent of the SPECT and 29 percent of the cCTA tests. An analysis of 2019 FY data from non-TFL beneficiaries undergoing further evaluation or procedures within 90 days of their initial diagnosis provides insight into the most recent trends. Of 26,997 beneficiaries undergoing further non-invasive testing, 88 percent of functional and anatomical non-invasive tests did not warrant further evaluation or revascularization referrals. Of the 12 percent of functional tests requiring further diagnostic testing, 35 percent underwent a repeat functional test, 25 percent underwent a cCTA, and 50 percent were referred for ICA. Despite the high number of referrals for ICA, only 25 percent of beneficiaries required further revascularization. By contrast, the 12 percent of beneficiaries with a cCTA that required further evaluation, 75 percent had a follow-up functional assessment, and 25 percent an ICA. Of the 25 percent of patients referred for ICA following a cCTA, 90 percent of beneficiaries underwent further revascularization. Overall in FY19, it is estimated that close to 1,000 ICAs following a non-invasive test did not require revascularization. Further analysis is ongoing.

Further cost and resource utilization rates will be collected and analyzed from the FFR_{CT} pilot program at eight sites within the MHS Direct Care system (Lackland Air Force Base and Brooke Army Medical Center. Additional pilot sites will include Walter Reed National Military Medical Center, Madigan Army Medical Center, Tripler Army Medical Center, Travis Air Force Base, Wright Patterson Air Force Base, and Portsmouth Naval Medical Center). This will provide direct cost data in routine clinical practice.

IMPLICATIONS ON USE OF FFR_{CT} IN THEATER

To have FFR_{CT} in theater, cCTA would need to become available in the theater of operations. The high quality cCTA scan needed to obtain a FFR_{CT} analysis comes with a high degree of technological demand and expertise. This requires access to a trained and qualified radiologist or cardiologist, and technicians to protocol, perform, and interpret cCTA in the theater of operations. The type of computerized tomography (CT) scanner needed to perform high quality cCTA has to meet certain minimum requirements (at least 64-row multidetector CT scan) and often has a large footprint, limiting their mobility. Most cCTAs require the administration of medications for heart rate control (oral or intravenous) to achieve a low heart rate (goal of less than 60 beats per minute) prior to the scan (often 60-120 minutes) in combination with medications for arterial vasodilatation (nitroglycerin 800 mcg sublingual) given at the time of the scan. These medications need to be administered by nurses with advanced cardiovascular life support training to ensure safe administration and adequate monitoring of the patient prior to, during, and after the scan if there are adverse effects.

Furthermore, due to cybersecurity concerns and issues with a secure, reliable connection to a Heartflow® server from remote overseas locations, and the time required to obtain results, the use of FFR_{CT} in the deployed setting is not feasible. Experience from deployed cardiologists during Operation Iraqi Freedom and Operation Enduring Freedom revealed that in-theater cardiology support, with the availability of treadmill stress testing and echocardiography, resulted in an 85 percent return to duty rate for Service members evaluated for chest pain. [55,56]

CONCLUSION

It is currently not practical to conclude cost savings to the MHS directly related to the addition of FFR_{CT}. Transitioning from a functional imaging to an anatomic strategy will be challenging and warrants exploration. While currently endorsed by international guidelines, U.S. guidelines do not support this approach at the time of this writing. It is important to note that while the U.S. guidelines will be updated in spring 2021, the updated recommendations for evaluating and diagnosing CAD are not currently available for public review.

There are several other factors to consider. In the MHS, there is widespread availability of nuclear medicine, stress treadmill, and stress echocardiography equipment that is likely contributing to the underutilization of cCTA. The availability of high-quality cCTA may not be available throughout the MHS, as it requires medical and technical expertise to produce consistent, high-quality imaging. Currently, there are less than 20 cCTA board-certified cardiologists and certified trained radiologists in the MHS, and only five have obtained additional dedicated training in advanced cardiac imaging. In the MHS, there are new generation scanners capable of performing cCTA, but cCTAs are often dependent on scanner availability to perform studies. In order to provide cCTA and meet access to care standards throughout the MHS, particularly if the utilization of cCTA is to increase, cardiovascular and radiology training programs need to ensure increased scanner availability and that their graduates are qualified and trained to perform high-quality cCTA.

Recent results from a large scale prospectively randomized clinical trial (ISCHEMIA Trial) sponsored by the National Institutes of Health have important implications on how cardiac imaging is used to evaluate patients for CAD.[57] Based on the recently published international guidelines for the evaluation of chest pain and the ISCHEMIA trial, cCTA will likely play an important role in the assessment of chest pain, implementation of aggressive medical therapy, and diagnostic efficiency, as a majority of patients who are evaluated with cCTA will have either no CAD or non-obstructive disease and will not need further testing. With the increased use of cCTA, the role of FFR_{CT} may increase in patients considered for ICA after an abnormal cCTA.

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APPENDIX A: ACRONYMS

CAD	coronary artery disease
cCTA	coronary computed tomography angiography
CMR	cardiac magnetic resonance imaging
CPT	current procedural terminology
CT	computerized tomography
DHA	Defense Health Agency
DoD	Department of Defense
ECG	electrocardiogram
FDA	Food and Drug Administration
FFR	fractional flow reserve
FFR_{CT}	fractional flow reserve computed tomography
FY	fiscal year
GXT	graded exercise treadmill testing
ICA	invasive cardiac angiography
MedCOI	Medical Community of Interest
MHS	Military Health System
MI	myocardial infarction
MTF	military medical treatment facility
NDAA	National Defense Authorization Act
NPC	network provided care
SE	stress echocardiogram
SPECT	single photon emission computer tomography
TFL	TRICARE for Life
U.S.	United States