

# Prevalence and factors associated with false positive suspicion of acute aortic syndrome: experience in a patient population transferred to a specialized aortic treatment center

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**Study objective:** Acute aortic syndrome (AAS) is a medical emergency that requires prompt diagnosis and treatment at specialized centers. We sought to determine the frequency and etiology of false positive activation of a regional AAS network in a patient population emergently transferred for suspected AAS.

**Methods:** We evaluated 150 consecutive patients transferred from community emergency departments directly to our Cardiac Intensive Care Unit (CICU) with a diagnosis of suspected AAS between March, 2010 and August, 2011. A final diagnosis of confirmed acute Type A, acute Type B dissection, and false positive suspicion of dissection was made in 63 (42%), 70 (46.7%) and 17 (11.3%) patients respectively.

**Results:** Of the 17 false positive transfers, ten (58.8%) were suspected Type A dissection and seven (41.2%) were suspected Type B dissection. The initial hospital diagnosis in 15 (88.2%) patients was made by a computed tomography (CT) scan and 10 (66.6%) of these patients required repeat imaging with an ECG-synchronized CT to definitively rule out AAS. Five (29.4%) patients had prior history of open or endovascular aortic repair. Overall in-hospital mortality was 9.3%.

**Conclusions:** The diagnosis of AAS is confirmed in most patients emergently transferred for suspected AAS. False positive activation in this setting is driven primarily by uncertainty secondary to motion-artifact of the ascending aorta and the presence of complex anatomy following prior aortic intervention. Network-wide standardization of imaging strategies, and improved sharing of imaging may further improve triage of this complex patient population.

**Keywords:** Acute aortic syndrome (AAS); aortic dissection; hospital transfer; false positive



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## Introduction

Patients with time sensitive acute medical emergencies often present to community hospitals and subsequently require transfer to tertiary centers for definitive treatment. Modeled on the success of statewide trauma networks, a number of regional systems for the management of acute medical emergencies including ST-elevation myocardial infarction (STEMI), cardiac arrest, stroke, and acute aortic syndrome (AAS), defined as acute aortic dissection, intramural hematoma, or penetrating atherosclerotic ulcer, have been developed (1-8). The creation of STEMI networks across

the United States and Europe has led to a dramatic increase in the availability of timely primary percutaneous coronary intervention (PCI) and reduced door to balloon times, both of which have translated into a decreased mortality rate with this condition (4,8-10).

Created in 1996, the International Registry of Acute Aortic Dissection (IRAD) is the largest dataset of AAS patients to date and has significantly advanced the recognition, diagnosis and treatment of patients presenting with this medical emergency. Eligible patients in IRAD have a confirmed AAS diagnosis based on medical history, imaging study, direct visualization at surgery, or post-

mortem examination (11-13). However, the initial diagnosis of acute aortic dissection and emergent triage is challenging due to the lack of biomarkers, complex differential diagnosis, and need for confirmatory imaging. Regional AAS networks have been created in order to accelerate diagnosis, transport, and treatment of these patients.

The upstream triage of care prior to arrival at a tertiary center, and the rate of diagnostic confirmation in patients emergently transferred for suspected AAS, is incompletely described. Understanding the frequency and causes of false positive activation in patients with suspected AAS provides opportunities to improve clinical care in AAS networks (14-16). The aim of this study is to report the prevalence and etiology of false positive activation for AAS in a consecutive series of patients transferred to a tertiary referral center.

## Methods

### *AAS network and emergency transport system*

The AAS network in the Cleveland Clinic Health System (CCHS) comprises of a tertiary academic center in downtown Cleveland and a number of referring hospitals in Ohio and neighboring states. At the main campus hospital, care for patients with AAS is organized within a specialized 'Aorta Center', staffed by a group of critical care cardiologists, cardiothoracic and endovascular surgeons, and cardiovascular imaging specialists/radiologists. Patients with confirmed or suspected AAS are emergently transferred by the Cleveland Clinic Critical Care Transport system (based on location, availability, weather and distance via ground, helicopter, or fixed-wing jet) directly to the CICU as described previously (17).

The Cleveland Clinic Critical Care Transport system can be activated for time sensitive medical emergencies via a single phone contact. While predominantly utilized for STEMI, this system is also designed and utilized for acute stroke as well as our AAS network. The central hospital and some hospitals within the CCHS share a 'Picture Archiving and Communication' PACS system, allowing shared access to radiologic studies. However, such sharing is not currently possible with the majority of other referring hospitals.

### *Selection of participants*

The study cohort consisted of 150 consecutive patients, with a community hospital/emergency department diagnosis of suspected AAS, transferred to our institution by the critical care transport team, via ground ambulance (n=27),

helicopter (n=110), or fixed wing jet (n=13) between March, 2010 to August, 2011. The initial data collection date of March, 2010 was chosen because our critical care transport team created a database of AAS transfers and began prospectively entering data on this date. Transport data was prospectively collected and added (CR and BA) to our Heart and Vascular Institute's RedCaps© AAS database, modeled similarly to IRAD. Final diagnosis in this cohort of subjects was made by consensus agreement of the cardiac intensive care unit, vascular surgery, cardiothoracic surgery and cardiovascular imaging teams utilizing all available clinical, imaging and surgical data, also modeled after IRAD (11-13). If there were no available diagnostic images from the initial hospital, computed tomography (CT) imaging was performed utilizing our institution's acute aortic dissection CT imaging protocols (*Table 1*). Patients were grouped into either confirmed dissection (Type A or Type B) or false positive suspicion (no pathology or no acute pathology). Patients with an initial ED diagnosis of penetrating aortic ulcer (3 patients) or intramural hematoma (4 patients) were reclassified as either Type A or Type B dissection based on the location of the lesion. The Cleveland Clinic Institutional Review Board approved this study, with a waiver of individual consent.

### *Analysis*

Baseline characteristics were compared between the groups with confirmed AAS and those with false positive activation. Continuous variables were compared between groups using Student's *t*-test with mean  $\pm$  standard deviation (SD) reported. Categorical variables were compared between groups using Pearson's chi-squared test with frequency and percent reported.

## Results

Overall, 150 patients were transferred with a suspected diagnosis of AAS from 60 different hospitals with a median distance of 40 [interquartile range (IQR), 14-75] miles. A total of 133 patients (63 Type A and 70 Type B) had the diagnosis of AAS confirmed at the tertiary center. In 17 patients (11.3%) the diagnosis was not confirmed ('false positive suspicion'), with 10 (58.8%) of these being suspected Type A and 7 (41.2%) suspected Type B. Baseline demographics for the confirmed AAS group and the false positive group are illustrated in *Table 2*. Demographics were similar in both groups.

**Table 1** Considerations for aortic dissection protocols

Use of ECG-synchronized acquisition with retrospective gating or prospective triggering for motion-less imaging of the aortic root and ascending aorta
Contrast-timing optimized for aortic enhancement
Protocol settings (tube-current and tube-voltage) sufficient for low-noise reconstruction and 1 and 3 mm slice thickness
Pre-contrast acquisition for easy identification of intramural hematoma and identification of surgical material
Additional delayed “venous” acquisitions in patient with prior endovascular stent grafting
Additional non ECG-synchronized acquisition of the abdomen and pelvis for distal aortic disease (more frequent with suspected Type-A pathology)
Additional non ECG-synchronized continuous acquisitions of the chest/abdomen/pelvis for endovascular stent graft planning (more frequent with suspected Type-B pathology)
Consideration of radiation exposure in particular in young and female patients
Consideration of contrast exposure in particular in patients with renal insufficiency or a contrast allergy
Consideration of alternative imaging modalities (TEE, MRI)
Abbreviations: ECG, electrocardiography; TEE, trans-esophageal eclocardiogrhy; MRI, magnetic resonance imaging.

**Table 2** Baseline demographics

Variable	Type A or Type B dissection, n=133	Normal or no acute pathology, n=17	P-value
Age, mean ( $\pm$ SD), yrs	65 $\pm$ 14.0	57 $\pm$ 23	0.04
Male (%)	75 (56.4)	9 (52.9)	0.78
Body mass index, mean ( $\pm$ SD)	28.2 $\pm$ 5.7	28.6 $\pm$ 5.8	0.78
Past medical history			
Hypertension (%)	100 (75.2)	15 (88.2)	0.23
Diabetes mellitus (%)	7 (5.3)	1 (5.9)	0.90
Hyperlipidemia (%)	32 (24.0)	7 (41.1)	0.14
ESRD (%)	0 (0.0)	0 (0.0)	-
COPD (%)	21 (15.8)	2 (11.8)	0.66
Known connective tissue disorder, Marfans (%)	1 (0.8)	0 (0.0)	0.72
Stroke/TIA (%)	13 (9.8)	1 (5.9)	0.60
Peripheral arterial disease (%)	4 (3.0)	1 (5.9)	0.53
Coronary artery disease (%)	26 (19.5)	2 (11.8)	0.44
Prior cardiovascular surgery (%)	27 (20.3)	9 (52.9)	0.003
Aortic valve replacement (%)	13 (9.8)	2 (11.8)	0.80
Mitral valve replacement (%)	5 (3.8)	1 (5.9)	0.67
Coronary bypass surgery (%)	17 (12.8)	5 (29.4)	0.07
Aortic surgery (dissection, aneurysm) (%)	23 (17.3)	5 (29.4)	0.23
Open aortic surgery (%)	20 (15.0)	4 (23.5)	-
Endovascular stent (%)	4 (3.0)	2 (11.7)	-
Abbreviations: SD, standard deviation; COPD, chronic obstructive pulmonary disease; ESRD, end-stage renal disease; TIA, transient ischemic attack.			

**Table 3** Imaging performed at initial institution and tertiary center

	False positive Type A dissection, n=10	False positive Type B dissection, n=7
Imaging from initial hospital/ER		
CT PE protocol	5	2
CT aortic/cardiac (nongated CTA)	2	2
CT chest/abdomen/pelvis	1	0
Non-contrast CT	1	2
None	1	1
Additional imaging performed at tertiary center to rule out AAS*		
ECG-synchronized CT	6	4
None needed (referral center CT satisfactory to rule out AAS)	2	2
Transesophageal echocardiography	1	0

\*, Additional imaging at the tertiary center was needed to rule-out Type A dissection in 9/10 patients and 6/7 patients for Type B dissection. Both patients did not require additional imaging because initial imaging was not performed at the community hospital. Instead, initial imaging at the tertiary hospital was performed. Abbreviations: AAS, acute aortic syndrome; CT, computed tomography; PE, pulmonary embolus; CTA, computed tomography aorta.

The overall in-hospital mortality for the 150 patients cohort was 9.3%. This included 13 patients in the confirmed dissection group ('true positive group' mortality =9.7%) and one patient in the false positive group (5.8%). One patient died during index hospital stay in the false positive cohort. A CT scan ruled out a Type B dissection in this patient who subsequently manifested mesenteric ischemia secondary to a superior mesenteric artery embolus and expired intra-operatively.

False positive suspicion by the referring institution was based on CT imaging in 15/17 cases. The remaining patients were transferred based on high clinical suspicion without pre-transfer imaging. Imaging utilized for the false positive group at both the initial and tertiary hospitals, is illustrated in *Table 3*.

The pre-transfer suspicion for Type A dissections was not confirmed in ten patients ('false positive Type A'). In one patient, the clinical suspicion (no pre-transfer imaging) was ruled out with a post-transfer ECG-synchronized CT imaging performed at the tertiary center. Review of the pre-transfer CT images from the initial hospital was satisfactory to rule out Type A dissection in two cases. In six patients, AAS was ruled out based on repeat imaging with an ECG-synchronized CT performed at the tertiary center. One patient had a TEE to rule out AAS due to renal insufficiency.

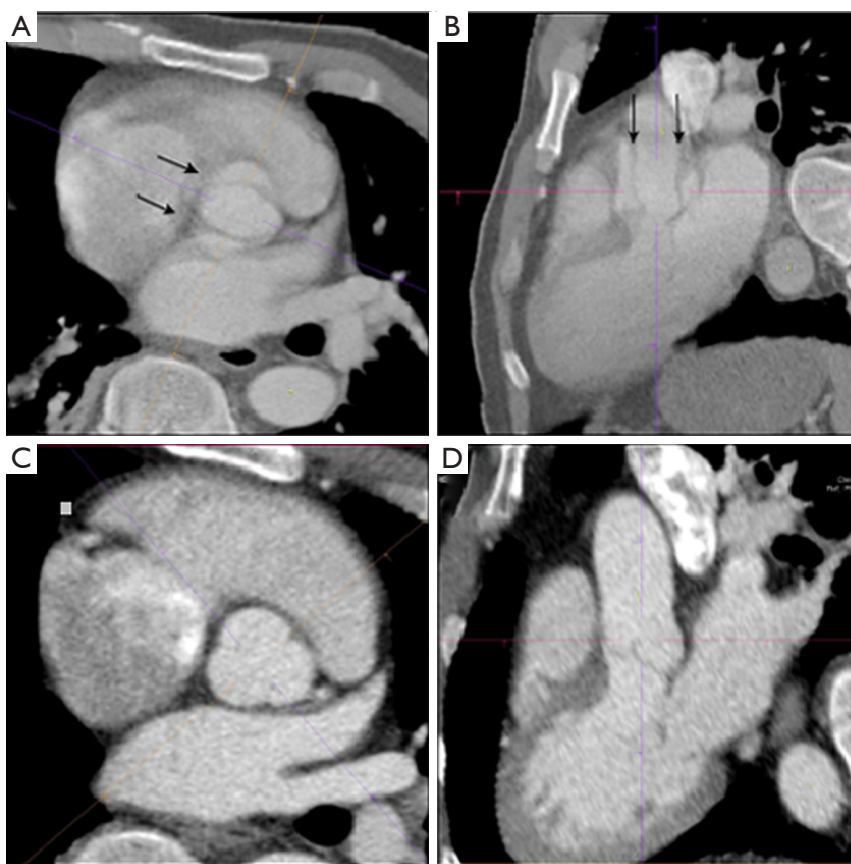
There were seven false positive suspicions of Type B

dissections. In one patient the clinical suspicion (no pre-transfer imaging) was ruled out with a post-transfer ECG-synchronized CT imaging performed at the tertiary center. Review of pre-transfer imaging from the referral hospital was considered satisfactory to rule-out Type B dissection in two patients. Four patients underwent repeat (ECG-synchronized) CT to rule out AAS (*Table 3*).

A history of prior surgical or endovascular repair was seen in 5/17 (29.4%) cases with one patient having both history of open and endovascular repair (*Table 2*). History of prior ascending aortic surgery was seen in three (30%) patients in the false positive Type A group.

## Discussion

This is the first study describing the prevalence and causes of false positive activation of emergency medical personnel for suspected AAS in an AAS network. In 11.3% of patients transferred to a tertiary center with an initial suspicion of an acute aortic dissection, the suspicion was not confirmed (false positive transfer). The unconfirmed suspicion was mainly a result of motion artifacts arising from non-ECG synchronized CT imaging that mimicked or could not clearly rule out an ascending aortic dissection. Just under one-third of the false positive transfers were associated with prior aortic surgery and 43% of false activation for Type B dissections had prior aortic intervention. These observations



**Figure 1** Example of a patient from this cohort study who presented with acute chest pain to a community hospital. The patient underwent initial non-ECG synchronized CT of the chest to rule out pulmonary embolism. Image reformation of the aortic root shows a symmetric flap-like appearance in the aortic root (arrow panel A,B). While the appearance was considered most consistent with motion artifact, in the clinical context of high clinical suspicion of an acute type A dissection, the patient was transferred to our tertiary care center and a repeat ECG-gated CTA was performed (panel C,D). In the repeat scan, there was no evidence of dissection flap and an acute aortic syndrome could be definitively excluded.

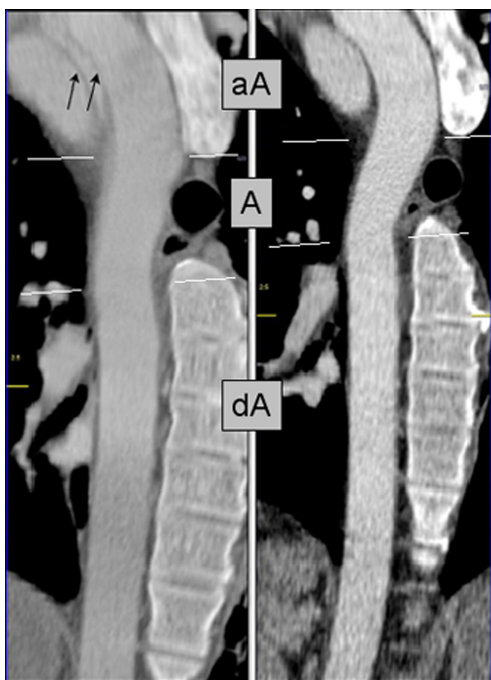
provide important insight for the future improvement of the organization and efficiency of acute aortic networks.

This reported rate of false positive activation lies between the reported false positive rate for other time sensitive emergencies including stroke treated with TPA (1.4-7%) (18,19) and STEMI (14-36%) (20,21), and should be considered in the clinical context of emergent presentation. Specifically, the referring emergency physician must weigh the risk of missing an uncertain but potentially lethal diagnosis of acute aortic dissection versus the negligible risk of transfer for further evaluation by experts.

AAS is complex, relatively rare when compared to PE and acute coronary syndrome (ACS), and can be difficult to diagnose (11,22). The emergency physician triages patients

based on clinical presentation and initial test results, weighing probabilities for various serious diseases including aortic dissection, pulmonary embolism, and ACS (23). For that reason and taking into account availability of CT protocols in most emergency departments, a chest CT primarily assessing and protocolized for PE (but also with attention for aortic dissection) is the most commonly performed study. These protocols have advantages in the evaluation of PE with regards to bolus timing and enhancement of the smaller, distal pulmonary branches; however motion of the aortic root during the cardiac cycle can create motion artifacts in a significant percentage of non-synchronized aorta studies (24-27). In contrast to prior reports of nearly 100% diagnostic accuracy of CT aorta (CTA), this study





**Figure 2** This figure shows a center-line reformation of the aorta from the same patient as *Figure 1*. The semi-automated centerline reformation shows a stretched out ‘curved MPR’ image of the aorta. On the non-ECG synchronized acquisition (left panel) the suspected flap is evident. The corresponding image from the repeat ECG-synchronized scan (right panel) provides proof that this is motion artifact. The segments of the aorta, including the ascending aorta (aA), arch (A), and descending aorta (dA) are illustrated.

also shows the potential for false diagnosis in non-ECG CTA studies (28).

Alternatively, ECG-synchronized protocols (retrospective gating or prospective triggering) reduce or eliminate motion artifact cause by the cyclic motion of the aortic root and ascending aorta (*Table 1* and *Figures 1-3*). These ECG-synchronized ‘gated’ protocols have a high sensitivity and specificity for evaluating AAS and are typically used if aortic disease of the aortic root and ascending aorta is the primary concern. However, their use is not universal for several reasons, including the cost of software, technical expertise, and increased radiation exposure (24,28). In fact, the vast majority of hospitals in our referral network do not have around-the-clock access to ECG-synchronized CT capabilities in the ED. Furthermore, for the reasons discussed above, these protocols would likely not be the first choice in patients presenting with poorly defined chest pain

syndromes.

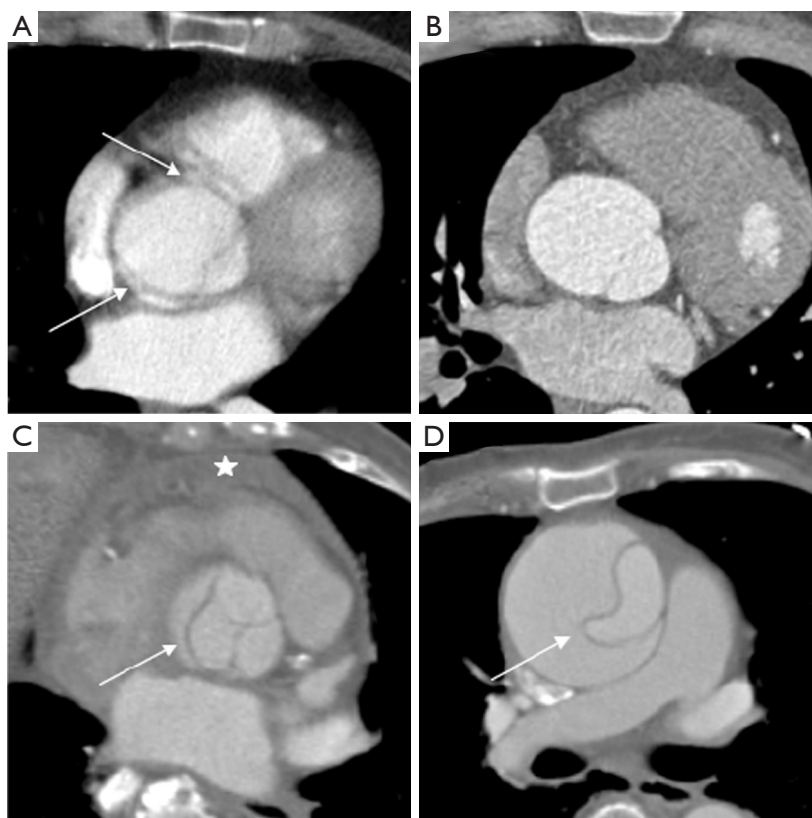
The emergent evaluation of AAS in patient populations with prior aortic surgery adds further complexity. Physicians and radiologists in community hospitals may be unfamiliar with the post-surgical anatomy of various surgical, endovascular, and hybrid repair techniques (29,30). Slightly <30% of the false positive cases occurred in patients with a prior history of aortic surgery or endovascular repair, with 60% of these cases requiring repeat imaging following transfer (*Figure 4*). In each instance the local hospital did not have access to prior imaging for comparison. Perhaps such patients should be encouraged to carry a copy of their most recent CT scan (on disc or USB drive) like we encourage many patients with chronic ST elevations to have a copy of their ECG. However, it is likely that both the referring hospital and tertiary center may still prefer patient transfer for definite diagnosis, image interpretation and close monitoring. From a tertiary center perspective, it is difficult to triage this complex disease over the phone. For example, in this analysis two separate patients presented one month post ascending aorta repair with chest pain. On both occasions, a non contrast CT performed at a local ED resulted in suspicion for new dissection. There was not access to prior CT imaging and both the initial and receiving hospitals favored transfer for definitive care. A subsequent ECG-synchronized CTA at our institution showed no change from prior CT.

Emerging concepts of telemedicine, based on shared picture archiving and communicating system (PACS) servers and cloud technology may have potential to increase communication and image sharing between referring EDs and tertiary centers (31). A regional network protocol in Minnesota has reported success with using a standard protocol with transmission of the CT images through a systems network (3). It is unclear whether the widespread use of ECG-synchronized CT and telemedicine would be safer and cost effective. Further study of this could prove useful.

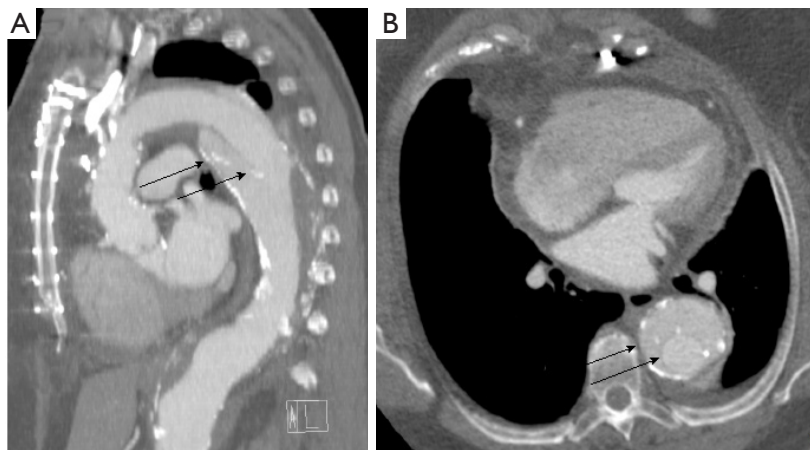
It could be argued that lack of reader experience may also contribute to the incidence of false positive suspicion of dissection. However, the number of false positive transfers in which subsequent review of the initial imaging study reversed the initial suspicion (without need for repeat imaging) was relatively limited.

### Limitations

This is a single center study with inherent bias and as such is not generalizable to all institutions or similar networks.



**Figure 3** In this figure an example of less prominent motion artifact in a non-ECG synchronized acquisition is shown (panel A). The same image obtained with ECG-synchronized acquisition shows no evidence of motion artifact (panel B). In contrast panel C and D show a type-A dissection flap in the aortic root and mid ascending segment, respectively.



**Figure 4** Patient with history of complex aortic surgery for extensive aortic aneurysmal disease. In a first stage surgery, a surgical graft was placed, including the supra-coronary ascending aorta and aortic arch. An additional part of the graft was left hanging into the dilated descending aorta for future replacement of this segment. This is called a ‘first stage elephant trunk graft’. The patient presented to a referring hospital with chest pain. The CT shows a graft hanging in the proximal descending segment (panel A, arrows). The axial image in panel B could be mistaken as a dissection flap. Correlation with operative reports and comparison with post-operative imaging studies typically allows definitive diagnosis.

Patients in this analysis were transferred by our institution's critical care transport team, therefore patients transferred by other transport teams or patients presenting directly our tertiary ER were not captured, however we believe this number to be small.

## Conclusions

The rate of false positive activation lies between the reported false positive rate for other time sensitive emergencies like stroke treated with TPA and STEMI, and has to be considered in the clinical context of emergent presentation. It is primarily driven by uncertainty secondary to motion-artifact of the ascending aorta and difficult to interpret complex anatomy following prior aortic surgery. Network-wide standardization of imaging strategies and improved consultation between referring and receiving centers may reduce the incidence of false positive activation.

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