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ORIGINAL RESEARCH

Misdiagnosis of Thoracic Aortic Emergencies Occurs Frequently Among Transfers to Aortic Referral Centers: An Analysis of Over 3700 Patients

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BACKGROUND: Acute aortic syndromes may be prone to misdiagnosis by nonreferral aortic centers with less diagnostic experience. We evaluated regional variability in these misdiagnosis trends among patients transferred to different regional quaternary care centers with presumed acute aortic syndromes.

METHODS AND RESULTS: Two institutional aortic center databases were retrospectively reviewed for emergency transfers in patients diagnosed with acute aortic dissection, intramural hematoma, penetrating aortic ulcer, thoracic aortic aneurysm, or aortic pseudoaneurysm between 2008 and 2020. Transferring diagnoses versus actual diagnoses were reviewed using physician notes and radiology reports. Misdiagnoses were confirmed by a board-certified cardiothoracic surgeon. A total of 3772 inpatient transfers were identified, of which 1762 patients were classified as emergency transfers. The mean age was 64 years (58% male). Patients were transferred from 203 medical centers by ground (51%) or air (49%). Differences in transfer diagnosis and actual diagnosis were identified in 188 (10.7%) patients. Of those, incorrect classification of Type A versus B dissections was identified among 23%, and 30% of patients with a referring diagnosis of an acute aortic dissection did not have one. In addition, 14% transferred for contained/impending rupture did not have signs of rupture. All misdiagnoses were secondary to misinterpretation of imaging, with motion artifacts (n=32, 17%) and postsurgical changes (n=44, 23%) being common sources of diagnostic error.

CONCLUSIONS: Misdiagnosis of acute aortic syndromes commonly occurred in patients transferred to 2 separate large aortic referral centers. Although diagnostic accuracy may be improving, there are opportunities for improved physician awareness through standardized web-based imaging education.

Key Words: acute aortic dissection ■ acute aortic syndrome ■ aortic aneurysm ■ misdiagnosis ■ transfer

Acute aortic syndrome (AAS) is a spectrum of emergent aortic pathologies. The collaboration of the American Heart Association and other professional societies adopted the concept into the guidelines for thoracic aortic disease in 2010.[1] In the guidelines, AAS referred to a group of acute aortic dissection (AAD), intramural hematoma, and penetrating atherosclerotic ulcer. Subsequently, the European

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CLINICAL PERSPECTIVE

What Is New?

- Misdiagnosis of acute aortic syndrome commonly occurred in patients transferred to 2 separate large aortic referral centers.

What Are the Clinical Implications?

- Recognition of common artifacts and postsurgical changes in imaging may help mitigate inappropriate transfers.
- Careful review of imaging and a multidisciplinary approach are essential.

Nonstandard Abbreviations and Acronyms

AAD	acute aortic dissection
AAS	acute aortic syndrome
UFH	University of Florida Health
UPMC	University of Pittsburgh Medical Center

Society of Cardiology guidelines added rupture of aortic aneurysm, traumatic aortic injury, inflammatory aortic disease, hereditary disease, and congenital abnormalities to the group.[2] A recent systematic review found the incidence of AAS approaching 6.0 per 100 000 patient-years, of which AAD accounts for 85% to 95%.[3] The pooled mortality of AAS was as high as 30% in the report.

The concept of "Centers of Excellence" has been widely disseminated in the United States. Lately, the concept of aortic center has gained traction, originating for ruptured abdominal aortic aneurysm. Survival difference after the treatment of ruptured abdominal aortic aneurysm has been shown between designated and nondesignated trauma centers as well as between high-volume institutions and others.[4–6] The concept of centralization has now expanded to thoracic aortic pathology.[7–10] The diagnosis and management of AAS is perhaps more complex, requiring multidisciplinary teams that may include cardiovascular surgeons, vascular surgeons, radiologists, noninvasive and interventional cardiologists, and anesthesiologists. An aortic center may provide services to treat AAS not offered at all centers, enhance research activities, and lead regional health care systems.[11]

The misdiagnosis of AAS is not uncommon, albeit the time-sensitive nature and complexity of management.[12] The presentation may mimic that of acute coronary syndrome and pulmonary or esophageal pathologies. Laboratory tests can be nonspecific. A myriad of studies investigated the diagnostic modalities to evaluate AAS, including transthoracic or transesophageal echocardiography, computed tomography, and magnetic resonance imaging. The aforementioned systematic review revealed that sensitivity and specificity of transesophageal echocardiography, computed tomography, and magnetic resonance imaging were higher than 90%.[3] Although these imaging studies are the mainstay of diagnosis, electrocardiogram-gated computed tomography is the most preferred modality because it is noninvasive and can render information quickly. However, the difficulty of prompt diagnosis remains with a concern for the availability of appropriate resources, including equipment and experienced image-reading physicians. Accordingly, we reported the incidence of misdiagnosis in 24% of transferred patients from 2002 through 2003.[13] However, that single institutional study limited generalizability. Furthermore, the contemporary trend of misdiagnosis in transferred patients is uncertain given advancements in aorta-related awareness as well as evolutions in technology and system-based practice.

The present study aims to describe the contemporary misdiagnosis rates for emergency aortic transfers and investigate the reasons for misdiagnosis in different regional aortic centers.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request. Institutional review board approval was obtained in each institution with a waiver of informed consent.

Data Collection

Both institutional transfer center databases were queried for emergency transfers in patients with a suspected diagnosis of AAD, intramural hematoma, penetrating aortic ulcer, thoracic aortic aneurysm, or aortic pseudoaneurysm. Patient inclusion was between January 2008 and May 2018 at University of Florida Health (UFH) in Gainesville, Florida and between January 2013 and March 2020 at the University of Pittsburgh Medical Center (UPMC) in Pittsburgh, Pennsylvania, respectively. Patients aged <18 years old were excluded. Outcomes of interest included the misdiagnosis and reason for misdiagnosis. The actual diagnosis was determined by experienced board-certified cardiothoracic surgeons in each institution after review of all imaging and operative records when appropriate. The misdiagnoses were categorized into 4 groups: incorrect classification of Stanford type A and B, the absence of dissection despite the referral diagnosis, the

absence of ruptured aneurysm despite the suspicion, and others. The referring physician was grouped into either (1) an emergency department physician or primary care physician, or (2) a cardiothoracic surgeon or vascular surgeon, based on the level of experience in thoracic aortic disease. After identifying misdiagnosis, transfer notes and patient charts were further reviewed to investigate the reason for misdiagnosis.

Patient Management/Transfer Protocol

When acute type A aortic dissection or ruptured/impending rupture of ascending aortic/aortic arch aneurysm was suspected or in the setting of a type B aortic dissection with malperfusion, the operating room was notified before patient arrival. Transesophageal echocardiography was used to confirm the diagnosis before chest exploration for type A aortic dissection. Transesophageal echocardiography was performed by a cardiac anesthesiologist and was reviewed with an experienced cardiothoracic surgeon. When outside imaging was unavailable or suboptimal, or endovascular repair was a potential treatment requiring detailed anatomy, diagnostic imaging was repeated. When a patient was deemed not to require emergent surgical intervention, the patient was admitted to a floor or intensive care unit for medical optimization.

RESULTS

We identified 3772 inpatient aortic-related transfers from a total of 203 referring facilities during the study period (Table 1). Overall, AAS was suspected in 1762 patients. The mean age was 64 years old. Among those transfers, 854 (48%) and 895 (51%) were transferred by air and by ground, respectively. We identified 188 (10.7%) patients who received an inaccurate diagnosis (Table 2). Among them, 134 (71%) were referred by emergency department physicians. Repeat imaging was obtained in 130 (69%). Overall, the most common misdiagnosis was the absence of dissection despite the referral diagnosis (30%, n=57). Although the wrong classification between the type of Stanford classification occurred in 44 (23%) patients, none received unnecessary surgery as the misdiagnosis was detected beforehand. Patients who were suspected of a ruptured aneurysm but did not have rupture were 14% (n=27). Among these categories, the inaccurate type of Stanford classification had the highest in-hospital mortality (20.5%) as compared with those who did not have dissection (7%) or rupture (7.4%) despite suspicion (Table 3). All of the misdiagnosis was due to imaging misinterpretation (Table 4). The reason for misinterpretation included imaging artifacts (17%, n=32) and expected postsurgical changes (23%, n=44).

Characteristics of Transfer in Each Center

A total of 784 and 978 patients with suspected AAS were transferred to UFH over 10 years and to UPMC over 7 years, respectively (Table 1). The mean age was 62 years old in USF and 66 years old in UPMC. In USF 61% of patients were male, and 56% were male in UPMC. The number of referring institutions to UFH and UPMC was 114 and 89, respectively. Ground transportation was more frequent in UFH (71%, n=557), and air transportation was predominant in UPMC (35%, n=338), which may reflect the difference in the distribution of hospitals or patient populations in the region. The frequency of misdiagnosis was nearly 10% in both centers despite the significant geographic differences (Table 2). Repeat imaging was obtained in 72% and 67% of patients in UFH and UPMC, respectively. Among patients with misdiagnosis, 82% (n=73) were referred by emergency department physicians to UFH, whereas only 51% (n=61) were transferred from emergency department physicians to UPMC. The category of misdiagnosis was equally distributed in UFH, ranging from 20% to 30%. In contrast, the absence of dissection was frequently seen in UPMC (34%, n=34). All misdiagnosis was secondary to imaging misinterpretation. Postsurgical changes were the most common reason for imaging misinterpretation in both centers (Table 4).

DISCUSSION

This study was an observational study that included 2 different institutions across 2 different geographic regions. We found the following: (1) 10.7% of misdiagnosis, (2) most misdiagnoses were referred by nonsurgeon physicians, (3) reason for misdiagnosis was imaging misinterpretation, and (4) postsurgical changes were a common reason for misinterpretation.

Table 1. Characteristics of Transfers for Patients with Presumed Acute Aortic Syndrome

Variables	UFH n=784	UPMC n=978	Total n=1762
Mean age, y	62	66	64
Male sex, %	478 (61)	550 (56)	1028 (58)
Transferred by air, %	227 (29)	627 (64)	854 (48)
Transferred by ground, %	557 (71)	338 (35)	895 (51)
Number of referring facilities	114	89	203

UFH indicates University of Florida Health; and UPMC, University of Pittsburgh Medical Center.

Table 2. Misdiagnosis of Transferred Patients

Variables	UFH n=89	UPMC n=99	Total n=188
Referral by emergency department physicians	73 (82)	61 (51)	134 (71)
Repeated scans	64 (72)	66 (67)	130 (69)
Category of misdiagnosis			
Incorrect classification of Type A/Type B	24 (27)	20 (20)	44 (23)
Suspected dissection but no dissection	23 (26)	34 (34)	57 (30)
Suspected rupture but no rupture	18 (20)	9 (9)	27 (14)

UFH indicates University of Florida Health; and UPMC, University of Pittsburgh Medical Center.

Diagnosis of AAS may be challenging particularly in physicians who are inexperienced with AAS.[12] In the present study, misdiagnosis was not uncommon and observed similarly between 2 separate geographic regions suggesting that misdiagnosis of AAS may be a nationwide issue. We did, however, find improvement in frequency of misdiagnosis from 24% to 10% compared with our previous reports.[13] Misdiagnosis may occur in the setting of either imaging misinterpretation or high-clinical suspicion without appropriate imaging resources. All of the misdiagnosis was imaging misinterpretation. Postsurgical changes were the frequent cause of misinterpretation. After aortic surgery, anatomy may be altered, being confused for AAD flap or graft dehiscence, and surgical material may mimic pseudoaneurysm.[14] Expected periaortic fluid and wall thickening after stent placement may appear as a ruptured aneurysm.[15] Acknowledging that many misdiagnoses were referrals from emergency department physicians, it suggests the importance of surgical anatomy understanding on imaging interpretation.[16–19]

A debate arises whether the 10% rate of misdiagnosis is unacceptably high. Certainly, "overdiagnosis" or misdiagnosis of acute coronary syndrome, pulmonary embolism, or esophageal perforation may harm patients. Additionally, mobilization of the aortic team, including staff in the intensive care unit and operating room, for misdiagnosis may add unnecessary workload and costs. Clinicians always attempt to pursue an accurate diagnosis. Cost analysis may be warranted to reveal an acceptable false positive rate of misdiagnosis in the future. On the other hand, we also believe a certain amount of misdiagnosis within aortic disease is acceptable during a transfer after excluding other conditions. This is because the downside of underdiagnosing AAD may lead to an exceedingly high rate of morbidity or mortality. In the present study, most of the misdiagnosis was the incorrect categorization of Stanford classification and misinterpretation between AAD and aneurysm. Irrespective of these misinterpretations, initial management of AAS is impulse control, pain management, and consultation and transfer to a referral aortic center.[20] If a referring physician is concerned for the accurate diagnosis and may be withholding consult or transfer for that reason, the hesitation may perhaps cause delay of treatment and subsequent detrimental outcomes. Without appropriate experience and certainty of non-AAS diagnosis, a referral should not be withheld. However, more broadly used web-based image sharing platforms may allow outside consultation and expedite appropriate transfers.

More than half of the patients in this study required repeat imaging. One of the primary reasons to repeat imaging is suboptimal outside imaging. Most computed tomography scans to diagnose AAS were pulmonary embolism protocol based, which does not allow for appropriate contrast in the thoracic aorta. Although these imaging methods were not ideal for diagnosing AAS, an imaging protocol depends on the differential diagnosis, and it is also important to exclude other possible diagnoses at a referral center before transfer in our opinion. It is not straightforward to define the minimal requirement for imaging protocol at this point. We found artifact resulted in almost 20% of misdiagnoses whereas our previous study detected only 1 patient with the pulsatile artifact. This increased incidence may be attributed to the increased use of

Table 3. Outcomes for Misdiagnosis in Subset of Categories

Outcomes	UFH n=65	UPMC n=63	Total n=128
Incorrect classification of Type A/Type B	24	20	44
In-hospital mortality	3 (12.5)	6 (30)	9 (20.5)
Suspected dissection but no dissection	23	34	57
In-hospital mortality	0	4 (11.8)	4 (7)
Suspected rupture but no rupture	18	9	27
In-hospital mortality	0	2 (22.2)	2 (7.4)

UFH indicates University of Florida Health; and UPMC, University of Pittsburgh Medical Center.

Table 4. Reason for Misdiagnosis

Reasons	UFH n=89	UPMC n=99	Total n=188
Imaging artifacts	14 (16)	18 (18)	32 (17)
Postsurgical changes	22 (25)	22 (22)	44 (23)

UFH indicates University of Florida Health; and UPMC, University of Pittsburgh Medical Center.

imaging modalities and our realization of this error as receiving centers. Aortic pulsatile movement may create a pseudo-intimal flap. Electrocardiogram-gating can alleviate motion artifacts, but the protocol is not always available at most emergency departments.[2,21] Alternatively, we repeated imaging for preoperative anatomic evaluation with an appropriate protocol, which was especially vital before endovascular treatment for appropriate orthogonal sizing in the setting of type B aortic dissection. This may also be because of frequent diagnoses of endoleaks after thoracic endovascular aortic repair.[22–25]

Misdiagnosis of transfer patients is a subject of interest outside of AAS diagnoses. A retrospective study from a level 1 trauma center in the Netherlands examined their 251 severely injured transferred patients from 2010 through 2015.[26] The authors discovered 150 new diagnoses after the transfer. Among those new diagnoses, 32 (21%) were misdiagnoses that were diagnosed by reexamination of outside imaging. They suggested an organized protocol to review outside imaging when a transfer patient is received. Some clinicians may rely solely on radiology reading because of their diffidence or more commonly for medicolegal reasons when transferring patients. However, it is well known that a radiologist interpretation may also contain errors.[27] Feedback of diagnoses to referring hospitals is commonly overlooked but should be highly encouraged to enhance regional quality improvement. A multidisciplinary conference, including emergency department and radiologists, may introduce an opportunity to share misdiagnosis and accurate diagnostic interpretation of AAS.

Given the complexity of diagnoses and subsequent management in AAS, other diagnostic algorithms have been investigated. The American Heart Association and other societies introduced a risk stratification for suspected dissection to the guidelines according to clinical features and presentations.[1] Subsequently, a retrospective study from the International Registry of AAD database investigated the diagnostic value of the aortic dissection detection risk score and showed the sensitivity of 95.7%.[28] D-dimer is another potential tool for risk stratification. An international multicenter prospective study, the IRAD-Bio (International Registry of Acute Aortic Dissection–Substudy on Biomarkers) study, demonstrated that a cutoff level of 500 ng/mL has a sensitivity of 96% to rule out aortic dissection within 24 hours from the onset of symptoms.[29] As a synopsis, the ADVISED (Acute Aortic Dissection Risk Score Plus D-Dimer in Suspected Acute Aortic Dissection) study examined the combination of the risk score and D-dimer. The risk score of 0 or 1 with D-dimer <500 ng/mL showed a failure rate of 0.3% to rule out AAS.[30] A prospective study is needed to see whether these integrated approaches reduce misdiagnosis of ASS or unnecessarily imaging in an outside hospital.

Development of regional systems may be suggested from these data. Transfer of imaging has been adapted in certain institutions while maintaining appropriate patient information security. These systems include a health information exchange, regional picture archiving and communication system, regional image exchange networks, and interoperable electronic health records. These technologies may reduce unnecessary patient transfers, costs, and repeat imaging.[31,32] A recent meta-analysis investigated image sharing system and reviewed 17 articles.[32] Among them, 58.8% of the technologies used were health information exchange or electronic health records. The study revealed that image sharing technology was associated with reducing repeat imaging. A future study may be suggested to evaluate whether these technologies decrease the amount of transfer. Although imaging misinterpretation resulted in all misdiagnosis cases in the present study, using other clinical/diagnostic algorithms may lower pretest probability and assist in ruling out AAS at a referring facility appropriately. When a transferred patient is stable enough, a structured review of imaging from referring institutions by an experienced multidisciplinary team is highly recommended. Lastly, specific education on postsurgical imaging may be advocated given the recognition of potential nationwide misdiagnosis issues.

Several limitations exist in the present study. First, we lack detailed information regarding referral centers, including the availability of radiologists reading, the presence of cardiothoracic surgeons or vascular surgeons. Although identifying a predictor of misdiagnosis was an interesting topic, this limitation precluded further analysis of misdiagnosis as important factors for misdiagnosis were perhaps a combination of the aforementioned limitations and physician characteristics including years from the graduation of residency, the experience level of AAS, and whether it was during day shift or night shift. A future prospective study is warranted to answer this question. Second, there was no standardized algorithm to identify misdiagnosis after a patient transfer, given the retrospective nature of the study. A decision for repeating a scan is the discretion of each surgeon. Third, we are unable to

obtain information about whether patients who were not transferred had AAS at an outside hospital.

In conclusion, misdiagnosis of AAS commonly occurred in patients transferred to 2 separate large aortic referral centers. Although diagnostic accuracy may be improving, there are opportunities for improved physician awareness through standardized web-based imaging education. Although accurate diagnosis is ideal, the transfer of patients by nonexperienced clinicians should not be discouraged when AAS cannot be excluded.

ARTICLE INFORMATION

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