Misdiagnosis of aortic dissection: A systematic review of the literature

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Declaration of Interest statement: Christian Mallen is funded by the National Institute for Health Research (NIHR) Applied Research Collaboration West Midlands, the National Institute for Health Research (NIHR) School for Primary Care Research and a National Institute for Health Research (NIHR) Research Professorship in General Practice (NIHR-RP-2014-04-026) for this research project. The views expressed are those of the author(s) and not necessarily those of the (partner organization), the NHS, the NIHR or the Department of Health and Social Care. The Keele School of Medicine have received funding from BMS to

support a non-pharmacological atrial fibrillation screening trial. None of the other authors have received any funding for this work.

Abstract

Background: Aortic dissection is a rare but potentially catastrophic condition. Misdiagnosis of aortic dissection is not uncommon as symptoms can overlap with other diagnoses.

Objective: We conducted a systematic review to better understand the factors contributing to incorrect diagnosis of this condition.

Methods: We searched MEDLINE and EMBASE for studies that evaluated the misdiagnosis of aortic dissection. The rate of misdiagnosis was pooled and results were narratively synthesized.

Results: A total of 12 studies with were included with 1663 patients. The overall rate of misdiagnosis of aortic dissection was 33.8%. The proportion of patients presenting with chest pain, back pain and syncope were 67.5%, 24.8% and 6.8% respectively. The proportion of patients with pre-existing hypertension was 55.4%, 30.5% were smokers while the proportion of patients with coronary artery disease, previous cardiovascular surgery or surgical trauma and Marfan syndrome was 14.7%, 5.8%, and 3.7%, respectively. Factors related to misdiagnosis included the presence of symptoms and features associated with other diseases (such as acute coronary syndrome, stroke and pulmonary embolism), the absence of typical features (such as widened mediastinum on chest X-ray) or concurrent conditions such congestive heart failure. Factors associated with more accurate diagnosis included more comprehensive history taking and increased use of imaging.

Conclusions: Misdiagnosis in patients with an eventual diagnosis of aortic dissection affects 1 in 3 patients. Clinicians should consider aortic dissection as differential diagnosis in patients with chest pain, back pain and syncope. Imaging should be used early to make the diagnosis when aortic dissection is suspected.

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Keywords: aortic dissection; diagnosis; misdiagnosis; outcomes

Article summary

1. Why is this topic important?

Aortic dissection is a rare but potentially catastrophic condition and misdiagnosis of aortic dissection is not uncommon.

2. What does this study attempt to show?

We conducted a systematic review to better understand the rate of misdiagnosis and factors contributing to incorrect diagnosis of aortic dissection.

3. What are the key findings?

Over 1 in 3 patients with aortic dissection are misdiagnosed. Patients with aortic dissection present with chest pain, back pain and syncope and many are smokers with pre-existing hypertension who have coronary artery disease, previous cardiovascular surgery or surgical trauma and Marfan syndrome. Factors related to misdiagnosis included the presence of symptoms and features associated with other diseases (such as acute coronary syndrome, stroke and pulmonary embolism), the absence of typical features (such as widened mediastinum on chest X-ray) or concurrent conditions such congestive heart failure. Factors associated with more accurate diagnosis included more comprehensive history taking and increased use of imaging.

4. How is patient care impacted?

Clinicians should consider aortic dissection as differential diagnosis in patients with chest pain, back pain and syncope. Imaging should be used early to make the diagnosis when aortic dissection is suspected.

Introduction

Aortic dissection (AD) is a rare disorder characterized by a tear in the layers of the aortic wall[1,2]. It is described as acute if presenting within 14 days, or chronic when the patient presents beyond 90 days[3]. Essential in the diagnosis of aortic dissection is its classification which is most commonly according to the Stanford or DeBakey classification[4]. The Stanford criteria divides aortic dissections into type A which involves the ascending aorta and type B which only involves the descending aorta[4]. Using the DeBakey criteria, type 1 involves the ascending aorta to at least the aortic arch and type 2 originates and is limited to the ascending aorta[4]. Type 3 begins in the descending aorta and extends distally[4]. Acute AD is associated with high mortality rates, cited between 1% and 2% per hour after the onset of symptoms[5]. Although the prognosis is better for those with chronic AD, a shorter life expectancy has been reported when compared with the general population[2]. Timely diagnosis of AD enhances a patient's chance of survival, and aversion of serious complications. The optimal management of this condition includes fastidious management of blood pressure, serial imaging of the aorta and surgical or endovascular repair where feasible[6].

Early diagnosis of AD may be challenging. Other more common conditions (acute coronary syndromes or pulmonary embolism) share a similar symptom profile with dissection, the correct diagnosis of the aortopathy is often made late once the other diagnoses have been ruled out. Many studies highlight these difficulties of correct and timely diagnosis. Misdiagnosis during initial assessment in the emergency department has been shown to be as high as 78%, with a wide array of conditions such as acute coronary syndrome, neurological, respiratory and gastrointestinal disorders being the most frequent alternative diagnoses[7]. Other studies show rates of misdiagnosis to be lower around 30% with clinical findings such as lack of widened mediastinum or presence of congestive cardiac failure being predictive of misdiagnosis[8]. Studies further highlight the diagnostic challenge suggesting those that attend

hospital as 'walk-in' patients with acute AD are more likely to be misdiagnosed[9]. It could also be added that about 50% of the acute type A ADs remain undetected as per autopsy results indicating that its incidence might be even higher in real life[10]. In view of the importance of understanding misdiagnosis of AD, we conducted a systematic review of the literature to understand how misdiagnosis is defined, how common it occurs, what factors are associated with misdiagnosis and whether it impacts patient outcomes.

Methods

This review was prepared in accordance to the recommendations of the MOOSE checklist[11].

Study inclusion criteria

We selected studies that evaluated the misdiagnosis of AD. Those included had to report one or more of the following: i) the number of misdiagnoses of AD cases within a defined population, ii) factors that differ between misdiagnosed AD, iii) outcomes associated with misdiagnosed AD or iv) reasons for misdiagnosed AD. There was no restriction on the definition of misdiagnosis of AD, and it was one of the aims to determine how it was defined in the literature. Outcomes included the rates of misdiagnosis and factors associated with the misdiagnosis. There was no restriction based on study design, or language of the report but original data had to be presented.

Search strategy

We searched MEDLINE and EMBASE using OVID with no date or language restriction in 24 March 2021. The exact search terms were: (missed aortic dissection) OR (missed diagnos* adj3 aortic dissection) OR (unrecogni* adj1 aortic dissection) OR

(misdiagnosis and aortic dissection) OR (missed diagnosis and aortic dissection). These search terms are a modified version of that conducted from a previous systematic review of misdiagnosis in acute myocardial infarction[11]. We reviewed the bibliography of relevant studies and reviews for additional studies that met the inclusion criteria.

Study selection and data extraction

Two reviewers (CSK and SL) screened all titles and abstracts retrieved from the search for studies that met the inclusion criteria. The studies that potentially met the inclusion criteria were reviewed and the final decision to include or exclude studies was made by consensus. The data extraction was carried out by SL and CSK and independently checked by CWW. Data was collected on study design, country of study origin, year, sample size, mean age, % male, inclusion criteria, definition of missed AD, rate of missed AD, patient outcomes, initial diagnosis of misdiagnosis and factors associated with misdiagnosis.

Risk of bias assessment

Methodological quality assessment of the included studies was conducted with consideration of the following: i) study design, ii) reliability of ascertainment of AD, iii) loss to follow up or missing data, iv) generalizability to a general AD cohort. For the definition of AD, studies were considered high quality if they evaluated the participants using imaging of the aorta to confirm the diagnosis of all patients. This was carried out by one reviewer (SL), and checked independently by another reviewer (CWW).

Data analysis

Data was extracted into pre-designed and piloted tables and the study findings were narratively synthesized. Considerable heterogeneity in the study methodology meant that we did not perform meta-analysis. The collective rate of misdiagnosis, symptoms among patients and co-existing conditions were determined by pooling across the studies.

Results

A total of 12 studies were included in the analysis after review of the potentially relevant studies identified on our search (Supplementary Figure 1)[7-9,13-20].

The study design patient characteristics and patient inclusion criteria are shown in Table 1. There were a total of 1663 patients included in this review and the mean age and proportion of male patients across 11 studies with this information was 60 years and 69.1% respectively. These studies took place in emergency departments and inpatient settings.

The quality assessment of the included studies is shown in Table 2. All the studies were retrospective in design. Ten studies reported clear ascertainment of AD and 9 had reliable ascertainment of outcomes. Aside from 2 studies where there was a significant degree of missing data, the other 10 studies had no missing data and only 2 studies were not generalizable to a contemporary population with AD because they were conducted over 20 years ago.

The description of patient symptoms, comorbidities, methods of evaluation and type of dissection are shown in Table 2. The proportion of patients with chest pain, back pain and syncope among the studies that reported these outcomes were 67.5%, 24.8% and 6.8% respectively. The proportion of patients with hypertension was 55.4% and the proportion of smokers were 30.5% while the proportion of patients with coronary artery disease, previous cardiovascular surgery or surgical trauma and Marfan syndrome was 14.7%, 5.8%, and 3.7%, respectively. Most studies used a combination of history, examination and investigations to evaluate patients. The proportion of patients with type A AD was 80.3%. Further descriptions of symptoms and comorbidities are outlined in Supplementary Table 2.

The definition of misdiagnosis of AD, setting, rate of misdiagnosis and conditions that were identified instead of AD is shown in Table 3. There was no consistent definition for

misdiagnosis of AD and 8 studies took place in emergency departments while 4 studies took place among inpatients. The overall rate of misdiagnosis of AD was 33.8% (562/1663). The range of misdiagnosed AD ranged from 14.1% to 78.3%. The most conditions that AD was mistaken for was acute coronary syndrome, stroke and pulmonary embolism.

Other comparisons of patients with misdiagnosis and correct diagnosis is shown in Supplementary Table 3. Patients with misdiagnosis had longer time to correct diagnosis and were more frequently found to have ECG changes or elevated cardiac troponins. Mortality was reported according to misdiagnosis or correct diagnosis in 5 studies and all of them reported no significant difference at longest time of follow up.

Five studies examined predictors of misdiagnosis of AD (Table 4). Hansen et al found that age and anterior chest pain were associated with increased odds of misdiagnosis[14]. Concurrent signs of heart failure and absence of widened mediastinum of chest X-ray was highly associated with misdiagnosis in the study by Ibrahim et al[15]. Kurayashi et al found that patient who were walk-in (patients not admitted via ambulance) and those with anterior chest pain were more likely to be misdiagnosed[8]. Ohle et al suggested that asking more questions about pain was associated with correct diagnosis[16]. In the study by Zaschke et al patients who had pain in the lumbar region, sweating and any paresis were associated with misdiagnosis of AD[7].

Discussion

AD is misdiagnosed 1 in 3 patients on presentation, where this proves to be the eventual diagnosis. The rate of misdiagnosis varies depending on the setting and study methodology. This is partly explained by the inconsistent definition used for misdiagnosis. Patients who are misdiagnosed have symptoms which mimic those of other disease such as in

acute coronary syndrome with ECG changes, anterior chest pain or elevated troponins. Misdiagnosis is also associated with lack of widened mediastinum on chest x-ray, mild symptoms and lack of pain. The evidence from a few studies suggests that incorrect diagnosis is not necessarily associated with worse outcomes compared to correct initial diagnosis. However further research is required to better understand how misdiagnosis and delay in diagnosis of AD could be reduced.

The individual rate of misdiagnosis varied across the included studies for a few reasons. First, the included studies did not use a consistent definition for misdiagnosis. Zaschke et al report that the rate of misdiagnosis as 78.3%[8], in contrast with other studies reporting rates of 15-39%. In Zaschke et al[8], this was defined by cases of patients where AD was not considered in the initial diagnosis of the first physician assessing the patient, and this was also prior to any further work up including imaging and invasive diagnostics. This is in contrast with the other studies where misdiagnosis was assumed if AD was not included in initial diagnosis after completion of imaging and other work up. With this further information it could be expected that the rates of misdiagnosis would be lower. The other major contributor to differences in rates between studies is heterogeneity in the studied population. The observed variation in the rates of known risk factors for AD which ranged from 5% to 71% for hypertension, 1% to 12% for Marfan syndrome and 0% to 21% for previous cardiac surgery or surgical trauma.

The rate of misdiagnosis across the studies is high with the most frequent alternative diagnosis being acute coronary syndrome. This is likely due to patients having symptoms which mimic those of acute coronary syndrome such as chest/trunk pain along with clinical features such as troponin rise and ST-segment elevation on electrocardiogram. This is combined the incidence of acute coronary syndrome being around 200 times higher[20] than acute AD and the time clinical urgency of both diseases requiring prompt decision making.

Our results suggest clinicians should consider AD in the differential diagnoses of patients with acute coronary syndrome and use appropriate imaging tests to rule out the disorder and avoid delaying treatment or prescribing inappropriate therapy.

In those patients presenting with atypical symptoms, a diagnosis of dissection is more likely to me missed. Kurabayashi et al[9] found the absence of widened mediastinum to be predictive of a misdiagnosis, a feature along with abnormal aortic contour shown to be useful in the diagnosis of AD[22]. Studies show that around 20% of patients diagnosed with AD however do not have these features[23] again demonstrating the diagnostic challenge. The problem is further highlighted by Ibrahim et al[16] who found that patients with concurrent signs of congestive cardiac failure were more likely to be misdiagnosed. Reported in the literature as a complication of AD[24] with an atypical presentation, clinicians should consider AD in patient presenting with congestive cardiac failure especially if acutely occurring and otherwise unexplained[16]. Patients presenting with mild symptoms were also found to be at greater risk of misdiagnosis. Kurabayashi et al[9] found that patients who attended the emergency department as a 'walk in' were significantly more likely to misdiagnosed compared to those attending through ambulance or other means. This again demonstrates the diversity in presentation of patients with AD with milder presentations perhaps not associated with expected critical illness of the condition. Other research suggests that the incidence of pain free AD may be as high as 17%[25] which may lead to patient attending with mild symptoms and being at risk of misdiagnosis.

Distinguishing type A and type B aortic dissection when considering misdiagnosis is important because symptoms, management and outcomes differ depending on the type. While both types may present with shortness of breath and loss of consciousness, type A aortic dissections present typically with a sudden onset of chest pain which may radiate to the neck, jaw or back whereas type B dissection present with sudden onset of severe tearing pain in the

back[26,27]. Once identified type A dissection requires urgent surgery with reconstruction of the aorta with or without aortic valve replacement whereas type B dissections may be managed without surgery in the absence of complications. Moreover, in-hospital mortality for Type A dissection has been reported to be 32.5%[28] compared to 10.6% for type B dissection[29].

The 2010 guidelines provide class I recommendation that patients that complain of symptoms that may represent acute thoracic aortic dissection should establish risk of disease with specific questions regarding medical history, family history, pain features and examination in order to consider if patients have high-risk conditions or historical features, high-risk chest, back or abdominal pain and high risk examination features[30]. Applying this comprehensive evaluation approach should be recommended to reduce the risk of misdiagnosis of aortic dissection and further help identify any underlying conditions that may be the risk factor predisposing the acute aortic dissection. In order to make it easier to implement in clinical practice, a risk score based on 12 proposed clinical markers was developed and shown to be a highly sensitive clinical tool for the detection of acute aortic dissection[31]. Such tools should be utilized to minimize the risk of mistaken other conditions for patients who have underlying acute aortic dissection.

A few explanations may account for the surprising observation that mortality was not significantly affected by misdiagnosis in patients with AD. Mortality in AD is high with variable presentation as some patients are peri-arrest at presentation and others more stable. It is possible that even with initial misdiagnosis patient will then go on to deteriorate and this leads to an eventual diagnosis. For example, if initial diagnosis is acute coronary syndrome and a coronary angiogram is performed subsequently showing normal coronaries a dissection should be suspected and it may prompt urgent referral for aortic imaging so the patients are less likely to suffer catastrophic consequences. The same applies to AD mistaken for pulmonary embolism except the AD may be visible on CTPA and observation that there is no

PE may lead to observing features of dissection. It is possible that stable patients present early with mild symptoms when their diagnosis is not yet recognized and represent later with more severe symptoms. The effect of this is that patients who have severe symptoms will always present, but some patients may present earlier because they had mild symptoms which they recognized not to ignore.

There are a number of key points in relation to reducing rates of misdiagnosis identified in the studies. Ohle et al[17] suggests that a more detailed history taking results in reduced rates of misdiagnosis. Specifically in relation to pain, asking two or more questions relating to character, onset, severity, duration and radiation of pain led to more accurate diagnosis[32]. This is in line with other research suggesting scoring tools which evaluate characteristics of pain such as the Acute Aortic Dissection Risk Score can reduce rates of misdiagnosis[33]. Kurabayashi et al[9] also highlighted how crucial imaging is in the correct diagnosis of AD with number of imaging studies performed being fewer in misdiagnosed than correctly diagnosed patients. This is likely due to patients not receiving imaging if AD is not suspected and this remaining the most sensitive method of accurate diagnosis[34]. In addition, Ibrahim et al[15] demonstrate how the availability of imaging such as contrast enhanced computed tomography or 24 hour specialist cover can result in a 17.3% increase in proportion of correctly diagnosed acute AD. Likewise, low-cost and fast solutions such as point-of-care ultrasound can facilitate diagnosis of AD and guide further treatment, with downstream effects similar to more advanced imaging methods such as CT angiography[35].

An important consideration is whether misdiagnosis should be considered a problem. It may be reasonable to expect that all emergency centers will have some degree of misdiagnosis of patients who have AD. It is likely that some cases with classical symptoms will get promptly identified but some present atypically and may be misdiagnosed. Literature suggests that features of other diagnosis like ECG change and troponin rises as well as heart

failure, anterior chest pain or mild symptoms will increase the likelihood of making a misdiagnosis. On the other hand, presence of tearing/ripping pain, hypotension, pulse deficit, neurologic deficits and a new murmur can help in making a suspicion of AD[32]. It is important for clinicians to be aware of this important diagnosis not to miss and that it can present with atypical features.

This review has several limitations. First, all of the studies included were retrospective in nature which has an inferior level of evidence compared to prospective studies as it may be at risk of selection and recall bias. Secondly, there is no agreed definition of misdiagnosis of AD which is an important consideration when interpreting the pooled results. Finally, case-by-case evaluation for why misdiagnosis occurred was not available from the reported studies and this information is important to inform how clinical practice could improve. For example, it is possible that the misdiagnosis or delay may be an error in clinical judgement but it may also be a consequence of other health service factors such as the availability of diagnostic tests at the center where the patient present to.

In conclusion, misdiagnosis of AD is common in both emergency department and inpatient settings with rates between 14 to 78%. The majority of cases are misdiagnosed due to common features with other conditions such as acute coronary syndrome, pulmonary embolism and stroke but some may be associated with an absence of typical features such as widened mediastinum on chest X-ray and mild symptoms such as lack of pain. While the diverse presentations for patients with AD may mean there is always some degree of misdiagnosis, clinicians can reduce this by undertaking a thorough history, and maintaining an index of suspicion for this condition in the differential diagnosis.

Acknowledgement: None.

List of Tables

Supplementary Material

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Table 1: Study design, patient characteristics and inclusion criteria in included studies

Study ID	Study design; Country; Year	No. of patients	Mean age	% male	Patient inclusion criteria
Asouhidou 2009	Retrospective cohort study; Greece; 2000 to 2004.	49	54.8	83.7	Patients referred or admitted to hospital with eventual diagnosis of acute aortic dissection.
Chua 2012	Retrospective cohort study; Singapore; 1998 to 2008.	68	54.9	79.4	Patients attended emergency department with diagnosis of aortic dissection, or death within 14 days due to aortic dissection.
Hansen 2007	Prospective and retrospective cohort study; Canada; 2000 to 2004.	66	62	76	Patients admitted with acute aortic syndromes confirmed by imaging, operative findings or post-mortem.
Ibrahim 2020	Retrospective cohort study; Singapore; 1998 to 2014.	145	57.3	70.3	Patients attended emergency department with discharge diagnosis of acute aortic dissection, or patients with acute aortic dissection as cause of death who presented to emergency department within 5 days of death.
Kurabayashi 2011	Retrospective cohort study; Japan; 2005 to 2010.	109	67.6	65.1	Patients visiting emergency department with eventual diagnosis of acute aortic dissection confirmed by imaging.
Ohle 2019	Retrospective cohort study; Canada; 2002 to 2014.	194	65.3	65.5	Patients who presented to two tertiary care emergency department or a regional cardiac referral center with acute onset non-traumatic truncal pain and a new diagnosis of acute aortic dissection.
Pare 2016	Retrospective cohort study; USA; 2013 to 2015.	32	61.5	53	Patients treated in the emergency department of 3 hospitals with diagnosis of acute aortic dissection at discharge or on autopsy. Only those with Stanford type A dissection included.
Patel 1997	Retrospective case review; USA; published 1997.	25	-	-	Patients with aortic dissection or questionable dissection by either TTE and/or TEE with diagnosis later confirmed by surgery, autopsy or CT/MRI.
Pourafkari 2016	Retrospective cohort study; USA; 2004 to 2015.	289	58.1	63	Patients admitted to the teaching heart center affiliated with Tabriz University of Medical Sciences with a final diagnosis of acute type A aortic dissection.
Scholl 1999	Retrospective cohort study; USA; 1985 to 1997.	75	65.5	65.3	Patients with acute or chronic type A aortic dissection treated at one center.
Zaschke 2020	Retrospective cohort study; Germany; 2012 to 2016.	350	63.2	63.4	Patients with non-iatrogenic type A aortic dissection transferred to a tertiary center for surgical treatment.
Zhan 2011	Retrospective cohort study; China; 2003 to 2008.	361	49.8	75.6	Patients with aortic dissection admitted to a tertiary hospital.

TTE=transthoracic echocardiography, TEE=transesophageal echocardiography, CT=computed tomography, MRI=magnetic resonance imaging

Table 2: Key symptoms, comorbidities, evaluation methods and type of dissection evaluated in included studies

Study ID	Chest pain	Back pain	Syncope	Hypertension	Marfan syndrome	Smoker	Coronary artery disease	Previous cardiac surgery or surgical trauma	Evaluation methods	Type of dissection
Asouhidou 2009	18/49 (36.7%)	-	3/49 (6.1%)	15/49 (30.6%)	1/49 (2.0%)	8/49 (16.3%)	-	0/49 (0%)	History, examination, ECG, CXR, bloods, TTE, contrast CT, coronary angiography in the emergency room.	DeBakey Type I 29/49, Type II 14/49, Type III 6/49.
Chua 2012	41/68 (60.3%)	23/68 (33.8%)	8/68 (11.8%)	41/68 (60.3%)	2/68 (2.9%)	-	-	4/68 (5.9%)	History, examination, CXR, ECG.	Type A, 43/68, Type B 22/68, Indeterminate 3/68.
Hansen 2007	48/66 (72.7%)	30/66 (45.5%)	6/66 (9.1%)	46/66 (69.7%)	8/66 (12.1%)	19/66 (28.8%)	17/66 (25.8%)	14/66 (21.2%)	History, examination, ECG, CXR, CT.	Type A 43/66, Type B 20/66, intramural hematoma 3/66.
Ibrahim 2020	79/145 (54.5%)	47/145 (32.4%)	11/145 (7.6%)	86/145 (59.3%)	6/145 (4.1%)	-	-	9/145 (6.2%)	History, examination, CXR, ECG, CT.	Type A 88/145, Type B 54/145, indeterminate 3/145.
Kurabayashi 2011	50/109 (45.9%)	64/109 (58.7%)	-	63/109 (57.8%)	-	63/109 (57.8%)	8/109 (15.6%)	2/109 (12.8%)	History, examination, blood test, CXR, CT, ECG, MRI.	Type A 42/109, Type B 67/109.
Ohle	-	-	-	-	-	-	-	-	History,	Type A

2019									examination, CT, MRI, TEE.	114/194, Type B 80/194.
Pare 2016	-	-	-	21/32 (65.6%)	1/32 (connective tissue disease) (3.1%)	16/32 (50.0%)	-	2/32 (6.3%)	History, examination, CXR, ECG, TTE, CT.	Type A 32/32.
Patel 1997	3/6 (50.0%)	1/6 (16.7%)	-	-	-	-	-	-	History, examination, TTE, TEE, MRI, CT.	Only 6 cases presented Type 1 4/6. No dissection 2/6.
Pourafkari 2016	133/189 (70.4%)	-	9/189 (dizziness and syncope) (4.8%)	120/189 (63.5%)	10/189 (bicuspid/ Marfan syndrome) (5.3%)	62/189 (32.8%)	26/189 (13.8%)	12/189 (6.3%)	History, examination, bloods, ECG, TTE, TEE, CTA, aortography	Type A 189/189.
Scholl 1999	-	-	-	-	-	-		-	Unclear.	Type A 75/75.
Zaschke 2020	240/350 (68.6%)	99/350 (thoracic and lumbar spine pain) (28.3%)	-	250/350 (71.4%)	[illegible]/350 (0.9%)	102/350 (29.1%)	43/350 (12.3%)	-	Unclear.	Type A 350/350.
Zhan 2011	279/361 (77.3%)	22/361 (6.1%)	13/361 (3.0%)	228/361 (63.2%)	16/361 (4.4%)	83/361 (23.0%)	-	16/361 (4.4%)	Observations, examination, bloods, ECG, CT 241/361 (66.8%), TTE 71/361 (19.9%), MRI 28/361 (7.8%), CXR 17/361 (4.7%), coronary angiogram 3/361	DeBakey Type I 252/361, Type II 28/361, Type III 81/361.

									(0.8%).	

ECG=electrocardiography, CXR=chest x-ray, TTE=transthoracic echocardiography, TEE=transesophageal echocardiography, CT=computed tomography, MRI=magnetic resonance imaging, CTA= computed tomography angiography

Table 3: Definition and rates of misdiagnosis of aortic dissection in included studies

Study ID	Definition of misdiagnosis	Setting	Misdiagnosis rate	Misdiagnosed conditions
Asouhidou 2009	Patients with other initial diagnosis when eventual diagnosis was AAD.	Emergency department.	Rate: 15/49 (30.6%).	Mistaken for myocardial infarction 12/15, cerebral infarction 3/15.
Chua 2012	AAD not a differential diagnosis, diagnostic imaging to diagnose dissection not performed or cardiologist or cardiothoracic surgeon consult not obtained whilst patient in the emergency department.	Emergency department	Rate: 26/68 (38.2%).	Alternative diagnoses: NSTEMI, angina, TIA, stroke, central cord syndrome, unspecified abdominal pain, unspecified chest pain, syncope and sepsis.
Hansen 2007	Incorrect initial diagnosis when eventual diagnosis aortic dissection.	Inpatient settings	Rate: 26/66 (39.4%).	Alternative diagnoses ACS 21/26, pulmonary embolism 2/26, musculoskeletal strain 3/26.
Ibrahim 2020	Not considering acute aortic dissection as differential diagnosis, not performing imaging to diagnose AAD. Prior to August 2009, no cardiology or cardiothoracic surgery consultation obtained were considered as misdiagnosis as well.	Emergency department	Rate: 42/145 (28.9%)	-
Kurabayashi 2011	Failure to diagnose AAD at the end of the initial assessment in the emergency room.	Emergency department	Rate 17/109 (15.6%).	Alternative diagnoses: ACS 10/17, pericarditis 2/17, hypertensive emergency 1/17, ureterolithiasis 2/17, acute gastritis 1/17, cerebral infarction 1/17.
Ohle 2019	Failure to diagnose AAD within the emergency department, treatment for alternative diagnosis started with in the emergency department, or representation within 14 days of the initial visit with new diagnosis of acute aortic dissection.	Emergency department	Rate: 34/194 (17.6%).	Alternative diagnoses: ACS 16/34, pulmonary embolism 5/34, stroke 4/34, others not reported.
Pare 2016	Initial failure to diagnose AAD in emergency department.	Emergency department	Rate: 7/32 (21.9%).	-
Patel 1997	False-positive, false negative or non-diagnostic TTE or TEE.	Inpatient setting	Rate: 6/25 (24.0%).	-
Pourafkari 2016	Patients in whom acute type A aortic dissection was not suspected in the emergency department.	Emergency department	Rate: 47/189 (24.9%).	-
Scholl 1999	Unclear.	Inpatient setting	Rate (misdiagnosis and delay): 17/75 (22.7%).	-
Zaschke 2020	Aortic dissection as sole or differential diagnosis included	Emergency department	Rate: 274/350	Alternative diagnoses: ACS 162/274, neurological disease

	in initial workup. Initial being the diagnosis of first physician with patient contact before the use of extended imaging or invasive procedures.		(78.3%).	69/274, respiratory disease 40/274, gastrointestinal disease 16/274, peripheral arterial disease 6/274, musculoskeletal disease 15/274, other cardiovascular disorders 15/274, psychological disorder 2/274.
Zhan 2012	Unclear.	Emergency department	Rate: 51/361 (14.1%).	Alternative diagnoses: pancreatitis 5/51, ACS 24/51, CVA 2/51, cholecystitis 3/51, acute gastroenteritis 3/51, acute renal failure 1/51, thyroid tumor 1/51, congestive heart failure 2/51, spinal pathology 1/51, cystitis 1/51, pulmonary tuberculosis 1/51, pneumothorax 1/51, pulmonary infection 4/51, acute gastroenteritis 1/51, mesenteric ischemia 1/51.

AAD=acute aortic dissection, ACS=acute coronary syndrome, NSTEMI=non-ST elevation myocardial infarction, TIA=transient ischemic attack, CVA=cerebrovascular accident

Table 4: Predictors of misdiagnosis of aortic dissection

Study ID	Setting	Predictors of misdiagnosis
Hansen 2007	Inpatient settings	Multivariable predictors: Age OR 1.06 95%CI 1.01-1.10, p=0.02. Anterior chest pain OR 7.12 95%CI 2.06-24.58, p=0.002.
Ibrahim 2020	Emergency department	Logistic regression analysis predictors of misdiagnosis: Concurrent signs of congestive heart failure OR 33.51 95%CI 1.42-789.2, p=0.024. Absence of widened mediastinum on chest X-ray OR 11.52 95%CI 1.37-96.8, p=0.029.
Kurabayashi 2011	Emergency department	Multivariable predictors: Walk-in patient OR 4.78 95%CI 1.27-18.01, p=0.021. Anterior chest pain OR 3.47 95%CI 1.06-11.31, p=0.040. Number of imaging studies per patient misdiagnosed vs diagnosed: 0.82 SD 0.81 vs 1.53 SD 0.52, p≤0.001.
Ohle 2019	Emergency department	The quality of the history taking was associated with an increase in likelihood of correct diagnosis: Asking more than two common pain questions (character, onset, severity, duration and radiation) suggests sensitivity of 93.3% 95%CI 82.4-97.6, p≤0.01 for correct diagnosis.
Zaschke 2020	Inpatient setting	Multivariable predictors: Pain in lumbar region OR 4.38 95%CI 1.94-9.90, p≤0.001. Angina pectoris OR 0.31 95%CI 0.15-0.61, p≤0.001. Sweating OR 1.86 95%CI 1.02-3.37, p=0.042. Any paresis OR 1.85 95%CI 1.04-3.31, p=0.037. Pain in scapulae OR 2.03 95%CI 0.94-4.39, p=0.072.

OR=odd ratio, CI=confidence interval, SD=standard deviation

Declaration of Interest statement: The authors declare no conflict of interest. Christian Mallen is funded by the National Institute for Health Research (NIHR) Applied Research Collaboration West Midlands, the National Institute for Health Research (NIHR) School for Primary Care Research and a National Institute for Health Research (NIHR) Research Professorship in General Practice (NIHR-RP-2014-04-026) for this research project. The views expressed are those of the author(s) and not necessarily those of the (partner organization), the NHS, the NIHR or the Department of Health and Social Care. The Keele School of Medicine have received funding from BMS to support a non-pharmacological atrial fibrillation screening trial. None of the other authors have received any funding for this work.