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Pulmonary artery dissection—A review of 150 cases

Dinesh Malcolm Gerard Fernando *, Solokara Mudiyanselage Nirmani Kaushalya Thilakarathne, Chathula Ushari Wickramasinghe

Department of Forensic Medicine, Faculty of Medicine, University of Peradeniya, Peradeniya 20400, Sri Lanka

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ABSTRACT

Pulmonary artery dissection (PAD) is considered to be a rare condition with a very high mortality. Since a comprehensive review on PAD has not yet been done, we analysed all the available reports on PAD. In this analysis and review we searched the databases; Medline, PubMed Central, Directory of Open Access Journals, Google Scholar using the search term "Pulmonary Artery Dissection" with no language restrictions. In the 150 cases of PAD reported from 1842 to June 2018, the average age at diagnosis was 44.8 years with a male to female ratio of 1.1:1. Diagnosis was made in 49.3% of the males in the third and fourth decades, and 55.4% of the females in the fifth and sixth decades. The primary underlying causes were pulmonary hypertension and heart diseases, both congenital (mainly PDA) and acquired. The commonest clinical presentations were dyspnoea and chest pain. The best investigation of diagnosis was CT scan. The pulmonary trunk was the site of dissection in 72.5%. Surgical treatment, or medical management followed by surgery, had the best success rates. The overall survival rate which was 10.9% up to the year 2000, increased to 59.3% thereafter. If PAD was diagnosed ante-mortem, 70.5% survived. Haemopericardium / cardiac tamponade was seen at autopsy in 84.2%. PAD is not as rare, nor as fatal as believed, and with a high index of suspicion and appropriate investigations, an early diagnosis of PAD can be made and successful treatment instituted.

Introduction

Although aortic aneurysms and dissections have been extensively studied and reported in the literature, pulmonary artery dissection (PAD) is not well documented.[1] PAD is considered to be a rare and lethal condition.[1–5] PAD commonly occurs at the site of a pulmonary artery aneurysm.[6] Dissection of the pulmonary artery occurs as a result of formation of a tear through the intima into the mid or deep media. Thereafter, the dissection tends to propagate along intramedial planes. Longitudinal dissection occurs due to the blood pressure developed within the media leading to a false lumen.[2] Due to the low resistance to blood flow inside the lungs, the pulmonary arterial media is thinner than the aorta. Usually, PAD results in a rupture, rather than re-entry, as occurs in aortic dissection.[2,7,8] Rupture may occur into the pericardium, mediastinum, lungs, or pleural cavity.[9]

A case of fatal PAD with rupture into, both, the pleural cavity and the lung, was encountered by the first author and reporting of this case was considered. While collecting data and perusing the literature, it was noted that there are numerous discrepancies and variations in the figures given by various authors. Even the information on the first reported case of PAD also varies; some authors state that the first description of PAD was by Helmbrecht in 1842,[2,9,10] while others cite Walshe in 1862.[4,11] In addition, figures for the number of cases reported since the first report also show inconsistencies. The number (50) quoted by Hako et al. in 2017 is less than the figure (64) quoted by Togo et al. and Sumi et al. (63) in 2015,[4,12,13] while a higher figure (70) is given by Li et al. in 2010.[3] Furthermore, even though most articles indicate that PAD has a very high mortality, we found that survival is not as rare as believed.

These incompatibilities prompted us to retrieve and analyse all the available reports on PAD. We retrieved 133 cases since the previous review of 17 cases by Shilkin et al. in 1969.[10] The gender, age, underlying cause, clinical presentation, investigations helpful in making a diagnosis, site of occurrence, treatment, their outcomes, and post-mortem features of all reported cases of PAD, including the 17 cases from 1842 to 1969, were analysed.

This review encompassing data of all reported cases of PAD (primary sources) since the first reported case, will be of benefit to all health care providers including, nurses, general practitioners, emergency department doctors, radiologists, including interventionists, treating physicians, surgeons and forensic pathologists.

Abbreviations: PAD, pulmonary artery dissection; PHT, pulmonary hypertension; PDA, patent ductus arteriosus; VSD, ventricular septal defect; ASD, atrial septal defect; CT, computed Tomography; MRI, magnetic Resonance Imaging; TTE, transthoracic echocardiography; MPA, main pulmonary artery; PT, pulmonary trunk; LPA, left pulmonary artery; RPA, right pulmonary artery; IPA, intra pulmonary arteries.

* Corresponding author.
E-mail address: dineshmgfdo@yahoo.com (D.M.G. Fernando).

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Methodology of the analysis

The entire data set consisted of all 150 cases reported from 1842 to 2018. The information given in the reports were categorized into age, gender, underlying disease, clinical presentation, diagnosis, site of occurrence, management, survival and post-mortem features. The cases that had given the relevant information in each category was analysed (Fig. 1) using statistical software, IBM SPSS Statistics for Windows, Version 20.0 to ascertain the frequencies and relationship between categories (e.g. association between gender and age at diagnosis).

Incidence

The literature is divided on who reported the first ever case of PAD. Some give credit to Helmbrecht in 1842,[2,9,10,14–18] while others cite Walshe in 1862.[4,7,11,19] According to the review by Shilkin et al. in 1969, Walshe has cited Helmbrecht in his report.[10] Hence, we conclude that Helmbrecht was the first to report a case of PAD in 1842.

Almost all the available literature consider PAD as an extremely rare condition.[1–7,9,10,12–18,20–54] In our series of 150 cases, only 54 case reports of PAD have been published in the 157 years from 1842 to 2000. A dramatic increase in PAD reports is noted thereafter, with 96 cases reported from 2000–2017 (Fig. 2), which is attributed to the advancement of diagnostic technologies.[17,19,24,26,31] The figures given on the reported number of cases show discrepancies.[2–4,7,9,11–13,15,16,18,19,23–25,30,32,35,42,49,50,52,53,55–57] For example, an article in 2017 states that there are 50 reported cases on PAD,[4] while an article in 2005 quotes a figure of 63.[24] The highest figure reported in the literature on the number of PAD cases in 2015[25] and 2018[55] is "<100". However, we found 150 reported cases of PAD.

Diagnosis and prognosis

Most of the literature consider PAD to be a fatal disease condition[1–8,12–15,17,24,26] while others give a mortality rate of 80%.[53] Of the 150 cases retrieved, 132 had given the outcome of the patient. We found that the overall survival rate of 42.4% was much higher than believed. When the number of survivors was plotted against the reported year (Fig. 3), an increased rate of survival was observed from 2004 onwards with a dramatic rise in survival after 2014.

Further analysis was conducted after categorizing the 132 cases which had mentioned survival into two sets based on the year of publication; cases reported up to the year 2000 and those reported thereafter, including 2000 (Table 1). The mortality rate of 89.1% up to 2000 was comparable to that given in the literature. However, from 2000 onwards the mortality rate had dropped to 40.7%. This is most probably due to the advent of the use of Computed Tomography; first used to diagnose PAD in 1986.

Most of the literature states that PAD is encountered post-mortem during autopsy.[44,46,58,59] The data on ante- mortem diagnosis of PAD also show discrepancies.[2,16,24–26,30,32,33,35,38,44,45,47,50,52,56] For example, an article in 2015 states that there are eight reported cases on living patients with PAD,[32] while an article in 2010 quotes a figure of 16.[16] The highest number reported in the literature so far is 26.[2] However, we found 90 cases where PAD was diagnosed ante-mortem, and also that the ante-mortem diagnosis of PAD has increased dramatically since the year 2000 (Fig. 4) from 19.6% to 85.3% (Table 2). Of the 90 cases of PAD diagnosed ante-mortem, 78 had mentioned the outcome of the patient. The survival rate in this 78 was 70.5% (55) and mortality was only 29.5% (23). Therefore, it may be concluded that PAD can be diagnosed and treated successfully.

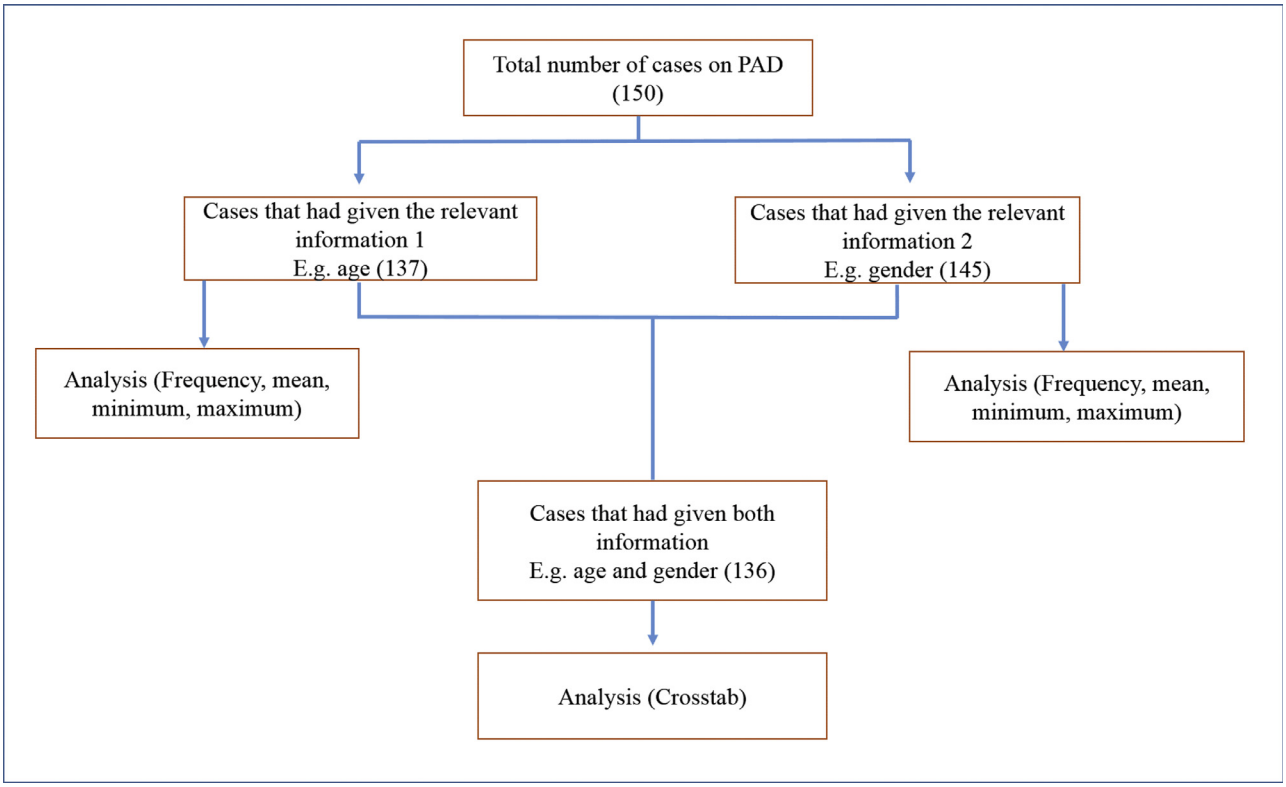

Fig. 1. Selection criteria of the cases for the analysis.

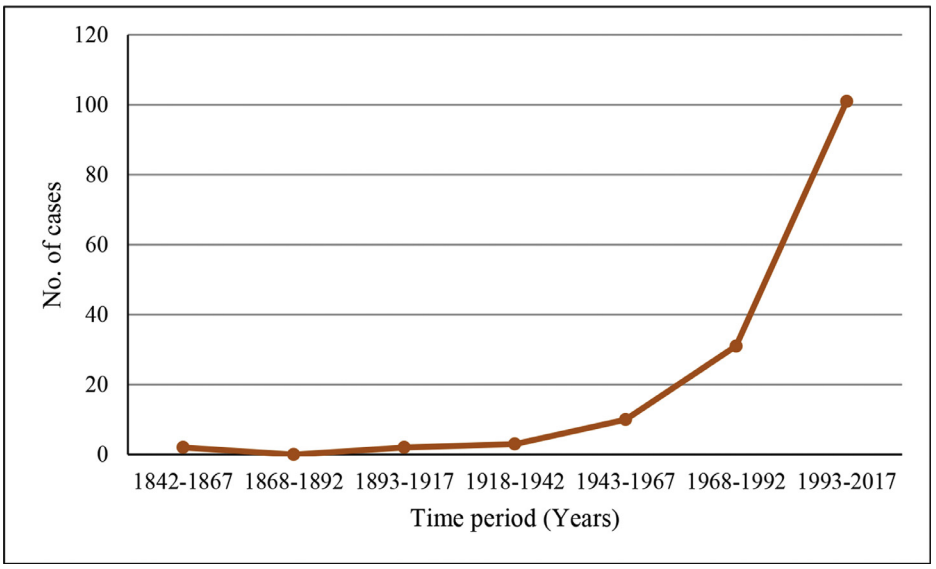

Fig. 2. Reported cases of PAD over time.

Association with gender

Some authors consider the incidence of PAD to be slightly higher in females than males giving a ratio of 1.2:1,[2,9,14,16,52] while Rosenblum et al. give a slightly higher figure of 60%[20] Conversely, Placik et al., state that the occurrence of non-aortic dissecting aneurysms is four times higher in males than females.[60] However, they have not differentiated the types of non-aortic (pulmonary, carotid, coronary, celiac, iliac etc.) dissections. Some others indicate that there is no gender predominance observed in occurrence of PAD.[26,35] Areco and Pizzano in 2003 state that more cases were reported in females during the last two centuries, although males are more prone to PAD.[11]

Out of 150 cases, five cases which had not mentioned gender were excluded from the analysis. In the 145 cases we analysed, there was a slight male predominance (53.1%) in PAD occurrence giving a male to female ratio of 1.1:1.

Association with age at diagnosis

PAD has been observed in an age range of 26 days to 85 years.[2,9,15,24,26,35,52] Variations were observed in this too, because some authors state that the diagnosis of PAD was at 26 to 85 years,[14,16] while others give a range of 17 to 85 years.[54] The given average age at diagnosis also differs; one article states it as 67.5 years[20] while another article mentions it as 39.6 years.[9,52] According to the literature, the highest number of PAD cases diagnosed was in the third and sixth decades.[2,9,15,24,35,52,53]

Out of the 150 cases, 13 that had not given age at diagnosis was excluded from our analysis. In the 137 cases, the age at diagnosis ranged from 26 days to 97 years. We found that 73% of the cases were between 21–60 years of age, with an average age of 44.8 years at the time of diagnosis. Peaks were observed in the sixth (21.2%), fifth (19.7%), and third (18.2%) decades of age (Fig. 5). The most frequent age at diagnosis (mode) was 56 years.

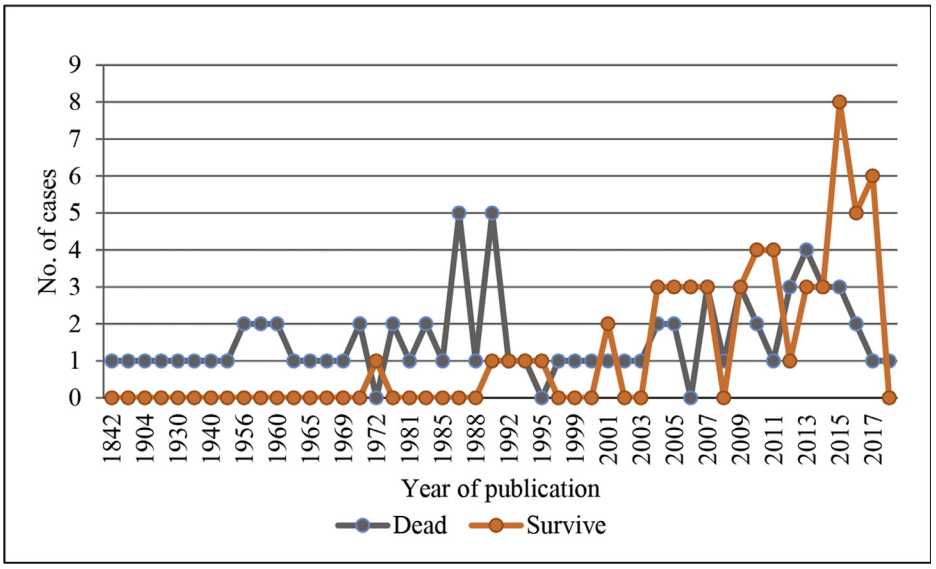

Fig. 3. Survival rate trend of patients with PAD over time.

Table 1
Analysis of the mortality based on the year of publication.

Time period (Year)	Total number of cases reported	No. of cases considered	Rate of survival	Rate of death
1842–1999	54	46	10.9% (05)	89.1% (41)
2000–2017	96	86	59.3% (51)	40.7% (35)
1842–2017	150	132	42.4% (56)	57.6% (76)

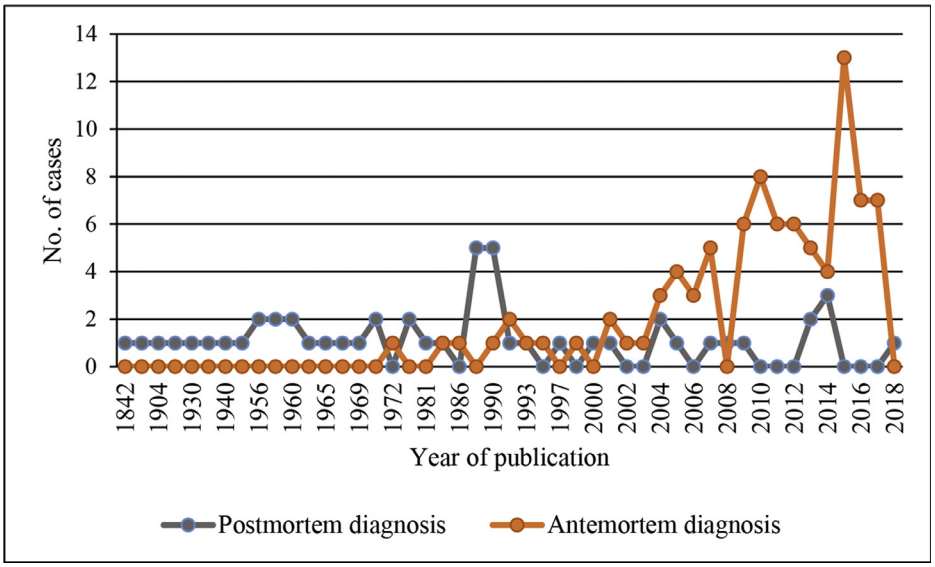

Fig. 4. Ante-mortem diagnosis of PAD over time.

Association between gender and age at diagnosis

Out of the 150 cases, 136 articles which had documented both gender and age at diagnosis were considered for the analysis. The highest number of cases diagnosed in males were in the third (26.8%) and fourth (22.5%) decades, while that of females was in the fifth (29.2%) and sixth (26.2%) decades (Fig. 6). There is a significant relationship between the age at diagnosis and gender ($p = 0.004$, <0.05). When the analysis was conducted separately for two data sets (that of Shilkin et al., from 1842 to 1969 and this study from 1970 to 2017), the same pattern was observed. In the 17 cases by Shilkin, the peaks for males were observed in the third and fourth decades while that of females was in the fifth decade. The separate analysis for the cases since 1970 to December 2017 revealed the same result as the analysis for the whole dataset since 1842.

Underlying disease/ aetiology

Adodo et al. have listed four major etiological groups; congenital malformation, infection or inflammation, acquired cardiac disease, and iatrogenic causes.[1] Throughout the literature, pulmonary hypertension (PHT) is identified and reported as the main underlying disease leading to PAD.[2,3,5,17,18,21,22,30,31,33,46,48,50,51,58,61] Some state that 75% had PHT as the underlying disease,[1,16,39] whereas Rosenblum et al. and Arena et al. give it as 78% and 81% respectively.[14,20] Patent ductus arteriosus (PDA),[4,27,34,47,55] infective endocarditis,[23] Eisenmenger syndrome,[21,53,55] chronic obstructive pulmonary disease,[16] vascular inflammatory disease, aorto-pulmonary fistula, catheter induced vessel wall injury,[25] and cardiac interventions[33] are some of the other conditions given in the literature as aetiological factors resulting in PAD.

In our analysis, of 150 cases, the underlying disease was unknown in 28. The balance 122 had documented one or more conditions, resulting in a total of 26 underlying disease conditions. Of those, PHT (including Eisenmenger syndrome) was present in 50% (61), congenital heart disease in 45.1% (55), cardiac valvular disease in 15.6% (19), lung diseases in 9.8% (12), and hypertension in 9.8% (12) of the cases. Of the 55 with congenital heart disease, PDA was the commonest with 31 cases (56.4%), followed by ventricular septal defect (VSD) with 11 (20%) and atrial septal defect (ASD) and aorto-pulmonary window/ aortopulmonary fistula with 5 (9.1%) cases each. Coarctation of the aorta (2), common truncus defect (1), and congenital pulmonary aneurysms (1) were some of the rare conditions documented. Some underlying disease conditions of PAD with a frequency lower than 6.0% were aortic aneurysm, coronary artery disease, diabetes mellitus, atrial fibrillation, anaemia, hypothyroidism, pregnancy, infective endocarditis, heart failure, and sepsis. It is possible that conditions that are difficult to diagnose clinically, such

Table 2
Ante-mortem diagnosis of PAD in relation to the year of publication.

Time period (Year)	Total number of cases reported	No. of cases considered	Ante-mortem diagnosis	Post-mortem diagnosis
1842–1999	54	46	19.6% (09)	80.4% (37)
2000–2018	96	95	85.3% (81)	14.7% (14)
1842–2018	150	141	63.8% (90)	36.2% (51)

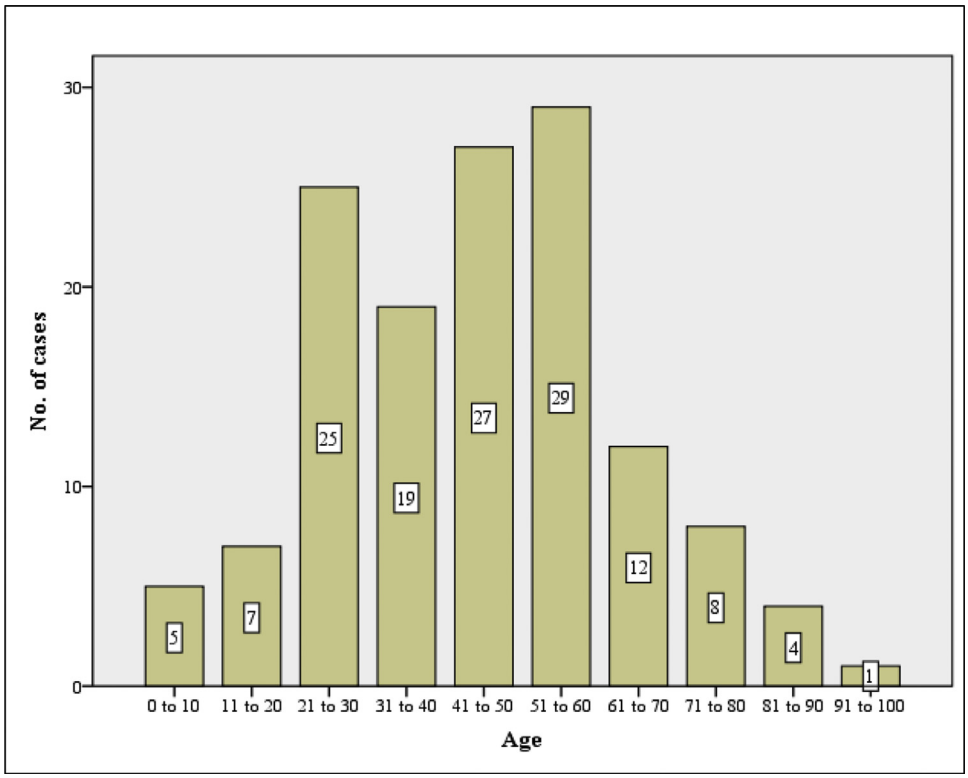

Fig. 5. The frequency of PAD incidence with age at diagnosis.

as connective tissue disorders (Marfan syndrome, Ehlers -Danlos etc.) were underlying conditions in the 28 cases where the underlying disease was unknown.

Therefore, we found that the primary underlying causes of PAD are PHT and heart diseases, both congenital (mainly PDA) and acquired.

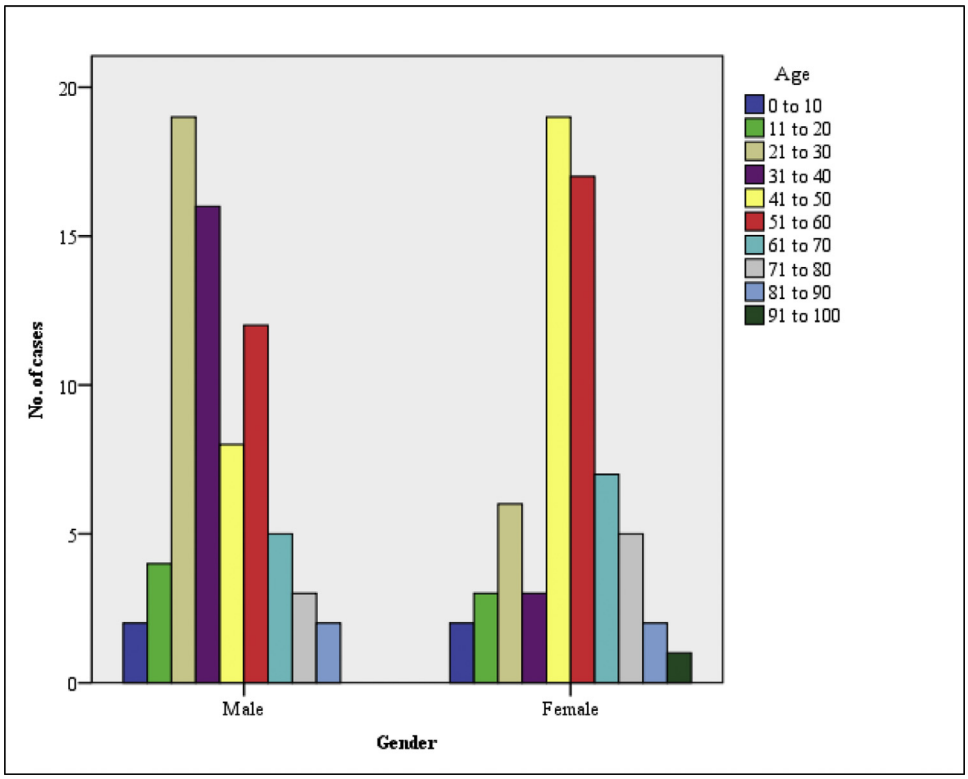

Fig. 6. The relationship between gender and the age at diagnosis.

Clinical presentation of PAD

According to the literature, clinical presentation of PAD is non-specific,[1,2,8,9,15,27,30,56] and the most common presentations are chest pain, dyspnoea, cyanosis, haemoptysis, shock, collapse, and death.[1,5,6,8,9,15,17,20,24,27,31,32,34,35,37,38,40,42,44,45,48,52,54–56,58] Dyspnoea has been the presenting complaint in 82% of the cases, while retrosternal chest pain and cyanosis have been present in 67% and 52% of the cases respectively.[2–4,30,40,42,45]

This analysis considered the 109 cases that had mentioned the presenting symptoms and excluded the 41 cases that had not. Some cases had mentioned more than one presenting complaint. The main symptoms of PAD were dyspnoea (66.1%) and chest pain (57.8%), followed by cyanosis (17.4%). Both dyspnoea and chest pain were present in 40.4%. The other presentations like shock, collapse, syncope, coma, cough, ankle oedema, fever, weakness/ fatigue, palpitations, haemoptysis, orthopnoea, vomiting, increased heart rate, anorexia, pallor, sweating, and diarrhoea were observed in only a few cases. Four cases had been asymptomatic, and had been detected incidentally, during routine postoperative follow-up in cases of pulmonary balloon valvuloplasty (2 cases), acute type 1 aortic dissection, and aortic canulation (1 case).

Therefore, it can be concluded that the most likely clinical presentation of PAD is dyspnoea associated with chest pain.

Diagnosis

With the improvement of technology, the availability of advanced investigation methods to evaluate PAD have also increased. Throughout the literature, Computed Tomography (CT) was identified as the best method to diagnose PAD, in comparison to alternate diagnostic methods.[1,2,8,16,17,26,27,30–33,48,53,55,58] Magnetic Resonance Imaging (MRI) was also considered as a good method to diagnose this entity.[8,16,17,26,27,30–33,48,55,58] The other investigations given in the literature as useful to diagnose PAD were chest radiography,[30] ultrasound scan, echocardiography,[1,8,27,33,53] and angiography.[48] Factors that need to be considered prior to determining an investigative methodology are, the stability of the patient, renal function, availability of the investigation modality, and postoperative complications.[2]

There were 95 cases in which investigative methods were documented and some radiography cases had used more than one investigation. The investigations useful to diagnose PAD in these cases, were CT (73.7%), transthoracic echocardiography (TTE) (33.7%), chest radiography (9.5%), electrocardiography (6.3%), MRI (5.3%). Transoesophageal echocardiography, magnetic resonance angiography and arteriogram were used in a few cases.

Since the first reported use of CT to diagnose PAD was in 1986, we excluded the three cases where a diagnostic technology was used prior to 1986 and analysed the success of the diagnostic modalities used, since then. There were 70 cases where CT ± other methods were used. Of these, in 64 cases (91%) PAD was diagnosed successfully using CT. However, in the 22 cases that CT was not used, it was still possible to diagnose PAD successfully in 18 cases (82%).

Multiple modalities of non-invasive investigations can be used to detect PAD.[2] TTE can be used as the initial investigation since it is quick, easy to use, low cost, and easily accessible. CT will confirm the diagnosis by demonstrating the intimal flap and provide additional information such as the extent of dissection, diameter of the aneurysm and the presence of intra luminal thrombi.[2,4,8] Although MRI provides additional information, its use is limited to situations like renal dysfunction or when there are contraindications for the use of iodinated contrast material.[2]

Therefore, we recommend immediate chest radiography and TTE followed by CT scan, if available.

Site of occurrence

The main pulmonary artery (MPA)/pulmonary trunk (PT) is said to be the commonest site for dissection to occur,[4,53] with a frequency ranging from 72%[2,14,31] to 80%.[16,17,24,33,35,47] The other possible sites given in the literature are the left and right pulmonary arteries[47] (LPA and RPA) and intra pulmonary arteries (IPA), with reported frequencies of 6% in LPA, 4% in RPA,[14,16,31] and 10%[2,14,31] in IPA,

Of the 150 cases, the 12 which did not give the site of occurrence were excluded from the analysis. Some reports had mentioned more than one site, and therefore the total of all sites exceeds 100%. The sites of dissection in the 138 cases we analysed was the MPA/PT in 72.5% (100), LPA in 23.9% (33), RPA in 18.8% (26), and IPA in 2.9% (4).

Management

Most articles state that there is no consensus on treatment strategy.[1,3,16,25,31,53] Although few reports suggest treatment strategies, the optimal management has not been defined.[1,3,17,25,31,34] Yaman et al. and Bhatia et al. state that there were successful reports of surgery,[47,48] and Tse et al. state that the first successful report on surgical treatment was in 2001.[55] Although some suggest surgical treatment as mandatory or as the optimal treatment strategy, they state that overall prognosis and chance of survival remains poor, as well as it has yet to be widely employed.[8,21,27,32,50,58] Some of the authors suggest both surgery and medical management,[28,30] while Birgy et al. state that both surgical and medical treatments have been used equally in the past.[18] Some authors believe that medical management is the best treatment option for PAD.[16,53] Zhu et al. suggest that endovascular treatment could be an attractive option to surgery and Birgy et al. emphasize the need of medical treatment for patients having a high risk for surgery.[18,34] Hako et al. states that surgery can be used as a treatment option for patients with symptoms and medical treatment can be implemented for asymptomatic patients.[4] Malm et al. emphasize the feasibility of both medical and surgical repair managements by considering the reports on surviving patients.[25]

Out of the 150 cases 77 were not considered for the analysis due to lack of information on the management used. Of the 73 cases that had documented the treatment, medical management and surgery were employed equally, in 35 (47.9%) cases each. In three (4.1%) cases medical treatment was followed by surgery. Medical management consisted mainly of oxygen, vaso dilators (ACE inhibitors, calcium channel blockers), diuretics and β blockers and was successful in 68.5%. Surgical treatment (including the three cases of medical management followed by surgery) was successful in 90.3%. Therefore, surgery should be the definitive management.

However, since the primary underlying causes of PAD are PHT and heart disease, both congenital (mainly PDA) and acquired, early detection by screening and treatment of heart disease and prevention of the development of PHT is of paramount importance.

Post-mortem features

The rupture of a PAD may cause haemopericardium, haemomediastinum, haemothorax, pulmonary haemorrhage, or a combination of these.[9,10] According to the literature haemopericardium and cardiac tamponade,[51,58] are the commonest post mortem findings in PAD.[4]

Death was reported in 71 of the 150 cases studied, of which post-mortem features were given in 38, which were considered for the analysis. In some, rupture had occurred into more than one site. Haemopericardium / cardiac tamponade was the commonest finding seen in 84.2% (32), while haemomediastinum and pulmonary haemorrhage, were seen in equal proportions, with a frequency of 10.5% (4) each. There were no cases of haemothorax reported.

The case autopsied by the first author, is similar to those discussed in the study in many aspects. The patient was a male in the 3rd decade, where the highest peak was observed in males. He had long standing PHT and an atrial septal defect. In our analysis, PHT was the commonest pre-disposing condition, as in this case. However, ASD has been reported in only 5 previous cases. Further, he had the most frequently encountered clinical presentation of dyspnoea, although he did not complain of chest pain. He also had fever and oedema which have been present in other cases of PAD, too. The site of occurrence was the RPA. However, rupture had occurred into both the pleural cavity and the lung, causing haemothorax and intra pulmonary haemorrhage respectively, which has not been reported previously.

If the details of the case seen by the first author are included to the 150 already analysed, the following changes occur. The average age at diagnosis becomes 44.7 years with a male to female ratio of 1.15:1, with the diagnosis being made in 50% of the males in the third and fourth decades. There is no change in the age of diagnosis in females, the primary underlying cause or clinical presentation. The site of dissection is the pulmonary trunk in 71.9%, the LPA in 23.7%, the RPA in 19.4%, and IPA in 2.9% of the 151 cases. During autopsy, haemopericardium, pulmonary haemorrhage, haemomediastinum and haemothorax are seen in 82.1%, 12.8%, 10.3%, and 2.6%, respectively. The mortality rate of 40.7% from the year 2000 onwards, increases to 41.4% with this case. However, there is no change to the survival rate of 70.5% of those who have had an ante-mortem diagnosis of PAD.

Conclusion

PAD is not as rare, nor as fatal as believed, and with a high index of suspicion and appropriate investigations, an early diagnosis of PAD can be made and successful treatment instituted, as survival has increased due to enhancement of diagnostic and treatment technologies. PAD should be part of the differential diagnosis in cases where patients present with dyspnoea, chest pain, with or without cyanosis. This is especially so, in cases of males in the third and fourth decades, and females in the fourth and fifth decades of life, where a significant association between the age and gender was identified. If the patient also has PHT, then PAD is highly likely, and immediate chest radiography and TTE followed by CT scan is recommended. The main pulmonary artery is the most likely site for PAD to occur. Immediate surgery, or initial medical management followed by surgery, is the best treatment option with a success rate of over 90%. If the patient is not fit, or refuses surgery, medical management alone can achieve a success rate of almost 70%. As time is of the essence in a patient with a dissecting pulmonary artery, health care staff in emergency departments, including nurses, physicians and surgeons should be armed with the knowledge and expertise to suspect, diagnose and treat promptly, in order to save the patients' life. However, it is stressed that prevention, early detection, and management of PHT is the best management strategy.

Declaration of interests

None.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.hrtlng.2019.02.007.

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