Austin Hypertension

Open Access

Austin Publishing Group

Research Article

The Relationship between Hypertension and Thoracic Aortic Aneurysm of Degenerative or Atherosclerotic Origin: A Systematic Review

Tong JKT and Rabkin SW*
Department of Medicine (Cardiology), University of British Columbia, Canada

***Corresponding author:** Simon W Rabkin, Department of Medicine (Cardiology), University of British Columbia, Vancouver, Canada

Received: April 11, 2016; **Accepted:** May 20, 2016; **Published:** May 23, 2016

Abstract

Background: The relationship between hypertension and 'so called degenerative or atherosclerotic' Thoracic Aortic Aneurysm (TAA), has not been subjected to rigorous systematic examination. The objective was to evaluate the association between hypertension and this type of TAA and compare it with other risk factors for atherosclerosis.

Methods: Studies of TAA that reported hypertension were extracted through MEDLINE using PubMed and OvidSP platforms.

Results: Fourteen articles fulfilled the eligibility criteria, with twelve having data on hypertension prevalence. The prevalence of hypertension was high; 70% in 1485 patients with TAA. In contrast the prevalence of cigarette smoking and dyslipidemia were considerably and significantly ($p < 0.01$) lower 42.2% and 43.4% respectively. Hypertension was most prevalent (80%) in ascending (80%) TAA. Studies reporting a relationship between hypertension and aneurysm progression, have larger initial aortic diameters and greater rates of TAA expansion.

Conclusion: These data provide evidence for a dominant role for hypertension in this kind of TAA and suggests that hypertension plays an important role in TAA expansion, especially in larger TAA perhaps due to increased wall stress. They also suggest the importance of hypertension in TAAs that are expanding in rapidly.

Keywords: Thoracic aortic aneurysms; Hypertension; Blood pressure; Aorta expansion rate

Introduction

Thoracic Aortic Aneurysm (TAA) is a serious condition because of the potential for aortic rupture and death [1,2]. Although TAA can be due to a variety of different genetic or inherited conditions, the majority of TAAs are ascribed to atherosclerosis or 'degenerative' factors that are not always clearly defined [3]. The prevalence of this kind of TAA is steadily increasing [2]. The development of thoracic aneurysm can be conceptualized as the balance of factors operating to distend and those that constrain aortic expansion [4]. Foremost amongst the factors operating to distend the aorta is blood pressure such that elevated blood pressure has been considered by some authorities to be an important risk factor for the development of TAA [5,6]. In contrast, other groups are more cautious in their opinion, suggesting that the role for hypertension and its management in TAA is not strong [7]. While there is general and longstanding acceptance of the relationship between hypertension and thoracic aortic dissection [8,9], there has not been a previous in-depth evaluation of the data on hypertension and TAA in the absence of aortic dissection. The objective of this study was to examine the data on hypertension and TAA due mainly to 'degenerative factors,' in the absence of aortic dissection and compare it with other atherosclerotic risk factors.

Methods

Search strategy

A systematic search was conducted to determine the relationship between hypertension and the prevalence and expansion of TAAs. We used MEDLINE with PubMed and OvidSP platforms as our main search strategy for relevant studies from the first available records on MEDLINE through to June 30, 2015. Search keywords included ("thoracic aortic aneurysm") AND ("hypertension" OR "blood pressure" OR "determinants") AND/OR ("progression" OR "growth" OR "expansion" OR "natural history). The search was limited to humans and English.

Eligibility criteria

The inclusion criteria were (i) an original study published in a peer-reviewed journal, (ii) subjects were adults (over 18 years of age), and (iii) used either chest radiography, echocardiograms, CT Scan or MRI for diagnosis or to measure aortic diameter. In addition, the study must either have (a) reported the prevalence of hypertension in patients with TAAs or (b) investigated how hypertension relates to the expansion of thoracic aneurysms. Studies were excluded if 30% or greater of the study population had aortic dissections, or if 30% or greater had genetic conditions and gene mutations producing TAA,

Citation: Tong JKT and Rabkin SW. The Relationship between Hypertension and Thoracic Aortic Aneurysm of Degenerative or Atherosclerotic Origin: A Systematic Review. Austin Hypertens. 2016; 1(1): 1004.

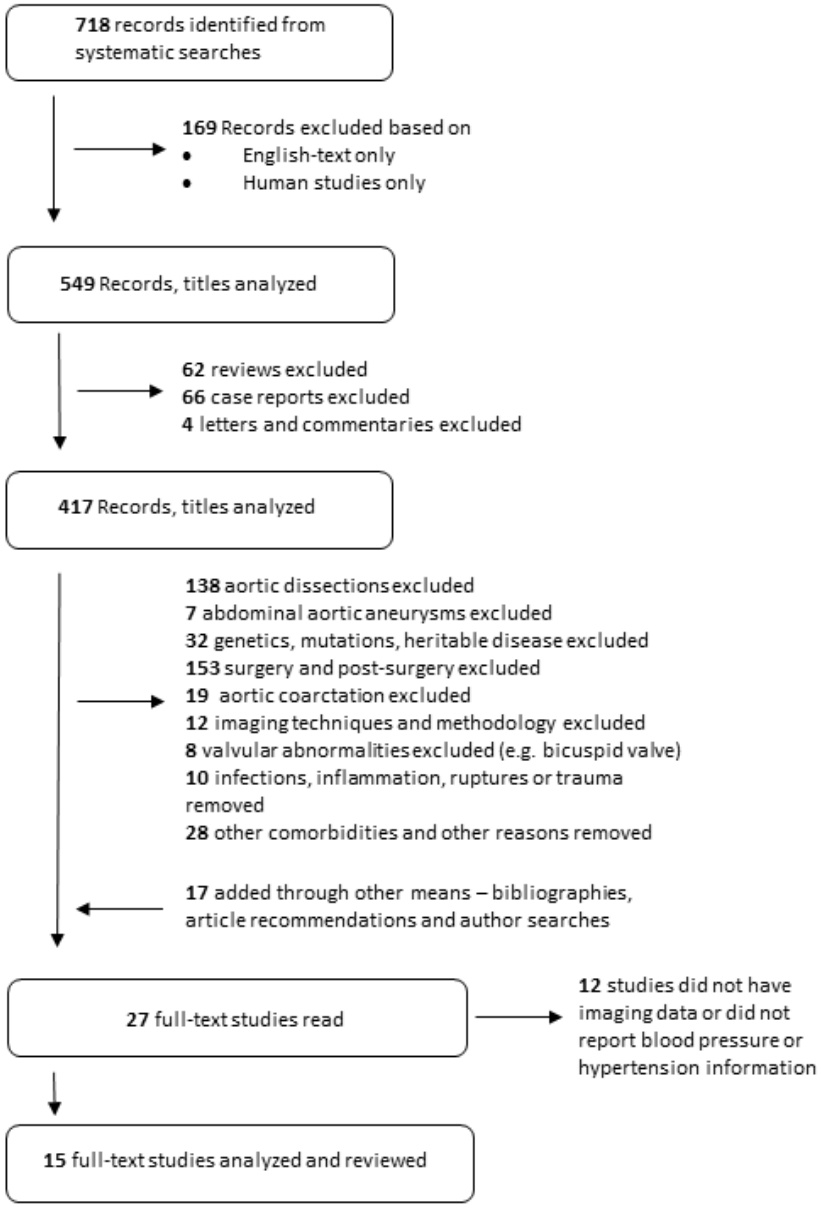

Figure 1: Shows the study flow diagram.

or valvular diseases, coarctation of the aorta, previous aortic surgery, aortic infections, trauma of the aorta or aortic ruptures. Studies that focused primarily or exclusively on abdominal aortic aneurysms were excluded. Review articles, case reports, letters, and abstracts were also excluded. Because publications with different analysis of the same patient population can occur, only the most recent study was used for our evaluation.

Data extraction

For each eligible study, the sample size, country of study, patient characteristics specifically BMI, history of dyslipidemia and cigarette use, definitions of hypertension and TAA, mean aortic diameter, expansion rates, the inclusion and exclusion criteria and main conclusions were recorded. For studies that had appropriate controls, the characteristics of the control group were also noted.

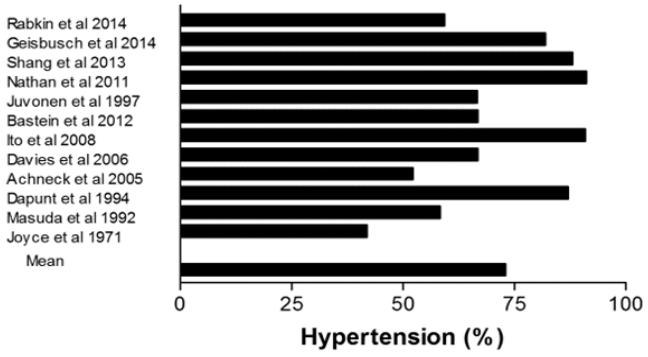

Figure 2: Shows the reported proportion of individuals with hypertension in cases with TAA.

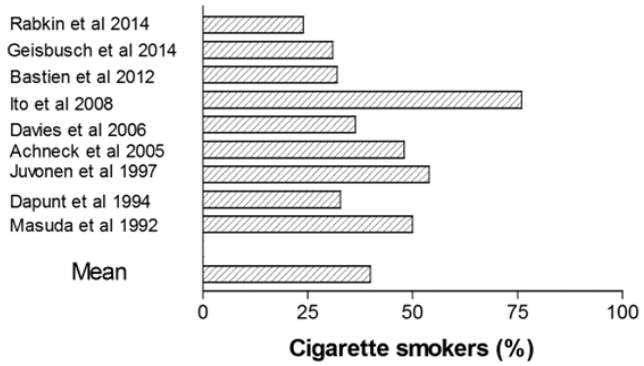

Figure 3: Shows the reported proportion of individuals with cigarette smoking in cases with TAA.

Statistical analysis

Data analysis calculated the mean and weighted mean. When a study reported only the median value it was considered to be the mean for our analysis. For comparison of two datasets the non-parametric Mann Whitney U test was used. Meta-analyses of the aggregate patient data were conducted using the Comprehensive Meta-analysis Version 2 (Biostat, Englewood, New Jersey, USA). Statistical significance was set as $p < 0.05$.

Results

The systematic search is summarized in (Figure 1), following the format for preferred reporting items for systematic reviews [10]. The systematic search yielded 718 unique records. Animal studies and non-English language studies excluded 169 citations. After screening the titles, 132 articles were removed because they were reviews, case reports, editorials or letters. The titles of 417 records were examined and studies were removed that did not fulfill the entry criteria. The remaining papers were read and 18 publications were identified from reference lists, author searches or article recommendations. We removed 12 studies that did not provide imaging information for TAA or did not report blood pressure or hypertension information. Fourteen fulfilled the eligibility criteria and were the basis for this review.

For evaluation of the prevalence of hypertension in persons with TAA, there were 1485 individuals with TAA (Table 1). They had a mean age of 65.4 years. There was a preponderance of men namely 66.9%. Studies were also sub-classified depending whether the TAA cases involved the ascending aorta, descending aorta or both.

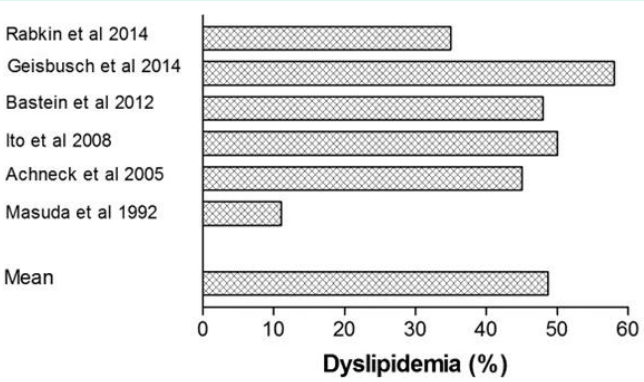

Figure 4: Shows the reported proportion of individuals with dyslipidemia in cases with TAA.

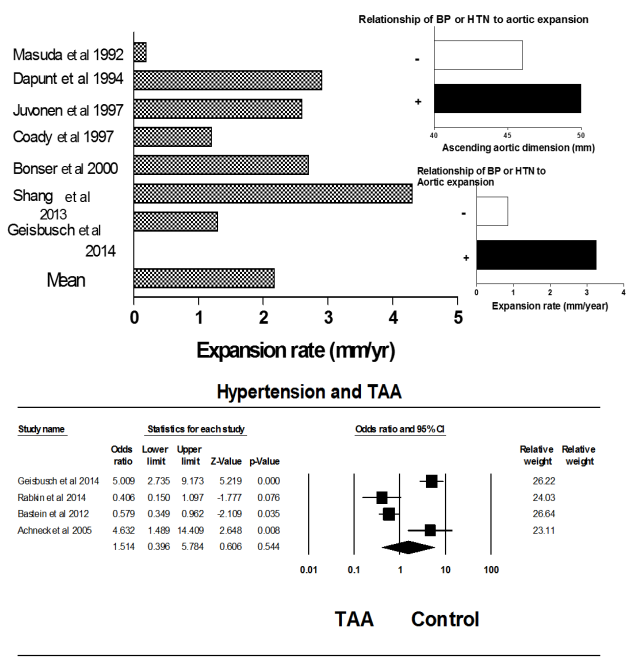

Figure 5: Shows the expansion rate for TAA in studies that reported the proportion of cases with hypertension. The inserts show the expansion rate and the initial ascending aortic diameter in studies that showed a relationship between hypertension and aortic expansion and those studies that did not show the relationship.

Overall the prevalence of hypertension in persons with TAA was 70.0% (Figure 2).

Considering the anatomical TAA location, the weighted average of the prevalence of hypertension was 80.1% in the ascending aorta (N=295) [11-13], 74.6% in the descending aorta (N=161) [14-16] and 66.3% in studies investigating both locations (N=1029) [17-22].

There were four studies with a control group. One study reported the proportion with a documented history of hypertension in persons with TAA at an aortic diseases clinic and an age matched group of persons without TAA attending a cardiology clinic [13]. Bastien *et al.* evaluated individuals with TAA but only 54% were reported to have had idiopathic-degenerative or so called atherosclerotic TAA [17]. Their control group was patients starting a cardiac rehabilitation program who were all considered to have cardiac disease [17]. Blood pressure was taken in a standard manner and hypertension diagnosed by guideline accepted criteria [17]. Another study compared TAA with a control group with no evidence of TAA on a CT done in the emergency department but did not provide details of the other characteristics of the control group and no definition of hypertension was stated [12]. Another study focused on aortic root aneurysms and had a control group from the emergency department [11]. Considering these studies with a control group, there were two studies showing an increased prevalence of hypertension in TAA and two showing a reduced prevalence of hypertension and TAA. The Odds Ratio for hypertension was 1.4 in TAA compared to control with p=0.08 which

Table 1: Studies reporting hypertension in Thoracic Aortic Aneurysms (TAA).

Study (Author(s), Year)	Country	TAA *N*	TAA *Average Age (Years)*	TAA *Male (%)*	Definition of HTN	Type of TAA
Joyce *et al*. 1964 [21]	USA	98	59.3	73%	DBP≥95 mmHg	Ascending and Descending
Masuda *et al.* 1992 [20]	Japan	36	61±15 (SD)	72%	Not defined	Ascending and Descending
Dapunt *et al.* 1994 [22]	USA	67	65.1±13	64%	DBP>100mmHg	Ascending and Descending
Juvonen *et al*. 1997 [16]	USA	102	72 (Median)	58%	Not defined	Descending and Thoracoabdominal only
Achneck *et al.* 2005 [11]	USA	31	59.6±14.9	61%	History of HTN or on antihypertensive medications	Ascending only
Davies *et al.* 2006 [19]	USA	410	61.9	63%	Not defined	Ascending and Descending
Ito *et al.* 2008 [18]	Japan	132	73.6±7.5 (Median±SD)	74%	SBP≥140mmHg, or DBP≥90 mmHg for atleast two repeated measurements or if they are on antihypertensive medications	Ascending and Descending
Nathan *et al.* 2011 [15]	USA	34	73.5±11.8 (SD)	50%	Not defined	Descending only
Bastien *et al*. 2012 [17]	Canada	286	67.5±10.1 (SD) TAD group	69%	BP>140/90mmHg	Ascending & Descending
Shang *et al*. 2013 [14]	USA	25	71.6±10.0 (SD)	48%	Not defined	Descending only
Geisbüsch *et al*. 2014 [12]	USA	232 166 had follow-up imaging	63.6±12.3 (SD)	72%	Not defined	Ascending only
Rabkin *et al*. 2014 [13]	Canada	32	66.5±10.9 (SD)	81%	History of hypertension	Ascending only

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; SD: Standard Deviation; +: When variance is reported as standard deviation

Table 2: Studies investigating the effects of blood pressure or hypertension on the progression of Thoracic Aortic Aneurysms (TAA).

Possibly Favors Expansion	Does Not Favor Expansion
Masuda *et al*. 1992 [20] N=36 Diastolic blood pressure, but not systolic blood pressure, was significantly (F=4.41, p<0.05) correlated with the expansion rate of TAA However, in multivariate risk factor analysis, blood pressure was no longer found to be significant.	Bonser *et al*. 2000 [23] N=87 In univariate analysis, hypertension did not significantly (p=0.24) influence growth rates of the aorta. Hypertension was also not a significant factor in stepwise multivariate regression of expansion rate.
Dapunt *et al*. 1994 [22] N=67 Hypertension had a borderline significance with regards to the expansion of TAA (p=0.0532) compared to normotensive group, but was not significant in multifactorial analysis of variance.	Geisbusch *et al*. 2014 [12] N=166 In univariate analysis, a history of hypertension was not a significant predictor for ascending aortic growth (p=0.67). Systolic blood pressure had a p value of 0.188.
	Coady *et al*. 1997 [24] N=230 "we found that we could not demonstrate a correlation between the level of blood pressure and the rate of growth"
	Shang *et al*. 2013 [14] N=25 The prevalence of hypertension was not significantly different between the rapidly expanding and slowly expanding TAAs

For the two studies no data was presented between TAA growth and blood pressure in Coady *et al.'s* study, and no correlation analysis was done in Shang *et al.'s* study.

was not significant at the 5% level. There was, however, significant heterogeneity across the studies (I^2=92.3, Q=38.9, p <0.001). This may in part be due to the nature of the control groups.

Cigarette smoking data was available in nine studies with a total of 1280 patients. The average prevalence of cigarette smoking was 40.1% (Figure 3). The prevalence of hypertension was significantly (p=0.0057) greater than the prevalence of cigarette smokers. Dyslipidemia prevalence was reported in six studies which totaled 701 individuals. The prevalence of dyslipidemia was 48.7% (Figure 4). The majority of studies did not provide a definition of lipid values that constituted dyslipidemia so that the definition was a usually 'history' of dyslipidemia. The prevalence of hypertension was significantly (p=0.009) greater than the prevalence of dyslipidemia.

Three studies also reported the mean BMI of their subjects [12,17,18]. The mean BMI would be considered overweight under standard BMI ranges, but the proportion of increased BMI was not provided and thus, comparisons could not be made with the cigarette smoking and dyslipidemia data.

Four of the identified studies also presented data on the relationship between aortic expansion and hypertension or blood pressure (Table 2). The results are conflicting. Masuda *et al.* examined 36 persons with TAA with a mean age of 61 years who were followed for at least 6 months [20]. The rate of aortic expansion was 1.3 mm/year and there was a significant correlation between expansion and diastolic but not systolic blood pressure in univariate analysis [20]. In multivariate analysis, only the size of the TAA was a significant

predictor of TAA expansion [20]. Dapunt *et al.* followed 67 persons with TAA for an average of 1.5 years [22]. A history of hypertension correlated with a greater diameter at TAA diagnosis and there was a borderline significant relationship between TAA expansion and hypertension (p=0.0532) [22]. In multivariate analysis, initial aneurysm diameter greater than 5 cm was the only independent predictor of expansion [22]. In contrast, there were two studies which did not find that hypertension was a significant risk factor for TAA expansion rates in univariate, multivariate or correlation analysis [12,23]. Bonser *et al.* conducted a retrospective evaluation of 87 persons with TAA, mean age 63 years, at a center for thoracic aortic diseases [23]. They did not find a significant correlation, in univariate analysis between TAA expansion and hypertension (treated or not treated) [23]. Geisbusch *et al.* examined the course of 166 persons with TAA who were on average 63.6 years and who were followed for an average of 1 year [12]. Systolic blood pressure was one of the top three factors correlating with TAA expansion although it did not reach statistical significance (p=0.19) and it was not significant in multivariate analysis [12]. Two studies that did not provide data on aortic expansion and blood pressure or hypertension, warrant additional comment. Coady *et al.* analyzed the determinants of aortic expansion in TAA and commented that they did not identify "a correlation between the level of blood pressure and the rate of growth" [24] but no data was presented (Table 2).

Shang *et al.* reported that the prevalence of hypertension was not significantly different between the rapidly expanding and slowly expanding TAAs but there was no data analysis correlating blood pressure and TAA expansion [14].

The aorta expanded significantly when one considers all of the studies on aortic expansion with blood pressure data (Figure 5). Aortic expansion was 2.17 mm per year [95% CI was 0.90 to 3.43]. We next examined the four studies with blood pressure and aortic expansion data. The rate of expansion was smaller than the average in studies that reported no relationship between blood pressure and aortic expansion. In contrast, the rate of expansion was greater than the average in studies that reported a relationship between blood pressure or hypertension and aortic expansion. The studies that reported a relationship between blood pressure or hypertension and aortic expansion, showed consistently a greater initial aortic dimension than studies that did not report such a relationship.

Discussion

This is the first detailed systematic review, to our knowledge, that examined the relationship between hypertension and TAA of 'so called' degenerative or atherosclerotic origin. We found a relatively high proportion of hypertension in persons with this kind of TAA. The prevalence of hypertension was greater than the prevalence of the other major risk factors for atherosclerotic vascular disease. In addition we provide a potential resolution of the reported controversial relationship between blood pressure and TAA progression.

Hypertension was present in 70% of persons with TAA. In two studies that were excluded for having 30-50% chronic dissections in their population, the prevalence of hypertension was 71% and 73% [25,26], which is similar to our findings that focused mainly on aneurysms without dissections. The prevalence of hypertension was highest in ascending TAAs which argues against the contention that ascending TAA is associated with less atherosclerosis [11].

Because most of the studies did not provide detailed age and blood pressure data, it was not possible to construct age-adjusted hypertension prevalence to permit comparisons with the general population. The 70% prevalence of hypertension for persons of 65 years of age, which was the mean age of the persons with TAA, in studies across different decades, is greater than the prevalence of hypertension in the general US population from NHANES population data for individuals of 60 to 69 years of age, with data collection from 1988 to 1991 [27]. As most of the TAA publications originated in the USA, the NHANES data is a reasonable comparator.

The relationship of blood pressure to the rate of TAA expansion has been controversial. Some studies report a significant correlation between blood pressure and TAA expansion [20,22] while other studies do not [12,23]. There may be several explanations for the divergent conclusions. First, the blood pressure selected for correlation with aortic expansion varied. One study reported that there was a correlation between diastolic, but not systolic blood pressure, and expansion rate [20]. Another study examined the relation of systolic blood pressure to aortic expansion and found it was almost significant in univariate analysis [12]. A second reason is that none of the studies were randomized control trials and therefore are subject to the biases of retrospective analysis. These include variations in the proportion receiving anti hypertensive medications and the degree of blood pressure control. Thirdly, the follow-up period for some studies was short, on average of six months to a year. A longer period maybe required to reveal the effects of hypertension on expansion rate. Fourthly, studies comment that patients were often already started on antihypertensive medications which makes it challenging to isolate the effects of blood pressure on growth as antihypertensive drugs may mitigate any effect that elevated blood pressure may have had [22,23]. Fifth, we propose an explanation based on aortic wall stress in TAA. Aortic wall stress is greater in larger compared to smaller aneurysms at the same level of blood pressure [28]. This is supported by our analysis that the two studies with larger aneurysms found that hypertension was a relevant risk factor for aortic expansion. The stress on the aortic wall should drive TAA expansion and this stress is greater in larger compared to smaller TAAs. In addition we found that studies showing a greater role for hypertension were those with higher rates of aortic expansion. While aortic expansion rates are linked with initial aortic dimension, the data suggest that hypertension maybe more important in rapidly expanding TAAs.

There are several potential limitations of our study that warrant consideration. First, we excluded studies published in non-English languages. This type of exclusion is reasonable as it does not affect the outcome of most meta-analysis [29]. Second, the absence of hypertension in all cases of TAA does not invalidate a role for hypertension in the pathogenesis of TAA. The development of TAA requires additional factors in the arterial wall which fail to oppose or accentuate aortic expansion [4]. Third, the major limitation of these kinds of reviews is the nature of the available reported data. While not a critique of those studies, most studies were focused on the nature of the aortic aneurysm, its co morbidity and its progression rather than a detailed description of blood pressure measurement or the nature of the hypertension. Furthermore there were differences in study criteria, differences in definitions, and lack of explicit definition

of key clinical terminology. The extent to which some studies have included a proportion of cases of aortic dissections, valvular diseases, previous vascular surgery or genetic diseases can create appreciable discrepancies between studies. Fourth, the role of antihypertensive drugs in TAA progression could not be assessed from this study. This subject is dealt with in randomized control trials although mainly in Marfan syndrome [30]. Lastly, we did not examine clinical endpoints of aortic rupture or dissection. We have previously examined this issue and found a trend of increasing prevalence of hypertension and aortic dissection [9]. Hypertension may be causative in the pathophysiology of aortic rupture. Blood pressure trends in men and women in 18 countries show a general parallel between reduction in blood pressure over time and reduction in mortality from thoracic aneurysms [31].

Conclusion

Analysis of pooled data from more than 1400 persons with TAA mainly of so-called 'degenerative or atherosclerotic' etiology shows a high proportion, specifically 70%, with hypertension. The prevalence of hypertension was highest (80%) in ascending compared to descending TAAs. These data in conjunction with the significantly higher prevalence of hypertension compared to cigarette smoking and dyslipidemia in TAA, suggest that hypertension is the leading risk factor for TAA of 'atherosclerotic or degenerative' origin. TAA is not just a condition of rare genetic or inherited diseases but is more commonly due to so called 'atherosclerotic or degenerative conditions' and these kind of TAAs are increasing in prevalence [2,32]. While recognizing that other factors are operative in the production of TAA, our analysis provides evidence for vigilance in the assessment and management of blood pressure especially in those with larger TAA and those with higher aortic expansion rates.

References

1. Coady MA, Rizzo JA, Goldstein LJ, Elefteriades JA. Natural history, pathogenesis, and etiology of thoracic aortic aneurysms and dissections. Cardiol Clin. 1999; 17: 615-635.
2. Olsson C, Thelin S, Stahle E, Ekbom A, Granath F. Thoracic aortic aneurysm and dissection: increasing prevalence and improved outcomes reported in a nationwide population-based study of more than 14,000 cases from 1987 to 2002. Circulation. 2006; 114: 2611-2618.
3. Norman PE, Powell JT. Site specificity of aneurysmal disease. Circulation. 2010; 121: 560-568.
4. Rabkin SW. Accentuating and Opposing Factors Leading to Development of Thoracic Aortic Aneurysms Not Due to Genetic or Inherited Conditions. Front Cardiovasc Med. 2015; 2: 21.
5. Goldfinger JZ, Halperin JL, Marin ML, Stewart AS, Eagle KA, Fuster V. Thoracic aortic aneurysm and dissection. J Am Coll Cardiol. 2014; 64: 1725-1739.
6. Hiratzka LF, Bakris GL, Beckman JA, Bersin RM, Carr VF, Casey Jr DE, et al. 2010ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease: executive summary. A report of the American College of Cardiology Foundation/American Heart Association Task Forceon Pra. Catheter Cardiovasc Interv. 2010; 76: 43-86.
7. Boodhwani M, Andelfinger G, Leipsic J, Lindsay T, McMurtry MS, Therrien J, et al. Canadian Cardiovascular Society position statement on the management of thoracic aortic disease. Can J Cardiol. 2014; 30: 577-589.
8. Hirst AE Jr, Johns VJ Jr, Kime SW Jr. Dissecting aneurysm of the aorta: a review of 505 cases. Medicine (Baltimore). 1958; 37: 217-279.
9. Chan KK, Rabkin SW. Increasing prevalence of hypertension among patients with thoracic aorta dissection: trends over eight decades-a structured meta-analysis. Am J Hypertens. 2014; 27: 907-917.
10. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol. 2009; 62: 1006-1012.
11. Achneck H, Modi B, Shaw C, Rizzo J, Albornoz G, Fusco D, et al. Ascending thoracic aneurysms are associated with decreased systemic atherosclerosis. Chest. 2005; 128: 1580-1586.
12. Geisbusch S, Stefanovic A, Schray D, Oyfe I, Lin HM, Di Luozzo G, et al. A prospective study of growth and rupture risk of small-to-moderate size ascending aortic aneurysms. J Thorac Cardiovasc Surg. 2014; 147: 68-74.
13. Rabkin S, Chan KK, Chow B, Janusz M. Pulse Wave Velocity Involving Proximal Portions of the Aorta Correlates with the Degree of Aortic Dilatation at the Sinuses of Valsalva in Ascending Thoracic Aortic Aneurysms. Ann Vasc Dis. 2014; 7: 404-409.
14. Shang EK, Nathan DP, Sprinkle SR, Vigmostad SC, Fairman RM, Bavaria JE, et al. Peak wall stress predicts expansion rate in descending thoracic aortic aneurysms. Ann Thorac Surg. 2013; 95: 593-598.
15. Nathan DP, Xu C, Pouch AM, Chandran KB, Desjardins B, Gorman JH 3rd, et al. Increased wall stress of saccular *versus* fusiform aneurysms of the descending thoracic aorta. Ann Vasc Surg. 2011; 25: 1129-1137.
16. Juvonen T, Ergin MA, Galla JD, Lansman SL, Nguyen KH, Mc Cullough JN, et al. Prospective study of the natural history of thoracic aortic aneurysms. Ann Thorac Surg. 1997; 63: 1533-1545.
17. Bastien M, Dagenais F, Dumont E, Vadeboncoeur N, Dion B, Royer M, et al. Assessment of management of cardiovascular risk factors in patients with thoracic aortic disease. Blood Press Monit. 2012; 17: 235-242.
18. Ito S, Akutsu K, Tamori Y, Sakamoto S, Yoshimuta T, Hashimoto H, et al. Differences in atherosclerotic profiles between patients with thoracic and abdominal aortic aneurysms. Am J Cardiol. 2008; 101: 696-699.
19. Davies RR, Gallo A, Coady MA, Tellides G, Botta DM, Burke B, et al. Novel measurement of relative aortic size predicts rupture of thoracic aortic aneurysms. Ann Thorac Surg. 2006; 81: 169-177.
20. Masuda Y, Takanashi K, Takasu J, Morooka N, Inagaki Y. Expansion rate of thoracic aortic aneurysms and influencing factors. Chest. 1992; 102: 461-466.
21. Joyce JW, Fairbairn JF 2nd, Kincaid OW, Juergen JL. Aneurysms of the Thoracic Aorta. A Clinical Study with Special Reference to Prognosis. Circulation. 1964; 29: 176-181.
22. Dapunt OE, Galla JD, Sadeghi AM, Lansman SL, Mezrow CK, De Asla RA, et al. The natural history of thoracic aortic aneurysms. J Thorac Cardiovasc Surg. 1994; 107: 1323-1332.
23. Bonser RS, Pagano D, Lewis ME, Rooney SJ, Guest P, Davies P, et al. Clinical and patho-anatomical factors affecting expansion of thoracic aortic aneurysms. Heart. 2000; 84: 277-283.
24. Coady MA, Rizzo JA, Hammond GL, Mandapati D, Darr U, Kopf GS, et al. What is the appropriate size criterion for resection of thoracic aortic aneurysms? J Thorac Cardiovasc Surg. 1997; 113: 476-491.
25. Svensson L, Crawford E, Hess K, Coselli J, Safi H. Variables predictive of outcome in 832 patients undergoing repairs of the descending thoracic aorta. Chest. 1993; 104: 1248-1253.
26. Pressler V, McNamara JJ. Aneurysm of the thoracic aorta. Review of 260 cases. J Thorac Cardiovasc Surg. 1985; 89: 50-54.
27. Burt VL, Whelton P, Roccella EJ, Brown C, Cutler JA, Higgins M, et al. Prevalence of hypertension in the US adult population. Results from the Third National Health and Nutrition Examination Survey, 1988-1991. Hypertension. 1995; 25: 305-313.
28. Rabkin SW, Janusz MT. Aortic Wall Stress in Hypertension and Ascending Thoracic Aortic Aneurysm: Implications for Antihypertensive Therapy. High Blood Press Cardiovasc Prev. 2013; 20: 265-271.

29. Grégoire G, Derderian F, Le Lorier J. Selecting the language of the publications included in a meta-analysis: is there a Tower of Babel bias? J Clin Epidemiol. 1995; 48: 159-163.

30. Lacro RV, Dietz HC, Sleeper LA, Yetman AT, Bradley TJ, Colan SD, et al. Atenolol *versus* losartan in children and young adults with Marfan's syndrome. N Engl J Med. 2014; 371: 2061-2071.

31. Sidloff D, Choke E, Stather P, Bown M, Thompson J, Sayers R. Mortality From Thoracic Aortic Diseases and Associations With Cardiovascular Risk Factors. Circulation. 2014; 130: 2287-2294.

32. Ince H, Nienaber CA. Etiology, pathogenesis and management of thoracic aortic aneurysm. Nat Clin Pract Cardiovasc Med. 2007; 4: 418-427.

Citation: Tong JKT and Rabkin SW. The Relationship between Hypertension and Thoracic Aortic Aneurysm of Degenerative or Atherosclerotic Origin: A Systematic Review. Austin Hypertens. 2016; 1(1): 1004.