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Clinical Characteristics of Symptomatic Vertebral Artery Dissection. A Systematic Review

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Abstract

Background—Vertebral artery dissection (VAD) is an important cause of stroke in the young. It can present nonspecifically and may be misdiagnosed with adverse consequences. We assessed the frequency of head/neck pain, other neurological symptoms, and cerebrovascular events in symptomatic VAD.

Methods—We conducted a systematic review of observational studies, searching electronic databases (MEDLINE, EMBASE) for English-language manuscripts with >5 subjects with clinical or radiological features of VAD. Two independent reviewers selected studies for inclusion; a third adjudicated differences. Studies were assessed for methodological quality and clinical data were abstracted. Pooled proportions were calculated.

Results—Of 3996 citations, we screened 511 manuscripts and selected 75 studies describing 1,972 VAD patients. The most common symptoms were dizziness/vertigo (58%), headache (51%) and neck pain (46%). Stroke was common (63%), especially with extracranial dissections (66% vs. 32%, $p < 0.0001$), while TIA (14%) and subarachnoid hemorrhage (SAH) (10%) were uncommon. SAH was seen only with intracranial dissections (57% vs. 0%, $p = 0.003$). Fewer than half of the patients had obvious trauma, and only 7.9% had a known connective tissue disease. Outcome was good (modified Rankin scale (mRS) 0-1) in 67% and poor (mRS 5-6) in 10%.

Conclusion—VAD is associated with nonspecific symptoms such as dizziness, vertigo, headache, or neck pain. Ischemic stroke is the most common reported cerebrovascular

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complication. VAD should be considered in the diagnostic assessment of patients presenting with dizziness or craniocervical pain, even in the absence of other risk factors. Future studies should compare clinical findings as predictors in well-defined, undifferentiated populations of clinical VAD suspects.

Keywords

vertebral artery dissection; dizziness; meta-analysis

INTRODUCTION

Vertebral artery dissection (VAD) is one of the most common identifiable causes of stroke in those aged 18-45,¹ with an estimated annual incidence between 1 and 1.5 per 100,000.² Since VAD is a potentially treatable cause of transient ischemic attack (TIA) and stroke,³ and the greatest risk of stroke in craniocervical dissections appears to occur in the first few weeks after dissection⁴, prompt diagnosis is essential. Unfortunately, VAD is not always easily recognized, and young patients with missed VAD may suffer potentially disastrous neurologic complications or death.⁵

Frank presentations of stroke, TIA, or subarachnoid hemorrhage (SAH) are likely to initiate an inpatient hospitalization and complete diagnostic workup, including vascular imaging, but patients with VAD may present with nonspecific complaints such as dizziness with neck pain, or headache with nausea and vomiting. Although VAD is more likely to be considered in patients with a clear history of trauma or with known underlying connective tissue disease, in some cases neither of these known risk factors is present.

The literature describing VAD is varying in quality and content, and many studies report on only a few patients. The purpose of this study was to conduct a systematic review of studies reporting clinical and radiographic data on individuals with VAD, to determine both the level of evidence available on this topic and to identify core clinical features of the syndrome. We sought to characterize the frequency of various symptoms, ischemic complications, and spectrum of outcomes in individuals with VAD.

METHODS

Search strategy

The search strategy was designed by a PhD-trained clinical investigator with relevant domain expertise and the co-director of our Evidence-based Practice Center with extensive experience in systematic reviews. We searched MEDLINE and EMBASE for English-language articles, using text words and controlled vocabulary terms including: vertebral, vertebro-basilar, dissection, pseudo aneurysm, and other terms related to craniocervical dissection. The search was not designed to identify studies reporting on asymptomatic dissections resulting from routine secondary or tertiary trauma screening assessments in multi-trauma victims. We did not restrict our search by date of publication or patient age. We also performed a manual search of reference lists from eligible articles. We did not attempt to contact corresponding authors and did not seek to identify research abstracts from meeting proceedings or unpublished studies. The search was updated through February 2009.

Selection criteria

All gathered literature was subject to title and abstract screening by two independent reviewers. Articles were selected using pre-determined criteria. These criteria excluded

papers that were not in English, lacked original patient data (or were duplicating data published in other included papers), were not about vascular disease or craniocervical dissection, focused on VAD resulting from surgical or penetrating trauma, did not include data about clinical or radiological features, or involved five or fewer subjects. We chose to exclude studies with small numbers of subjects because of concerns about how patients were recruited, including selection based on specific clinical features that might make the reported cases non-representative of other VAD patients.

Although exclusion by sample size at the abstract review stage was for studies with fewer than 5 subjects, we also chose to exclude all studies with only 5 subjects after full text review because of residual concerns about the methodology in these smaller studies (thus, the final review excluded all studies with 5 subjects).

We included studies with radiological or pathological confirmation of dissection. Both intracranial and extracranial dissections were included. We did not establish preconditions on the presence of specific radiological features for diagnosis of VAD. We chose this approach because we suspected from the outset that most studies would not provide sufficient detail regarding diagnostic criteria for patient selection.

Full-text screening was applied to all abstracts considered eligible or possibly eligible by at least one reviewer (i.e., labeled “yes” or “maybe” in the abstract review). Two independent reviewers identified whether full-text manuscripts were eligible and provided a reason for exclusion. At the full text level concordance was mandated for reason of exclusion. When coders disagreed about the reason for exclusion it was resolved by discussion. A third reviewer verified the eligibility of selected articles and settled any discrepancies in selection status.

Assessment for study quality

Two unmasked raters and a third adjudicator also assessed the methodological quality of included studies based upon criteria derived from the Standards for Reporting Diagnostic Accuracy Statement,⁶ and recommended for use with studies of history and physical examination as diagnostic tests.⁷ Specifically, we rated the quality of the studies based on the following parameters: (1) participant recruitment and sampling—whether there was systematic recruitment/diagnosis of all patients with specific symptoms/signs or systematic case identification from radiographic files/databases, (2) data collection—whether there was prospective systematic data collection with a standardized data collection form applied to all patients; and (3) masking—whether examiners were masked to the VAD diagnosis. The quality of the studies was rated as high if all criteria were adequately addressed, medium if any criteria were adequately addressed, and low if none of the criteria were adequately addressed. If the two initial reviewers disagreed on the study quality, a third adjudicator settled the discrepancy.

Within-study data extraction

Data extraction was performed by a single author. Subsets of these data were checked by a second author. Information extracted from each article included study type, number of subjects with VAD, the frequency of head and neck pain, various neurological symptoms, cerebrovascular events, prognosis, associated risk factors, radiological features, and the site of dissection. For data about prognosis, in most cases, actual Rankin scores were provided in the manuscripts; in some papers, however, prognosis was described as by level of impairment, often using descriptive terms such as good, mild impairment, moderate impairment, or bad outcome. We used these descriptions to categorize patients into the equivalent modified Rankin score categories 0-1 (good outcome), mRS 2-4 (fair outcome),

or mRS 5-6 (poor outcome). Data were extracted at the subject level as provided in the included manuscripts, and only those patients meeting inclusion criteria were analyzed (e.g., in studies reporting both carotid and vertebral dissection patients, only those with VAD were considered). Some outcomes could only be assessed in aggregate (e.g., mean age), in which case sample-size weighted means were calculated.

Data synthesis

We restricted our analysis for each research question (i.e., within each table) to those studies that were felt to be free of bias with respect to those data for the particular question. For example, for assessment of headache frequency, we did not include studies that required headache as a diagnostic requirement for inclusion into that particular study. Bias was assessed per individual symptom or outcome, so a study could be rated as unbiased regarding one symptom but biased regarding another. In addition, assessment of stroke, TIA, and SAH were synthesized both overall (in studies with mixed samples of extracranial and intracranial dissections) and separately for those which reported separate numbers for intracranial versus extracranial dissections.

We calculated proportions with standard errors. Pooled standard errors were calculated separately for each symptom or outcome type. No formal tests of heterogeneity or subgroup analyses were performed. Data were handled in Reference Manager v11 (Stamford, CT), ProCite v5.0.3 (Stamford, CT), EndNote (Stamford, CT) and Microsoft Excel 2003 (Redmond, WA). Standard errors and kappa values were calculated using Microsoft Excel and Stata v8.0 (College Station, TX).

RESULTS

Our search identified 3996 unique citations, of which 3485 (87.2%) were excluded at the abstract level (Figure). Agreement was 98.5% for yes/no ratings at the abstract level, with kappa=0.65.

We did not demand concordance on reason for abstract exclusion. At the abstract level, concordant exclusions (66%) were as follows: not about craniocervical dissection 54% (1238/2289), no clinical feature data 19% (437/2289), not about vascular disease 16.6% (380/2289), <5 subjects 6.3% (145/2289), no original patient data 3.8% (87/2285), not English 0.04% (1/2289), and VAD from penetrating trauma 0.04% (1/2289).

We sought to examine 511 full manuscripts, 6 of which were unretrievable despite multiple attempts from multiple sources. After initial screening, there were 20 disagreements about study inclusion (kappa 0.74) and 99 on reason for exclusion when the two raters agreed regarding the eligibility of the study. Disagreements about study inclusion were resolved by a third reviewer. Concordance was forced on the reason for exclusion by discussion between the two coders. After our full-text review, 430 articles were excluded and 75 were considered eligible. These eligible studies represented 2% of the total (n=75/3996). The principal reasons for exclusion of full text manuscripts after concordance was forced were 5 subjects 32% (138/430), no original patient data 28% (122/430), combined data about vertebral and carotid artery dissection that could not be segregated 18% (77/430), not about craniocervical dissection 9% (38/430), not about vertebral artery dissection 8% (35/430), focused solely on treatment 3% (14/430) and other 1% (6/430).

All 75 included studies were of modest quality (Table 1). No studies met criteria for high quality, which required presence of the three parameters described above. Medium quality rating was given to 48% of the studies, with the others rated as low quality. Individual sample sizes ranged from 6 (based on our exclusion of any studies with 5 or fewer subjects)

to 332 subjects. When pooled together, a total of 1,972 individuals with vertebral artery dissection were available for study. Of the 512 of these individuals in whom information was provided as to the location of the dissection, 134 (26%) were extracranial and 378 (74%) were intracranial. Most studies included adults only, with one only studying children⁸ and 10 others including a mix of pediatric and adult subjects. Most studies analyzed retrospectively-collected data in a series of patients. The mean age of the population studied was 46.5 years.

Symptoms associated with VAD

When studies presenting unbiased estimates of particular symptoms were pooled together, dizziness or vertigo was the most common symptom among individuals with vertebral artery dissection, in approximately 58% of VAD patients, followed by headache (51%) and then neck pain (46%) (Table 2). Headache or neck pain as the initial symptom was present in 67% (pooled), although the range of frequency reported was between 24% and 100%. Seventy-six percent of the individuals in studies with unbiased estimates had either head or neck pain at some point during their presentation (SE 0.02); thus, nearly one in four patients had no craniocervical pain either as an index symptom or evolving by the time of diagnosis.

The standard errors were quite large for these pooled proportions, demonstrating the significant heterogeneity across studies in estimating the prevalence of these symptoms. Fewer studies provided information on more specific neurologic symptoms such as gait problems or ataxia, nystagmus, dysphagia, and tinnitus than about nonspecific symptoms such as dizziness, headache, neck pain, nausea/vomiting, and visual symptoms.

Cerebral ischemic events and SAH

Stroke was commonly reported in VAD subjects, occurring in 63% of cases, with a higher prevalence among those with extracranial than intracranial VAD (66% vs. 32%, $p<0.0001$) (Table 3). TIA was much less commonly reported, occurring in only 14% of VAD subjects analyzed, with a trend towards being more common among those with extracranial than intracranial VAD (21% vs. 11%, $p=0.25$). SAH was the least common cerebrovascular complication, occurring in 10% of cases, and exclusively among those with intracranial VAD (57% vs. 0%, $p=0.003$) when location was reported.

VAD and trauma

Minor trauma was relatively uncommon in association with VAD, with even lower frequencies of sporting injuries, chiropractic manipulation, and “major trauma” (primarily motor vehicle accidents) (Table 4). Examples given of minor trauma cited in the referenced papers include abrupt head turning, massage, falls, bending over, positioning for surgery, or riding a roller coaster. Sports identified as possible risk factors included jogging, horseback riding, skiing, surfing, and playing tennis. Studies on dissections from penetrating trauma were excluded from this systematic review.

Outcome after VAD

Despite variability across studies, in general, individuals with VAD appear to have relatively good outcomes when treated in routine clinical fashion. Outcomes using a modified Rankin Scale between 0 and 1 are reported in Table 5. Poor outcomes occurred only in 10% of the total group of 570 individuals in whom outcome was reported, with the highest proportion of poor outcome just over 35% in one study of 17 individuals;⁹ this study still observed that the majority of patients had good outcomes.

Other factors associated with VAD

In the 12 studies¹⁰⁻²¹ that addressed history of connective tissue disorders (some with known diagnosis before VAD, others diagnosed after VAD), only 7.9% (SE 21.6%), on average, had a known connective tissue disorder, including fibromuscular dysplasia. However, this varied between 1.1% in one larger study¹¹ to as high as 56% in a smaller series.¹⁹ Results for history of smoking were slightly less heterogeneous, with an overall proportion of 170/496 individuals with history of smoking (34%, SE 38%).

DISCUSSION

Our systematic review of 75 papers demonstrates that reports on clinical features associated with VAD are heterogeneous, with very few (only two) studies including sample sizes over 100, and no studies of high quality by methodological criteria. We found that nonspecific symptoms (dizziness/vertigo, headache, and neck pain) are the most frequent clinical manifestations in patients with VAD, but no particular clinical symptom was sufficiently common as to exclude VAD when absent (e.g., absence of neck pain is not a sufficient predictor against VAD to rule out the disease). Unfortunately, most studies did not report data required for synthesis of clinical feature combinations that might have helped physicians identify a distinctive clinical profile for VAD. Given the mean age of reported VAD patients (46.5 years) is roughly 20 years younger than in unselected stroke populations,²² however, our study results do suggest that clinicians should be particularly vigilant when assessing young adults with these symptoms.

While our review did not identify studies that allowed pooled estimates of VAD prevalence in unselected clinical populations, a recently published study suggests that VAD may not be rare (~5%) even among patients with non-specific, mild symptoms such as headaches or dizziness.²³ Taken together with well-documented reports of these as isolated presenting symptoms of VAD,^{24, 25} our study strongly suggests that VAD should be considered in the differential diagnosis in patients with these common symptoms, even in the absence of more obvious (e.g., hemiparesis) or specific manifestations (e.g., cranial nerve palsies). This is particularly important for younger patients where the combination of dizziness with craniofacial or cervical pain might otherwise be mistaken for a benign diagnosis such as vestibular migraine.⁵

Stroke was surprisingly common in our review, particularly in extracranial vertebral artery dissection. TIA, by contrast, was surprisingly uncommon (though, like completed stroke, more common with extracranial VAD). Whether these prevalence findings reflect detection bias (i.e., dissections were more often sought and discovered in patients with stroke) is unknown. A recent study, however, found no completed strokes and 6 possible TIAs among 14 VAD patients who presented with mild, non-specific symptoms such as headache or vertigo.²³ Prospective diagnostic studies in unselected patients presenting with dizziness, vertigo, headache, and neck pain would be required to identify the full spectrum of patients with VAD and determine the true population proportion with stroke or TIA.

SAH was clearly more prevalent in patients with intracranial VAD. The one small study reporting extracranial VAD found no associated SAH, and the prevalence of SAH in studies failing to report dissection location was far lower than that of studies reporting intracranial VAD. Although the focus of this review was not treatment of VAD, this diagnostic finding relates to choice of therapy. Anticoagulation is often given for VAD, despite some controversy and a lack of guidelines advising this practice.²⁶ In cases of intracranial extension of the dissection, however, the clinician is generally advised to avoid anticoagulation because of the concern for SAH.²⁷ Our review corroborates the fact that SAH was much more common in the presence of an intracranial VAD, and ischemic stroke

was more common in the presence of extracranial VAD, adding to the evidence base supporting current practice. This does not, however, answer the question as to whether an individual with intracranial VAD who presents with a stroke should be anticoagulated or not. Whether the relatively good clinical outcomes for patients identified in this study reflect benefits of therapy or simply natural history of disease remains unknown. We found no information in these studies about the effects of treatment with antithrombotic medications, which would be an important area for future research.

The risk factors generally sought when considering a diagnosis of VAD, such as connective tissue disorders or history of trauma, were not seen in a majority of individuals, with fewer than 8% of reported subjects having connective tissue disorders and fewer than half having obvious trauma, even using fairly liberal definitions of “trauma.” This is not to suggest that VAD patients without known collagen-vascular diseases might not have occult abnormalities of their connective tissue,²⁸ but it does emphasize the need to shift clinical focus away from seeking VAD only in patients with underlying conditions of this type—particularly in light of recent studies demonstrating that connective tissue abnormalities are no more common in VAD than in non-VAD stroke controls.²⁹ Similarly, absence of a trauma history should not cause a clinician to remove VAD from consideration as a possible cause of stroke, TIA, or SAH.

Our study is limited principally by the quality of the source data. In general, most studies that met medium quality criteria did so only because of adequacy of subject recruitment or case ascertainment. Most studies did not provide adequate information about data collection or masking of examiners. No study met all three criteria for quality (required to be considered high quality, as discussed above), and very few met two. Similarly, the lack of control groups in the large majority of these papers makes it impossible to compare frequencies of symptoms in VAD to patients with other vascular presentations or to generate odds ratios for VAD given a particular symptom (or vice versa). Finally, most studies do not provide data on particular combinations of symptoms, so we cannot estimate the frequency of certain symptom constellations (such as headache and vertigo alone, for instance) in VAD patients.

To mitigate the effects of design flaws, we reviewed studies not only for quality but for bias with respect to individual symptoms or features being analyzed when determining which results should be included; nevertheless, there was likely some residual bias or variability. We could not exclude all papers using “clinical history consistent with dissection” as a diagnostic criterion, because one would anticipate that all cases diagnosed as dissection had at least some consideration of the clinical history. The extent to which an individual manuscript disclosed risks related to diagnostic work-up, review, or incorporation bias³⁰ may have limited our ability to weed out biased samples from the data analysis. Similarly, the extent to which investigators systematically inquired about history of trauma was probably quite variable, and it would be expected that making a diagnosis of VAD would make it more likely that an individual would identify a recent minor trauma (so-called rumination bias). These differences in recruitment and case ascertainment are likely to explain some of the heterogeneity we found for many of the symptoms and features reported here. We also excluded from review the trauma literature, in which dissection would be identified through systematic screening of asymptomatic patients. This limits our conclusions somewhat, particularly regarding rates of trauma when extrapolating to all patients with VAD (as opposed to that subset who present with various specific or nonspecific neurologic symptoms).

For stroke, TIA, and SAH we separated those studies that identified the location of the dissection and found differences. Given the relatively small number of studies that provided

detailed information about dissection location, we chose to analyze symptom results in combined fashion, but the admixture of intracranial and extracranial dissections might partially explain the large standard errors and wide ranges of prevalence of particular symptoms or outcomes. For example, an estimation of neck pain frequency might be very different in one study with primarily extracranial dissections, as compared to another with a larger number of intracranial dissections, in which headache might be more common. The heterogeneity of the included studies, as well as the heterogeneity of the definitions of clinical symptoms within the studies, limits our conclusions somewhat. It highlights the challenges inherent in determining unbiased symptom prevalence values, but also the importance of compiling these into a systematic review to demonstrate the range of frequencies seen across the literature and offer summary prevalence estimates for frequent symptoms.

Despite these limitations, we feel that our study findings will assist physicians in recognizing the clinical phenotype of VAD. Given the large number of subjects across all of the pooled studies, we have described important patterns in symptomatology and outcome. We used standardized search strategies and specific criteria for rating study quality and appropriateness for inclusion in this review. We are confident that we were able to identify most published, relevant studies pertaining to VAD. There were 6 manuscripts that we could not retrieve, but, given the large overall sample size, we do not anticipate that these would have meaningfully influenced our results, as they had relatively small sample sizes individually. Our review is strengthened by the requirement of included studies to have radiographic or pathologic confirmation of VAD.

Conclusions

Our systematic review of subjects with VAD demonstrates that vertigo, dizziness, headache, and neck pain are the most common presenting symptoms in individuals with VAD. Diagnostic assessment of individuals with these complaints should include consideration of VAD, perhaps even when more specific neurologic symptoms are absent. Although we are not recommending that a complete imaging workup for VAD is needed in all individuals with headache or dizziness, we do wish to draw attention to the fact that VAD may present with relatively common symptoms, and that many VAD patients do not have symptoms typically linked to VAD. As an example, the pooled prevalence of neck pain in VAD is only 46%, emphasizing that the majority of patients with VAD do *not* report neck pain. It remains uncertain at this point whether patients presenting with isolated symptoms, such as dizziness, are at high risk for VAD, or what the predictive values for certain symptom combinations may be. A history of trauma or connective tissue disease is not found in the majority of symptomatic cases. Most individuals are identified when they present with either stroke (particularly if the VAD is extracranial) or, less frequently, SAH (particularly if the VAD is intracranial). Most appear to have relatively good outcomes when treated in accordance with routine practice. Large-scale, prospective studies imaging systematically for VAD in undifferentiated clinical populations (e.g., emergency department patients with dizziness or vertigo), and comparing VAD patients with non-VAD controls will be needed to refine prevalence estimates for clinical findings and determine their diagnostic value (i.e., sensitivity, specificity, likelihood ratio).

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Figure. Citation search and selection

¹ MEDLINE was accessed via PubMed; EMBASE – the Excerpta Medica database

² Abstracts coded as “yes” or “maybe” by at least one reviewer

³ Adjudication by third reviewer

Table 1

Studies selected for inclusion.

Study	Age Range	Year published	N	Study method	Quality rating
Ahmad ¹	28-53	1999	8	retrospective	2
Ahn ²	33-67	2006	14	retrospective	3
Anxionnat ³	45-61	1994	7	retrospective	3
Arnold ⁴	27-53	2006	12	retrospective	2
Arnold ⁵	21-69	2006	169	retrospective	2
Auer ⁶	23-60	1998	19	retrospective	3
Bartels ⁷	18-59	1996	20	retrospective	3
Bartels ⁸	18-60	2006	24	retrospective	3
Beletsky ⁹	>18 y	2003	67	prospective	2
Berger ¹⁰	21-57	1984	6	retrospective	3
Boet ¹¹	16-63	2002	9	retrospective	3
Campos ¹²	13-57	2007	22	retrospective	2
Chen ¹³	27-57	2004	17	retrospective	2
Chiche ¹⁴	33-71	2005	10	retrospective	3
Chiras ¹⁵	26-64	1985	15	retrospective	3
Chung ¹⁶	4-67	2002	29	retrospective	3
Clevert ¹⁷	21-95	2007	35	prospective	3
Clevert ¹⁸	22-83	2005	9	retrospective	3
Dae Hee ¹⁹	15-58	1998	15	retrospective	2
De Bray ²⁰	unknown	2000	22	prospective	3
De Bray ²¹	21-64	1997	16	retrospective	2
De Sousa ²²	30-67	2005	10	prospective	2
Dittrich ²³	44.1 y (mean)	2006	31	retrospective	2
Dziewas ²⁴	43.2 y (mean)	2003	46	retrospective	2
Ganesan ²⁵	8 mo- 13 yrs	2002	10	retrospective	3
Gelbert ²⁶	unknown	1991	6	unknown	3
Greselle ²⁷	24-63	1987	13	retrospective	3
Han ²⁸	15-58	1998	16	retrospective	3
Hashimoto ²⁹	46-82	2008	6	retrospective	3
Hicks ³⁰	8-61	1994	47	prospective	2
Hoffmann ³¹	24-58	1993	10	retrospective	2
Hosoya ³²	25-82	1999	31	retrospective	3
Hosoya ³³	40-64	1994	13	prospective	3
Hufnagel ³⁴	27-46	1999	8	retrospective	3
Josien ³⁵	17-66	1992	9	retrospective	3
Kim ³⁶	4-67	2006	35	retrospective	2
Kitanaka ³⁷	33-65	1994	24	retrospective	3

Study	Age Range	Year published	N	Study method	Quality rating
Leclerc ³⁸	27-54	1999	16	retrospective	2
Lee ³⁹	46.9 y (mean)	2006	22	retrospective	2
Lee ⁴⁰	34-71	2007	28	retrospective	2
Lee ⁴¹	23-77	2006	18	retrospective	2
Lu ⁴²	24-53	2000	8	retrospective	3
Mas ⁴³	24-64	1987	15	retrospective	2
Metso ⁴⁴	17-68	2007	70	retrospective	2
Mokri ⁴⁵	29-54	1988	25	retrospective	2
Naito ⁴⁶	33-68	2002	21	retrospective	3
Nakagawa ⁴⁷	37-70	2000	17	retrospective	3
Nebelsieck ⁴⁸	22-57	2009	26	prospective	2
Pelkonen ⁴⁹	1-62	2004	40	retrospective	2
Peluso ⁵⁰	10-64	2008	14	retrospective	3
Pozzati ⁵¹	34-68	1994	10	retrospective	3
Provenzale ⁵²	19-54	1996	14	retrospective	3
Pugliese ⁵³	28-58	2007	15	retrospective	3
Ramgren ⁵⁴	41-73	2005	23	retrospective	2
Reuter ⁵⁵	40 y (mean)	2006	36	retrospective	2
Rother ⁵⁶	31-83	1995	11	prospective	3
Saeed ⁵⁷	27-76	2000	26	retrospective	2
Sakata ⁵⁸	32-51	2000	6	retrospective	3
Sheah ⁵⁹	42-59	2005	6	retrospective	2
Shibata ⁶⁰	50-80	2006	30	retrospective	3
Shimoji ⁶¹	39-58	1984	7	retrospective	3
Shin ⁶²	27-59	2000	22	retrospective	3
Shin ⁶³	36-45	2007	8	unknown	2
Silbert ⁶⁴	26-69	1995	26	retrospective	2
Sturzenegger ⁶⁵	36-67	1994	14	retrospective	2
Sturzenegger ⁶⁶	34-67	1993	14	prospective	2
Takagi ⁶⁷	51.7 +/- 8 yrs	2007	62	retrospective	3
Vertinsky ⁶⁸	29-62	2008	10	retrospective	3
Wessels ⁶⁹	18-71	2008	33	prospective	2
Yamada ⁷⁰	35-71	2004	24	retrospective	3
Yamaura ⁷¹	8-86	2000	332	retrospective	2
Yamaura ⁷²	37-67	1990	24	retrospective	2
Yoshimoto ⁷³	21-64	1997	16	retrospective	3
Zhao ⁷⁴	6-67	2007	16	retrospective	2
Zuber ⁷⁵	28-54	1994	7	prospective	2

Quality rating: 1=High; 2=Medium; 3=Low

Table 2

Symptoms and signs associated with VAD.

	# Studies	Total sample size (N)	Number of subjects with symptom	Pooled proportion (pooled SE)	Range of proportions
Dizziness/ Vertigo	18 8, 16, 19, 28, 30, 32, 44, 47, 52, 55-57, 60-62, 65, 73, 74	467	273	0.58 (0.53)	5-100%
Headache	32 2, 9, 11, 12, 15, 19, 21, 22, 24, 25, 27, 28, 30, 32, 33, 35, 38, 41-46, 52, 53, 57, 60, 64-66, 69, 73	689	348	0.51 (0.7)	6-93%
Neck Pain	27 11, 12, 14, 15, 21, 22, 24, 25, 30, 35, 37, 38, 41, 43-45, 52, 53, 56, 57, 60, 61, 64-66, 69, 73	526	244	0.46 (0.69)	10-80%
Gait problems/ Ataxia	10 1, 6, 8, 16, 52, 53, 56, 57, 61, 65	150	57	0.38 (0.43)	7-71%
Visual symptoms	17 1, 6, 8, 12, 16, 30, 32, 37, 47, 52, 53, 56, 57, 61, 65, 72, 73	314	114	0.36 (0.53)	4-88%
Nausea/ Vomiting	13 1, 8, 12, 30, 32, 44, 52, 56, 57, 60, 65, 73, 74	306	108	0.35 (0.42)	5-79%
Nystagmus	7 6, 8, 30, 37, 56, 61, 65	150	44	0.29 (0.30)	4-55%
Homer's syndrome	11 30, 41, 44, 47, 52, 55, 60, 61, 65, 72, 73	265	58	0.22 (0.03)	6-36%
Sensory deficits	17 1, 8, 16, 30, 32, 37, 47, 52, 53, 55-57, 60, 61, 65, 72, 73	335	70	0.21 (0.43)	4-58%
Cranial nerve palsies	11 8, 30, 37, 47, 52, 53, 55, 56, 65, 72, 73	241	51	0.21 (0.32)	4-43%
Dysphagia	6 16, 53, 57, 60, 65, 74	102	13	0.13 (0.20)	5-29%
Tinnitus	4 5, 32, 44, 65	238	17	0.07 (0.09)	5-13%

Table 3

Cerebrovascular complications of VAD by location of the dissection.

Cerebrovascular complication	Dissection Location	# Studies	Total sample size (N)	Number of subjects with complication	Pooled proportion (pooled SE)	Range of proportions
Stroke	Any	36 1, 2, 5, 8, 9, 13-15, 19, 20, 23, 24, 27, 28, 32, 35, 36, 38, 40-43, 45, 46, 49, 51, 52, 55-57, 60, 62-65, 72 }	944	571	0.60 (0.71)	10-89%
	Intracranial	7 2, 19, 32, 40, 46, 60, 72	176	57	0.32 (0.26)	13-48%
TIA	Extracranial	6 8, 14, 19, 35, 43, 65	74	50	0.68 (0.38)	10-89%
	Any	20 2, 5, 6, 8, 9, 13, 15, 19, 20, 23, 24, 27, 35, 38, 41, 43, 45, 52, 63, 65	571	80	0.14 (0.37)	7-26%
	Intracranial	2 2, 19	28	3	0.11 (0.12)	7-14%
SAH	Extracranial	5 6, 8, 19, 35, 65	70	15	0.21 (0.30)	7-75%
	Any	17 5, 9, 19, 21, 32, 37, 40, 42, 45, 50-52, 57, 60, 62, 64	865	304	0.35 (0.42)	0-93%
	Intracranial	8 19, 21, 32, 37, 40, 50, 60, 71	481	274	0.57 (0.31)	5-93%
	Extracranial	1 21	7	0	0.00	0%

Table 4

History of trauma associated with VAD

	# Studies	Total sample size (N)	Number of subjects with symptom	Pooled proportion (pooled SE)	Range of proportions
Major trauma (primarily MVA)	6 1, 8, 27, 31, 53, 69	103	15	0.15 (0.22)	10-25%
Minor trauma *	16 1, 6, 9, 16, 21, 28, 30-32, 35, 43, 57, 62, 65, 66, 69	371	150	0.40 (0.47)	15-70%
Sporting injuries	13 1, 6, 8, 16, 25, 30-32, 35, 57, 62, 65, 66	261	40	0.15 (0.33)	3-42%
Chiropractic injury	14 1, 8, 14, 21, 24, 30, 35, 42, 43, 53, 57, 65, 66, 69	283	46	0.16 (0.36)	7-30%

* Some manuscripts included sports-related injuries or chiropractic manipulation as "minor trauma," so this category likely includes some VAD patients with these exposures.

Table 5
Outcomes following routine clinical care for VAD in 570 individuals with reported outcome^{*}

	N with outcome	Pooled proportion	SE	Range of proportions
Good outcome (mRS 0-1)	394	0.67	0.60	33-100%
Fair outcome (mRS 2-4)	105	0.18	0.49	0-53%
Poor outcome (mRS 5-6)	59	0.10	0.38	0-35%

^{*} Studies including outcome information: 5, 6, 13, 14, 16, 19, 21, 24, 28, 31, 36-38, 41, 43, 45, 47, 50, 51, 55, 62, 69, 70, 72, 73