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Association of Mental Health Disorders and Aortic Dissection

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Abstract

Introduction.—Mental health disorders (MHD), including substance abuse, have been associated with aortic dissection (AD). Aneurysmal degeneration in the residual untreated aorta after both open and endovascular treatment is not uncommon in AD. Thus, diligent long-term follow-up is necessary and MHD may play a role in treatment plan and surveillance. The impact of MHD on management, outcomes and follow-up after AD treatment is unknown and here we sought to evaluate these associations.

Methods.—A retrospective review was performed on all patients diagnosed with Stanford Type A and B dissections from 2008–2018 at a tertiary referral center. MHD was defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-V). Patient demographics, procedural characteristics, and outcomes were analyzed.

Results.—A total of 649 non-traumatic aortic dissections were identified in the study timeframe. The cohort consisted of 51% Type A (n=334) dissection and 49% Type B (n=315) dissection. Mental health disorders were present in 49.3% of the cohort. Notably, the timing of MHD diagnosis relative to development of AD is unknown in the majority of patients. Within the Type A population, a MHD was present in 50.6% (N=162) of patients, of which the most common indication for MHD was the presence of antidepressant or antipsychotic medication (28.6%). In patients with Type A dissections, the presence of a MHD did not significantly affect the rate of index hospitalization intervention (68%) or long-term mortality (12.5% in patients with a MHD). Within the Type B population, a MHD was present in 49.4% (n=158) of patients, of which the most common indication for MHD was the presence of antidepressant or antipsychotic medication (30.5%). In patients with Type B dissections, the presence of a MHD did not significantly affect the rate of index hospitalization intervention (50.3% in patients with a MHD) or long-term mortality (10.1% in patients with a MHD). The overall rate of follow-up was not significantly

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decreased based on the presence of a MHD compared to those without a MHD (1.66 ± 2.16 years vs. 1.68 ± 2.20 years, p=0.93).

Conclusion.—MHD is more prevalent in AD patients than in the general population, but demonstrating the direction of cause and effect is challenging. Despite a high prevalence of MHD in AD patients, in-hospital mortality and follow-up compliance was similar to non-MHD patients.

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Mental Health Disorders (MHD) were demonstrably prevalent within a retrospective review of 649 non-traumatic aortic dissections. The presence of a MHD was not significantly associated with worsened clinical outcomes in this cohort, but authors suggest further evaluation amid high co-prevalence and previously documented impact of MHD on cardiovascular disease.

Keywords

Aortic dissection; mental health disorder; depression; anxiety; drug abuse

Introduction

Aortic dissection (AD) is the most common acute aortic syndrome world-wide and mental health disorders (MHD) may play a role in the development and management of this challenging clinical problem[1]. MHD are one of the leading health diagnoses globally[2–5] and are associated with significant morbidity and mortality across multiple cardiovascular disease processes[6–14] in part due to observed difficulty with ability to adhere to medical management plans[15–17]. AD has a documented association with substance abuse (e.g. cocaine, methamphetamines), a subtype of MHD, which likely complicates the long-term medical management and surveillance of AD[18–20].

The role of MHD in clinical outcomes within the vascular surgery patient population is an ongoing area of exploration[3,18,21], but initial studies suggest that patients with MHD are likely to be one of the highest risk populations for AD[22–24]. Post-operative compliance with medications and follow-up imaging is essential to successful long-term management of AD given the high reintervention rate in both open and endovascular repairs[25–27]; therefore the difficulty with medical adherence that has been documented within the Psychiatry literature may present a significant barrier to establishing and maintaining appropriate diligent long-term post-intervention surveillance. The purpose of this study is to determine rates of MHD within the AD population at a single institution and determine the effect, if any, MHD has on immediate and long-term clinical outcomes.

Methods

A retrospective chart review was performed on all patients diagnosed with an aortic dissection from January 2008 to December 2018 at a single tertiary referral center. Patients included in the study were at least 18 years old and had a primary diagnosis of either a type A or type B aortic dissection. Traumatic aortic injuries were specifically excluded from analysis. Standard dissection definitions per Society of Vascular Surgery guidelines were used[28]. The presence of a MHD was determined by documentation of the diagnosis in the

medical record and was defined by DSM-V criteria. All patients taking antidepressant and/or antipsychotic medications prior to admission, regardless of whether they were documented as having a MHD, were included in the MHD group, under the assumption that these medications were prescribed for an underlying mental illness. Patients taking Buproprion, which is often used for smoking cessation, were included in the MHD category if they had no history of smoking or if the dosage of medication was consistent with a therapeutic dosage. Patient demographics, procedural characteristics, treatment and outcome data, and follow-up data were obtained from chart review and included in the analysis.

The overall prevalence of MHD in patients diagnosed with an aortic dissection was the primary outcome. Secondary outcomes included treatment performed (surgical or medical management), in-hospital and long-term mortality, and long-term follow-up duration. Mortality was determined through the Hospital EMR and was not linked to SSDI. Descriptive statistics were reported using mean ± standard deviation (SD) for continuous variables, or as a percentage when categorical. Univariate analysis of clinical characteristics, demographic data, interventional methods, and postoperative events was conducted for continuous variables with Student's T-tests or Wilcoxon rank-sum tests. Categorical variables were evaluated using Fisher's exact or Pearson's Chi-squared tests. Significant factors on univariate analysis were included in multivariable logistic models to evaluate associations between perioperative conditions and secondary outcomes. Statistical significance was defined as having a p-value < 0.05. All statistical analysis was performed using SPSS version 25.0 (IBM Corp. Armonk, NY). This study was approved by the Institutional Review Board at the University of Alabama at Birmingham.

Results

Demographics

We identified 649 patients with a diagnosis of aortic dissection, of which 51% were Stanford type A (n=334) and 49% were Stanford type B (n=315). The demographics of the cohort are presented in Table 1.

A mental health diagnosis (MHD) was documented in 49.3% (n=320) of the cohort. Within the 320 patients, there were a total of 322 diagnoses present. Within the entire cohort, MHD were equally distributed between Stanford type A dissection (n=162, 50.6%) and Stanford type B dissections (n=158, 49.4%) (Table 1). The distribution of MHD within the entire cohort (N=649) are shown in Table 2. A total of 186 patients (28.6%) were on at least one antidepressant or anti-psychotic medication, making this the most common inclusion criteria. The second most common MHD was anxiety or depression (n=60, 9%), followed by substance abuse (n=57, 8.8%). Roughly 1.5% (n=9) patients had more than 1 MHD, with the most common combination being substance abuse and anxiety or depression. The presence of any MHD was associated with significantly higher rates of End Stage Renal Disease (13% vs. 7%, p=0.019), Chronic Obstructive Pulmonary Disease (20.3% vs. 8.9%, p<0.001), and history of stroke (18% vs. 9.7%, p=0.004) (Table 1)

Effect of Mental Health on Surgical Intervention

Within the entire cohort, the rate of surgical intervention for any type of dissection was 60% (n=393) (Table 3). Stanford type A dissections had a significantly higher rate of surgical intervention compared to Stanford type B dissections (69.4% vs. 51.1%, p<0.001), and of those who underwent treatment, type A were more likely to be repaired within 2 weeks of diagnosis (90% vs. 80%, p<0.001). The presence of a MHD did not significantly affect intervention rates within either dissection type nor did it have any significant effect on the timing of intervention (Table 3). Table 4 shows the rates of intervention within each subgroup of mental health disorders. Within the entire cohort, interventions were highest within patients on an antidepressant or antipsychotic medication (n=120, 64.5% intervention rate) followed by a 61.4% intervention rate in patients with substance abuse. Within Stanford type A dissections, substance abuse patients had the highest rate of intervention (n=21, 75%), however this was not significantly different from any of the other MHD subgroups. Within Stanford type B dissections, patients on an antidepressant or antipsychotic medication had the highest rate of interventions (n=51, 54.8%), but this was not significantly higher than any other mental health subgroups. (Table 3).

Effect of Mental Health on Survival

Outcomes related to survival are presented in Table 5. The overall average follow-up time for the cohort was 1.7 ± 2.2 years, and was not affected by the presence of any mental health diagnosis (1.66 ± 2.16 vs. 1.68 ± 2.20, p=0.93). The all-cause 5 year mortality rate over the study period was 14% (n=92). Mortality was significantly higher in patients without any mental health diagnosis (17.3% vs. 10.9%, p=0.03). For patients that had a MHD, mortality was greatest within those that had dementia (33% mortality rate) followed by those that had Schizophrenia or Bipolar (25% mortality rate)(Table 6). Mortality was significantly higher in patients with Stanford type A dissections compared to type B dissections (19.1% vs. 8.8%, p<0.001). When isolated to just Stanford type A dissections, the presence of any MHD was associated with significantly lower mortality (12.5% vs. 25%, p=0.004). In patients with a type A dissection and a MHD, the mortality rate was highest among those that had dementia (33.5% mortality rate) followed by those that had substance abuse (17.8% mortality rate). When isolated to just Stanford type B dissections, patients with MHD had a higher mortality (9.6%) compared to those without a MHD (8.2%), however this result was not statistically significant. In patients with a type B dissection and a MHD, the mortality rate was highest among those that were on an antidepressant or antipsychotic medication (54.8% mortality rate).

Discussion

The findings of this study suggest an association between aortic dissections and the presence of a mental health diagnosis. Within this patient population, the overall rate of MHD was 49.3%, which was comprised of 51.5% Type A dissection and 48.5% Type B dissection. This rate is significantly higher than the NIH reported 19% rate of MHD within the general population[29], suggesting a relationship between MHD and aortic dissection. This result aligns with significant previous research demonstrating a relationship between MHD and cardiac disease; with over 60% of patients with MHD dying from coronary artery

disease[23]. In response to the abundant research linking MHD to CAD, the American Heart Association listed depression as a significant independent risk factor for CAD[30]. This strong association is in large part due to a documented trend of uncontrolled modifiable risk factors (hypertension, hyperlipidemia, and diabetes mellitus)[3,21,18] within patients with a MHD; making this population particularly high risk for cardiovascular disease[22–24]. The same factors that make patients high risk for coronary disease translates as expected into a higher rate of MHD within the AD population. However, given the nature of this study, the directionality of this relationship between mental health and AD unfortunately cannot be established.

Although this study cannot evaluate whether MHD has any part in the causality or is a result of the dissection, MHD is clearly important in the long-term treatment of these patients. The development of a MHD following a new serious health diagnosis has been well established with in cardiovascular literature, where rates of depression can rise up to 20% after a myocardial infarction[31,32]. Prior studies have demonstrated patients with multiple chronic comorbidities had high rates of depression, and, further, those with unplanned hospitalizations had even higher rates of depression[33]. In our particular patient population, the diagnosis of a MHD was associated with ESRD, COPD, history of stroke, and diabetes mellitus. Unfortunately, we were unable to determine the timing of MHD diagnosis with relation to the timing of hospitalization. Therefore, the question remains as to whether the MHD contributes to the development of these conditions, or if it is a result of them – the direction of this causal relationship is unclear.

Our study did not find a difference between treatments received (surgical vs. medical management) amongst those with MHD and those without. One possibility for this would be that perhaps those with MHD were younger and more likely to have a drug induced or hypertension induced dissection as opposed to an older patient without MHD presenting with a degenerative or atherosclerotic induced dissection, as has been demonstrated previously[19,20]. While there are trends to indicate this may be occurring in our patient cohort with the MHD population being younger and having a higher prevalence of hypertension, neither of these reached statistical significance between the two groups. Further, due to deficits in the medical records and availability of imaging, we are unable to identify the etiology of each patient's dissection.

Patients with a MHD within the studied population did not differ in their overall length of follow-up, which is a reassuring finding given that the importance of compliance with medications and follow-up imaging cannot be overstated in the management of aortic dissection. We were unable to reliably explore compliance with relevant anti-hypertensive medications following hospital discharge as this is a large tertiary hospital with a significant portion of patients receiving primary care follow-up outside of the hospital system. Studies within the Psychiatry literature have demonstrated trends of decreased ability to adhere to medical plans[34] and medications[16,35] with the population of patients with a MHD; which has led to a documented association with uncontrolled modifiable risk factors (hypertension, hyperlipidemia, and diabetes mellitus)[3,21,18] within patients with a MHD; making this population particularly high risk for cardiovascular disease and worse clinical outcomes[22–24]. Given the documented difficulty with follow-up in this patient population,

while we were unable to demonstrate a difference between groups in our study with regards to follow-up, this remains an important consideration for future studies given a frequent need for re-operation on the residual aorta after open or endovascular repair[25,26].

Within this dataset the presence of a MHD did not translate into lower rates of overall survival. This result was generally unexpected, given the historical data that suggests patients with a MHD have higher rates of mortality at baseline and are associated with significant morbidity and mortality across multiple cardiovascular diseases[3]. It has been well documented that patients with MHD receive below standard of care across all basic health needs[6], leading to significantly higher mortality at baseline compared to the general population[7–10]. Increased mortality is in part due to extrinsic factors such as suicide, vulnerability to violence, and side effects of neuroleptic medications[12–14]; however, studies have shown that depression is an independent risk factor for mortality and poor clinical outcomes following cardiovascular intervention. Following CABG, the persistence of depression at 6 months post-operatively was associated with significantly higher long-term mortality (17% vs, 3%, $p<0.001$)[36]. Similarly, depression in vascular patients hospitalized for critical limb ischemia was significantly associated with increased rates of major amputation[18]. It is possible that the results of this study do not align with previous trends because this study focused on all mental health disorders, while previous studies have isolated analysis to depression.

The retrospective, single center nature of this study increases the probability of selection bias. Due to changes in the medical record storage during the study period, earlier patients were lacking detailed comorbidity records compared to those available for later patients, which could have consequently affected tabulation of those patients' demographics, characteristics, and outcomes; consistent and long-term follow-up would be required for more confidence in results, especially in the drug abuse patient cohort[11]. Due to the same limitations in the medical record, we were unable to pinpoint when a diagnosis of MHD was made or when an antidepressant/antipsychotic was prescribed (i.e. before or after the diagnosis of aortic dissection), which leaves open the question of chronicity of the relationship between aortic dissection and a MHD. The decision to exclude patients on Bupropion with a history of smoking or at doses consistent with smoking cessation aligns with studies that demonstrate Bupropion is used for smoking cessation in up to 25% of prescriptions and is FDA approved for smoking cessation[37]. In this study, none of the patients on isolated bupropion had a history of smoking and therefore all of these patients were included in the MHD cohort. To confirm this decision, the analysis of survival was performed excluding Bupropion patients from the MHD cohort and there was no significant change in clinical outcomes.

Conclusion

While privacy concerns regarding sensitive health information have made the role of mental health conditions in surgical care less studied in the past, the evidence base in cardiovascular disease and preliminary findings of high prevalence of MHD in AD from our large single institution analysis suggests that further understanding of the role of coexistent mental health disorders could allow for improvements in care strategies in this population. Mental

health disorders are demonstrably prevalent in the aortic dissection patient population, with a prevalence of 51% in a large tertiary care academic center. The presence of a MHD did not correspond to worsened in-hospital mortality or follow-up compliance. The relationship of mental health with dissection diagnosis, management, treatment, and outcomes is yet to be fully understood but merits further evaluation amid its high co-prevalence in aortic dissections and previously documented impact of MHD on cardiovascular disease.

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ARTICLE HIGHLIGHTS

Type of Research:

Single Center Retrospective Cohort Study

Key Findings:

Mental Health Diagnoses (MHD) were present in 49.3% of all non-traumatic aortic dissections (N=659, 51% Type A, 49% Type B). The most common MHD was substance abuse. Within all dissections, the presence of a MHD was not significantly associated with lower rates of intervention or higher mortality.

Take home Message:

MHD are demonstrably prevalent in the aortic dissection population. While the presence of a MHD did not correspond to worsened mortality or follow-up compliance; the relationship of MHD with dissection treatment, and outcomes is yet to be fully understood but merits further evaluation amid its high co-prevalence in aortic dissections.

Table 1:

Demographic Characteristics

Diagnosis	Entire Cohort (N=649)	MHD (N=320)	No MHD (N=329)	p
Type A Dissection	334 (51%)	162 (50.6%)	172 (52.2%)	0.672
Type B Dissection	315 (49%)	158 (49.4%)	157 (47.7%)	0.57
Age (years)		59.17 ± 14.17	60.95 ± 15.10	0.12
Gender				
Male	448 (69%)	212 (66.2%)	236 (71.7%)	0.206
Female	201 (31%)	108 (33.4%)	93 (28.8)	
Race				
Unknown	20 (3%)	8 (2.5%)	12 (3.6%)	
White	369 (57%)	184 (57.4%)	185 (56.3%)	0.665
Non-White	260 (40%)	127 (40.3%)	133 (39.2%)	
Smoking				
Never	273 (42%)	125 (38%)	148 (45.8%)	
Former	235 (36%)	120 (38%)	115 (34.4)	0.287
Current	141 (22%)	75 (24%)	66 (19.7%)	
Hyptertension	574 (88%)	285 (90.1%)	289 (87%)	0.142
Diabetes Mellitus	100 (15%)	47 (14.6%)	53 (16.1%)	0.581
ESRD	64 (10%)	40 (13%)	24 (7.1%)	0.019
COPD	94 (14%)	64 (20.3%)	30 (8.9%)	<0.001
CAD	183 (28%)	100 (31.2%)	83 (25.2%)	0.088
CHF	123 (19%)	59 (18.4%)	64 (19.4%)	0.733
History of Stroke	91 (14%)	59 (18.4%)	32 (9.7%)	0.001
Connective Tissue Disorder	32 (5%)		17 (5%)	0.848

ESRD = Endstagc Renal Disease, COPD = Chronic Obstructive Pulmonary Disease, CAD=Coronary Artery Disease, CHF=Congcstivc Heart Failure

Table 2:

Mental Health Characteristics of the Entire Cohort

Mental Health Diagnosis	All (N=649)	Type A Dissection (N=334)	Type B Dissection (N=315)	p
Anxiety/Depression	60 (9%)	32 (9.5%)	28 (8.5%)	0.761
Schizophrenia/Bipolar	8 (1.2%)	1 (.3%)	7 (2.2%)	0.027
Dementia	12 (1.8%)	6 (1.8%)	6 (0.3%)	0.918
Substance Abuse	57 (8.5%)	28 (8.3%)	29 (8.6%)	0.711
More than 1 MHD	9 (1.4%)	2 (0.6%)	7 (2.2%)	0.077
Antidepressant/Antipsychotic Medication	186 (28.6%)	93 (27.8%)	93 (30.5%)	0.755

Tabic 3:

Treatments and Outcomes of Cohort

Outcome	Entire Cohort (N=649)	MHD (N=320)	No MHD (N=329)	p
Surgical Intervention	393 (60%)	189 (59%)	204 (62%)	0.446
Timing of Intervention				
Acute (Within 2 Weeks)	339 (86%)	159 (85%)	180 (87%)	0.684
Delayed	54 (14%)	27 (15%)	27 (13%)	
Outcome	**All (N=649)**	**Type A Dissection**	**Type B Dissection**	**p**
Surgical Intervention	393 (60%)	232 (69.4%)	161 (51.1%)	<0.001
Timing of Intervention				
Acute (Within 2 Weeks)	339 (86%)	209 (90%)	130 (80%)	<0.001
Delayed	54 (14%)	23 (10%)	31 (20%)	
Outcome	**Type A Dissection (N=334)**	**MHD (N=162)**	**No MHD (N=172)**	**p**
Surgical Intervention	232 (69.4%)	110 (67.9%)	122 (70.9%)	0.548
Timing of Intervention				
Acute (Within 2 Weeks)	209 (90%)	96 (59.5%)	113 (66%)	0.265
Delayed	23 (10%)	14 (8.8%)	9 (5.1%)	
Outcome	**Type B Dissection (N=315)**	**MHD (N=158)**	**No MHD (N=157)**	**p**
Surgical Intervention	161 (51.1%)	79 (50.3%)	82 (51.8%)	0.779
Timing of Intervention				
Acute (Within 2 Weeks)	130 (80%)	66 (42%)	64 (40.5%)	0.65
Delayed	31 (20%)	13 (8.2%)	18 (11.3%)	

Table 4:

Surgical Interventions in MHD Subgroups

Entire Cohort (N=649)	**Intervention Rate**
Anxiety Or Depression (n=60)	26 (43.4%)
Schizophrenia or Bipolar (n=8)	4 (50%)
Dementia (n=12)	6 (50%)
More than 1 MHD (n=9)	6 (66.6%)
Substance Abuse (n=57)	35 (61.4%)
Antidepressant/Antipsychotic Medication (N=186)	120 (64.5%)
Type A Dissection (N=334)	**Intervention Rate**
Anxiety or Depression (n=32)	15 (46.8%)
Schizophrenia or Bipolar (n=l)	1 (100%)
Dementia (n=6)	3 (50%)
More than 1 MHD (n=2)	2 (100%)
Substance Abuse (n=28)	21 (75%)
Antidepressant/Antipsychotic Medication (n=93)	69 (71.1%)
Type B Dissection (N=315)	**Intervention Rate**
Anxiety or Depression (n=28)	11 (39.2%)
Schizophrenia or Bipolar (n=7)	3 (42.5%)
Dementia (n=6)	3 (50%)
Substance Abuse (n=29)	14 (48.2%)
Antidepressant/Antipsychotic Medication (n=93)	51 (54.8%)

Table 5:

Mortality Rates

	Entire Cohort (N=649)	MHD (N=320)	No MHD (N=329)	p
Mortality	92 (14%)	35 (10.9%)	57 (17.3%)	0.02
	All (N=649)	**Type A Dissection (n=334)**	**Type B Dissection (n=315)**	**p**
Mortality	92 (14%)	64 (19.1%)	28 (8.85%)	<0.001
	Type A Dissection (N=334)	**MHD (N=162)**	**No MHD (N=172)**	**p**
Mortality	64 (19.1%)	20 (12.5%)	44 (25%)	0.004
	Type B Dissection (N=315)	**MHD (N=l 58)**	**No MHD (N=157)**	**p**
Mortality	29 (8.85%)	16 (10.1%)	13 (8.2%)	0.679

Table 6:

Mortality in MHD Subgroups

Entire Cohort (N=649)	**Mortality Rate**
Anxiety Or Depression (n=60)	8 (13.3%)
Schizophrenia or Bipolar (n=8)	2 (25%)
Dementia (n=12)	4 (33.3%)
More than 1 MHD (n=9)	3 (33.3%)
Substance Abuse (n=57)	9 (15.7%)
Antidepressant/Antipsychotic Medication (N=186)	15 (8.0%)
Type A Dissection (N=334)	**Mortality Rate**
Anxiety or Depression (n=32)	5 (15.6%)
Schizophrenia or Bipolar (n=l)	0 (0%)
Dementia (n=6)	2 (33.3%)
More than 1 MHD (n=2)	2 (100%)
Substance Abuse (n=28)	5 (17.8%)
Antidepressant/Antipsychotic Medication (n=93)	10 (10.3%)
Type B Dissection (N=315)	**Mortality Rate**
Anxiety or Depression (n=28)	3 (7.6%)
Schizophrenia or Bipolar (n=7)	2 (28.5%)
Dementia (n=6)	2 (33.3%)
Substance Abuse (n=29)	4 (13.7%)
Antidepressant/Antipsychotic Medication (n=93)	5 (5.4%)