5-2017

Quality of Life and Psychosocial Impacts of Persons With a Genetic Predisposition to Thoracic Aortic Dissections or Aortic Aneurysms

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QUALITY OF LIFE AND PSYCHOSOCIAL IMPACTS OF PERSONS WITH A GENETIC PREDISPOSITION TO THORACIC AORTIC DISSECTIONS OR AORTIC ANEURYSMS

May 4, 2017

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Submitted in partial completion of the Master of Science Degree at Sarah Lawrence College, May 2017

Abstract

BACKGROUND: Thoracic aortic dissections (TAD) and thoracic aortic aneurysms (TAA) can cause significant disabilities and premature sudden deaths. Modern advances in medicine and technology have increased the life expectancy for survivors of TAD or TAA; however, limited studies have measured the quality of life of affected individuals, especially those with genetically triggered aortic diseases. The National Registry of Genetically Triggered Thoracic Aortic Aneurysms and Cardiovascular Conditions (GenTAC) measured the Health Related Quality of Life (HRQoL) in survivors of a TAD or TAA. Another area of impact on quality of life includes depression. One accurate measurement for depression is the 16-item Quick Inventory of Depressive Symptomatology (QIDS-16). With 20% of individuals who survived an AD or AA having a family history, little is known regarding the impact of genetic specialists such as genetic counselors and geneticists.

METHODS: Using data collected by the GenTAC registry from patients with genetically triggered aortic diseases and recruited from the University of Texas Health Science Center at Houston and Baylor College of Medicine, this study examined health-related quality of life (i.e. physical role limitations, pain, physical functioning and general health; HRQoL) and prevalence of depression in patients who completed a survey including questions from the 36-Item Short Form Survey (SF-36). Effects of demographic factors (age, gender, race, education, marital status, health insurance, income, and employment status) and diagnosis of a known genetic syndrome or mutation, TAA or TAD, including rupture and marked tortuosity on HRQoL was analyzed. A survey was created via SurveyMonkey to measure the

impact of genetic specialists and depression severity, as well as demographics, on HRQoL and was distributed via Facebook. Seventy-five survivors of an aortic dissection or an aneurysm completed the survey. Correlational studies were performed to draw conclusions regarding the results.

RESULTS: Overall, mean score for physical functioning was 26.8 (SD 26.5), 40.1 (SD 43.1) for role-limitations, 61.8 (SD 29.9) for pain, and 55.0 (SD 25.8) for general health. Univariate analysis showed significantly lower physical functioning among White patients with college or postgraduate education, and diagnosis of TAA or TAD. Role limitation was significantly higher among patients in the youngest age group (33 years and younger), with college or postgraduate education, private insurance, and those who are employed/student/ homemaker. Pain was reported to be significantly higher among the youngest patients with college or postgraduate education, private insurance, and who are employed/student/homemaker. Finally, self-reported general health was significantly higher among males, White patients, with college or postgraduate education, private insurance, highest income group (>$100,000), employed/student/homemaker, with no diagnosis of a known genetic syndrome/condition, and with TAA or TAD. Approximately 32% of the patients reported depression. The 75 individuals who experienced an aortic dissection or an aneurysm demonstrated an average QIDS-16 score of 13.05 (SD=4.90), which was indicative of moderate depression. The most impacted area for depression was sleep change with a mean score of 2.49 (SD= 0.64) and appetite/weight change with a mean score of 2.03 (SD= 1.10). Sixteen individuals that met with a genetic counselor or geneticist stated it was more

valuable in areas such as providing resources and education regarding depression when comparing the individuals who did not meet with a genetic counselor or geneticist ($p<0.05$). CONCLUSION: Overall findings showed that HRQoL particularly physical functioning and role limitation was poor, and depression was prevalent in this patient population with genetically triggered TAA and TAD. Different demographic factors had significant but variable effects on the HRQoL domains, while diagnosis of a known genetic syndrome/condition, TAA or TAD significantly affected physical functioning and general health. Effects of diagnosis and treatment on quality of life and psychosocial functioning should be considered when conducting a genetic counseling session so that appropriate referrals for interventions can be made. These findings show the need for a more thorough investigation of mental health in this patient population, including the impact of sleep patterns, appetite/weight change, and genetic services for survivors of an aortic aneurysm or an aortic dissection.

Keywords: GenTAC, health-related quality of life, depression, aortic aneurysm, aortic depression, Marfan syndrome

Introduction

Cardiovascular disease is one of the leading causes of death in the United States (Mozaffarian et al., 2015). Cardiovascular anomalies such as thoracic aortic dissection (TAD) and thoracic aortic aneurysm (TAA) are known to cause sudden death. While medications and medical procedures have extended the life expectancy for many individuals with TAD or TAA, there is a gap in the literature concerning their mental health. The psychological impact of a TAD on a patient, or the impact of a genetic predisposition towards a TAD, is rarely studied. Similarly, there is limited information about the quality of life of patients with TAD or TAA, especially those with a genetically triggered aortic disease. The aim of this study is to examine depression and quality of life in individuals who have experienced a TAD or TAA.

A TAA presents as a bulging, balloon-like dilation in the aorta in the thoracic cavity due to weakness in the aortic wall. Aneurysms tend to be asymptomatic before dissection and/or rupture. A TAA can be the result of certain risk factors, including hypertension and bicuspid aortic valve (Ramanath, Oh, Sundt, & Eagle, 2009). An aortic dissection involves the tearing of the lumen, forcing blood between the layers of the aortic wall. As blood leaks into the false lumen, that pressure weakens the aorta and blocks the arteries that branch off of the aorta, restricting blood flow to other organs. TADs are often classified through the Stanford system based on whether the dissection involves the ascending aorta; if the TAD involves the ascending aorta, regardless of its origin, it is considered a type A dissection, and if it does not, it is considered a type B dissection (Nienaber & Eagle, 2003).

TADs, if untreated, can potentially lead to catastrophic events such as pericardial tamponade, aortic rupture, and death. The incidence of acute TAD per year in the general population is estimated to be 2.6 to 3.5 per 100,000 (Clouse et al., 2004). There is an estimated 20% mortality rate for individuals who have experienced a TAD, and this rate continues to increase by 1-2% every hour following the TAD that an individual goes without medical treatment (Olsson et al., 2006). One estimate using the IRAD registry showed a 10% in-hospital mortality for individuals with type B AD (Suzuki et al., 2003). The reported long-term survival rate with medical therapy is estimated to be between 60-80% at 4-5 years and 40-45% at ten years (Doroghazi et al., 1984; Umaña et al., 2002; Bernard et al., 2001). Individuals with type A dissections have an estimated 26% in-hospital mortality rate (Tsai et al., 2006) and have an estimated survival of 91% at three years (Knipp et al., 2007). These survival rates suggest that patients with smaller and distal dissections have more favorable outcomes.

Both TAA and TAD are linked to various genetic syndromes and also non-syndromic familial inheritance. Syndromic conditions related to TAA and TAD include Marfan syndrome, Loeys-Dietz syndrome, and vascular Ehlers-Danlos syndrome (Beighton, De Paepe, Steinmann, Tsipouras, & Wenstrup, 1998; Loeys et al., 2005; Matura, Ho, Rosing, & Bondy, 2007; Westaby, 1999). Some individuals with TAA and TAD have been found to carry a familial mutation in one of seven known genes conferring predisposition to TAA and TAD, including but not limited to MYLK, MYH11, PRKG1, and ACTA2. Though researchers have found that there is an increased to have a TAA or TAD with a mutation in

one of these genes, the exact risk for each is unknown. (Milewicz & Regalado, 2003).

The National Registry of Genetically Triggered Thoracic Aortic Aneurysms and Cardiovascular Conditions (GenTAC) has compiled a database of people with genetic predispositions towards aortic disease (Eagle, 2009). The study population includes participants with an aortic disease as well as those who are genetically predisposed but unaffected. Individuals enrolled in GenTAC completed a Health-Related Quality of Life (HRQoL) survey. Abstracted information from their medical records and self-reported medical information were collected. GenTAC specifically utilized portions of the Medical Outcomes 36-Item Short-Form Health Survey (MOS SF-36). The MOS SF-36 asks patients about limitations in physical activity because of health problems, bodily pain, general mental health, role limitations due to both physical and emotional health, energy level, general health perception, and constraints in social activity (Ware & Sherbourne, 1992). GenTAC assessed four domains of the MOS SF-36 including physical functioning, role limitations due to physical health, pain and general health.

As vital as the GenTAC data is for measuring the HRQoL, more thorough examinations of depression are critical to fully comprehend the psychological impacts of TAD and TAA. One accurate measurement of depression is the 16-item Quick Inventory of Depressive Symptomatology (QIDS-16). The QIDS-16 was developed to assess the severity of depression and derived from the DSM-IV criterion diagnostic symptoms (Rush et al., 2003). Another impactful aspect of medical care is accessing the role of a genetic professional in the patient's treatment after a TAD or TAA repair. To date, there has been no

published literature investigating the impact of genetic services in this patient population. Given the traumatic nature of an acute TAD or TAA and repair, it is necessary to examine the possible effects this experience has on a person's mental well-being post-event and/or diagnosis and make recommendations for appropriate mental health follow-up if the data indicates symptoms of depression or anxiety. This study aimed to evaluate the HRQoL with genetically triggered TAA/TAD using data from the GenTAC study. The second part of this study measured depression and impact of genetic services after an individual has experienced a TAA/TAD.

Methods

Participants

These studies were approved by IRBs at both the University of Texas Health and Science Center at Houston and Sarah Lawrence College. For analysis of the individual's HRQoL, anonymized patient data collected through GenTAC from two sites, University of Texas Health Science Center at Houston and Baylor College of Medicine, were used. Participants had to be over the age of 18 and have a genetic predisposition to aortic aneurysms or dissections, including patients who had been diagnosed with TAA, TAD, rupture or marked tortuosity or a known genetic syndrome or causative mutation predisposing to TAA/TAD.

The anonymous SurveyMonkey depression survey was distributed to survivors of aortic dissections and aneurysms through various Facebook support groups and was posted on The John Ritter Research Program in Aortic and Vascular Disease's Facebook page. This

study was available for completion for two months and was reposted once during that time on the various Facebook pages that agreed to aid in recruitment. All participants were required to be 18 years of age and older and had to complete the informed consent before participating in the survey. All survey data was self-reported by the participants.

Instrumentation

The GenTAC data was comprised of an enrollment patient questionnaire. This survey collected self-reported data regarding the patient's demographics, lifestyle, medical history, and family history. It also included a modified 36-Item MOS SF-36 that measured HRQoL domains: physical functioning, role limitations due to physical health, pain and general health. The questions relating to role limitations due to emotional problems, energy/fatigue, emotional well-being and social functioning were not assessed by the survey due to the focus of physical health aspects of HRQoL. Each question was assigned to a particular domain listed above and scored from 0 to 100 with 100 being the highest HRQoL. Additionally, this data was linked to the primary diagnosis at the time of enrollment, a data point completed by the study personnel. Diagnoses included: Marfan syndrome; Turner syndrome; Ehlers-Danlos syndrome (vascular type); Ehlers-Danlos syndrome (other type with aortic enlargement); Loeys-Dietz syndrome; genetic mutation of FBN1, TGFBR1, TGFBR2, ACTA2 or MYH11; bicuspid aortic valve with aortic enlargement; family history or aortic coarctation; Shprintzen-Goldberg syndrome; familial thoracic aortic aneurysm and dissection with aortic enlargement; other aneurysms/dissections of the thoracic aorta in persons age 50 years or younger; other congenital heart disease with aortic enlargement; or

first-degree family member of proband already enrolled in the registry.

SurveyMonkey was used to distribute a survey that measured depression and experience with genetic services to survivors of an AD. The study consisted of the QIDS-16 in addition to their history of aneurysms, depression, any genetic diagnosis and testing, a previous diagnosis of anxiety or depression along with demographic information. Additionally, the survey asked them to rate their experience with a genetic professional. This survey was only available in English. The QIDS-16 incorporated the nine DSM-IV symptom criterion domains, including: sleep disturbance (initial, middle, and late insomnia or hypersomnia) (questions 1-4), sad mood (question 5), decrease/increase in appetite/weight (questions 6-9), concentration (question 10), self-criticism (question 11), suicidal ideation (question 12), interest (question 13), energy/fatigue (question 14), psychomotor agitation/retardation (questions 15-16). Responses were based on a Likert scale of 0 to 3 (Acosta et al., 2014).

For scoring the QIDS-16, the highest score from each domain was added for a total. Each domain includes highest sleep item (1-4), the score for item 5, the highest score on any of the appetite/weight items (6-9), the score for item 10, the score for item 11, the score for item 12, the score for item 13, the score for item 14, the highest score for either of the two psychomotor items (15 and 16). Then, the scores were added for a total score. The total score range can be 0-27. Scores correlated to estimated severity of depression as follows: scores of 0-5 = no depression; scores of 6-10 = mild depression; scores of 11-15 = moderate depression; scores of 16-20 = severe depression; scores of 21-27 = very severe depression

(Acosta et al., 2014).

Procedures

A subset of anonymized patient data, consisting of 474 unique patient identification numbers (13.5%,) from the GenTAC database collected at University of Texas Health and Science Center at Houston and Baylor College of Medicine was assessed. Two-hundred and sixteen patients were excluded due to incomplete HRQoL data and 64 patients under the age of 18 were also excluded; the data from the remaining 194 patients (40.9% of UTH subset, 5.5% of the entire GenTAC database) was included in the analysis.

Each question from the modified MOS SF-36 used in the GenTAC survey was matched to the specific question in the original MOS SF-36. Each response to the modified MOS SF-36 used by GenTAC corresponded to an individual score between 0 and 100; these were coded according to Table 1 on "36-Item Short Form Survey (SF-36) Scoring Instructions" (RAND Corporation, n.d.). Questions 13-16 of the MOS SF-36 were modified in the GenTAC survey to be a Likert scale of 1 to 5 instead of the original yes or no answer choice; questions originally scored with 1 to 4 were converted to "yes" and questions scored with 5 on the Likert scale were converted to "no." Then, each question was grouped into one of the four domains (physical functioning, role limitations, pain and general health) and scores in each domain were averaged as per Table 2 (RAND Corporation, n.d.). After the modified MOS SF-36 has been scored for each, the data was analyzed as described below.

The depression survey distributed through Facebook had 150 participants, 75 of which were disqualified due to an incomplete QIDS-16 and the remaining 75 were analyzed.

Each answer choice from the QIDS-16 survey corresponded to a Likert scale of 0 to 3 (University of Pittsburgh Epidemiology Data Center, 2017).

Data analysis

Data for categorical variables were summarized using frequencies and percentages. Continuous variables were summarized by means and standard deviations. Univariate analysis was completed on the GenTAC data to test the association of each variable with the four domains of HRQoL assessed by the MOS SF-36. For each variable, either a t-test or an ANOVA analysis was performed to compare the categories or groups, and p-values less than 0.05 were considered statistically significant.

The depression survey data was uploaded from SurveyMonkey into SPSS Version 24 for analysis of relationships between variables. The depression scale, an interval variable, was the primary dependent variable used in this study. The independent-samples t-test (t-test) were used to compare mean scores when independent variables were categorized into two groups. The independent variables that were categorized into three or more groups such as categories of mental health diagnosis, one-way ANOVA was used to assess mean differences and Tukey's post hoc analysis was used to determine which groups had the largest mean differences. Correlation coefficients were used to assess relationships between continuous variables such as depression, age, and income.

Results

GenTAC Health-Related Quality of Life

Of the 194 eligible participants from the GenTAC dataset, 193 had a primary

diagnosis at enrollment. Sixty-seven (34.7%) had a diagnosis of a known genetic syndrome or mutation with the average age of diagnosis being 33.1 years (18.4); of these, 32 (16.5%) were diagnosed with Marfan syndrome. One hundred and sixty-four (85.4%) had experienced an aortic aneurysm, dissection, rupture, or marked tortuosity. However, only 28 (51.9%) out of 54 participants reported having vascular heart surgeries or procedures.

Each HRQoL domain is scored on a scale of 0 to 100, whereas 100 is the top performance in the domain with no limitations due to health or pain (Ware & Sherbourne, 1992). The HRQoL domains in the GenTAC data showed that the mean for physical functioning is 26.8 (26.5). The average for role-limitations is 40.1 (43.1). The domain pain's mean is 61.8 (29.9). Lastly, the mean in the general health domain is 55.0 (25.8).

Age of the study population was divided by quartile: 48 participants (25.1%) between the ages of 18-32, 49 (25.7%) between 33-43 years, 49 (25.7%) between 44-52 years, and 45 (23.6%) between 53-83 years of age. One hundred and eight participants (56.0%) identified themselves as male and 169 (89.9%) identified as White/Caucasian. Ninety-four participants (50.8%) either had graduated from college or postgraduate school and 112 (59.3%) were married. One hundred seventy-five individuals (93.6%) had insurance coverage. From these, 129 individuals (73.7%) reported their insurance was private. Sixty-five participants (39.4%) had an income below $50,000, 60 (36.4%) had income between $50,000-$100,000 and 40 (24.2%) had income greater than $100,000. One hundred twenty-eight (68.5%) were either employed, a student or homemaker, while 40 (21.4%) were unemployed and 19 (10.2%) were retired. For the full summary of demographics, please refer to Table 1.

When reviewing the individual domains, overall General Health was most significantly impacted across variables. Ten of the 12 variables showed a statistically significant association with demographics (gender, race, education, insurance, income and employment), diagnosis (depression, Marfan syndrome, other known genetic syndrome or mutation, and TAAD, rupture or tortuosity). Gender impacted ($p=0.0379$) scores in General Health, with men scoring significantly higher (58.3 [SD=24.6] vs. 50.6 [SD=26.7] for women). With regards to race ($p=0.0013$), non-white individuals scored lower with 38.0 (SD=22.1). When looking at insurance ($p=0.0027$), individuals with private insurance scored higher 59.1 (SD=24.0). With income ($p=0.0008$), individuals earning more than $100,000 scored highest with 62.4 (SD=22.6), those earning between $50,000-$100,000 in the middle with 61.3 (SD=26.7) and those earning less than $50,000 scored lowest with 46.5 (SD=23.9). When looking at employment ($p<0.0001$), those who were employed, a homemaker or student scored highest with 61.5 (SD=23.2), those who were retired the second highest with 60.1 (SD=27.9) and those who were unemployed the lowest with 32.8 (SD=22.2). People who self-reported depression also significantly impacted ($p=0.0187$) general health 48.6 (SD=24.2). Those with a diagnosis of Marfan syndrome were also ($p=0.0124$) lower with 44.6 (SD=23.4), as were those with any genetic syndrome or mutation diagnosis ($p=0.0002$) with 45.7 (SD=24.1). However, those with a diagnosis of thoracic aortic dissection/aneurysm, rupture or marked tortuosity reported significantly higher general health than those without this diagnosis (56.8 ± 26.0, $n=28$), p-value = 0.0181.

Physical functioning had 6 out of 12 variables that showed statistical significance.

With race (p=0.0074), white participants scored lower 24.8 (SD=25.7) than non-white participants 42.9 (SD=31.2). Education was significant (p=0.0032) with those who graduated from college or postgraduate scoring lower, 20.6 (SD=22.7), compared to those who had some college or less, 32.1 (SD=28.3). When looking at marital status (p=0.0340), individuals who were married have higher physical functioning 30.7 (SD=27.9). Employment was also significant (p<0.0001) with individuals who were employed having the lowest score 21.6 (SD=24.5), those who were retired 31.3 (SD=28.7) scored in the middle, and those who were unemployed had the highest with 43.2 (SD=26.5). Those who had a diagnosis of a genetic syndrome or mutation reported higher physical functioning 33.2 (SD=27.7) than those without a known genetic syndrome or diagnosis, p=0.0148. Lastly, those diagnosed with a thoracic aortic aneurysm/dissection, rupture or marked tortuosity reported lower physical functioning (24.9 ± 25.8), p=0.0254.

Role limitations had 4 out of 12 variables that showed statistical significance. In regards to age (p=0.0124), ages 54-84 scored at 25.6 (SD=36.5), then ages 45-53 scored at 38.3 (SD=43.6), then ages 34-44 at 39.9 (SD=44.4) and finally those age 33 and younger at 56.0 (SD=43.8). With education, (p=0.0007) those who graduated from college or postgraduate scored higher 50.5 (SD=44.0) than those who had some college or less education 28.7 (SD=38.7). Those with private insurance scored (p=0.0160) higher 45.6 (SD=43.5) than those with public insurance. Lastly, job status was significant (p<0.0001) with those who were employed, student, or homemaker scoring highest with 49.6 (SD=43.8), retired scoring 23.6 (SD=37.8), and unemployed scoring 14.2 (SD=30.4).

Pain had 4 out of 12 variables that showed statistical significance. With age (p=0.0116), ages 33 and younger scored the highest 74.7 (SD=25.5), and then ages 54 to 84 scored next with 59.9 (SD=29.6), ages 34-44 at 57.4 (SD=29.8) and lastly, ages 45-53 after that with 57.2 (SD=31.8). Education was significant (0.0017) with those who graduated from college or postgraduate scoring higher with 68.4 (SD=27.1). Those with private insurance scored (0=0.0440) higher with 65.4 (SD=28.9) than those with public 55.0 (SD=29.1) Lastly, with employment (p=0.0012), those that were employed, a student or homemaker scored highest with 66.8 (SD=28.2), those who are retired 57.6 (SD=28.8) and those who are unemployed at 46.7 (SD=31.0). For a full summary of all variable correlations to the four domains, please refer to Table 2.

Depression Measurements in AD and AA Survivors

Seventy-five individuals completed the survey. The mean age of participants was 54.25 (9.438), with the youngest participant being 36 and the oldest being 78. Thirty-seven (49.3%) identified as male-gendered, 35 (46.7%) identified as female, and one (1.3%) identified as a transgender female. Sixty-seven (89.3%) identified as White, one (1.3%) identified as Black or African-American, two (2.7%) identified as Asian, and three (4%) identified as multiple races. Only one individual (1.3%) identified their ethnicity as Hispanic or Latino. Fifty-two participants (69.3%) were married, 18 (24%) were divorced, and three (4%) were never married. Thirty-six (48%) individuals graduated from college and gone on to postgraduate schooling. Thirty-six (48%) individuals earned less than $50,000 income, 14 (18.7%) earned $50,0001-$100,000, and 19 (25.3%) earned more than $100,000. Twenty-

seven (36%) were unable to work due to disabilities. Lastly, 39 (52%) of individuals were on private health insurance, whereas 18 (24%) were on Medicare or Medicaid.

Sixty-two participants (82.7%) had been diagnosed with an aortic dissection. Out of these individuals, 16 (21.3%) had a descending dissection, and 46 (61.3%) had an ascending dissection. Eight (10.7%) individuals had been diagnosed more than ten years ago, 15 (20%) were diagnosed between 5-10 years ago, 17 (22.7%) were diagnosed two-five years ago, 13 (17.3%) were diagnosed one-two years ago and seven (9.3%) were diagnosed less than a year ago. Ten (13.3%) of individuals had been diagnosed with an aortic aneurysm before to their aortic dissection. Forty-six individuals (61.3%) had been diagnosed with an aortic aneurysm. Forty-one (54.7%) had their aneurysm surgically repaired. Of those with a surgical repair, 7 (9.3%) had it repaired less than a year ago, eight (10.7%) 1-2 years ago, 11 (14.7%) 2-5 years ago, 10 (13.3%) 5-10 years ago and 4 (5.3%) more than ten years ago. Forty participants (53.3%) denied a first-degree relative with an aortic aneurysm or dissection.

The average QIDS-16 score was 13.05 (indicating moderate depression) with a standard deviation of 4.9. Table 4 demonstrates how each category of the QIDS-16 impacted the patient populations score for depression. Each category is measured 0-3. Sleep disturbance was the greatest area with an average score of 2.49 (SD= 0.64), followed by appetite/weight change 2.03 (SD=1.10), and energy 1.67 (SD=0.89). The least impacted area was the suicidal indication with a mean score of 0.49 (SD=0.74) and general interest/involvement with a score of 1.15 (SD=1.06). The QIDS-16 results are detailed in Table 3. From the 75 individuals who completed the QIDS-16 portion of the survey, six (8%)

had scores indicating very severe depression, 19 (25.3%) scored in the range indicating severe depression, moderate and mild depression each included 23 (30.7%) individuals with this score, and four (5.3%) individuals' scores indicated no depression.

Nine individuals (12%) were referred to see a mental health professional after their diagnosis, but 23 (30.7%) reported seeing a mental health professional after their diagnosis. Eighteen (24%) were referred to a genetic professional or genetic counselor following their diagnosis and 19 (25.3%) reported seeing a genetic professional or genetic counselor. Twenty-two (29.3%) reported having genetic testing.

Genetic services demonstrated a significant impact of the survivor's mental health and understanding the disease. The survey demonstrated that their genetic counselor/geneticist helped the patient make the best decision and was positively correlated with reduced depressive thoughts ($r(16) = 0.56$, $p < 0.01$) and reduced overall anxiety ($r(16) = 0.56$, $p < 0.01$). Ratings that the genetic counselor/geneticist provided the patient with useful resources was correlated with ratings that the genetic counselor/geneticist reduced depressive thoughts ($r(16) = 0.42$, $p<0.05$), and helped in understanding the patient's condition ($r(16) = 0.41$, $p<0.05$) It was also shown that the genetic counselor/geneticist helped patients understand their condition, as it was positively correlated with rating that "the genetic counselor/geneticist helped make the decision that was best for me" ($r(16) = 0.42$, $p<0.05$).

One area of this study that had a negative correlation with depression was employment status ($F(6/63) = 2.94$, $p<0.05$). Individuals that were unable to work due to

disability (M=14.73), were self-employed (M=17.25), or were unemployed (M=13.60) had higher depressions scores than individuals that were employed full-time (M=11.26), employed part-time (M=9.50), were homemakers (M=9.33), or were retired (M=11.33).

Factors that did not have a significant impact on depression included a patient's prior knowledge of being at a higher risk for an AD or AA, their age, or gender. Females did have a higher rate depression scores than males; however, it was not significant. Depression was also not related to marital status (F (2/70) = 2.50) or a previous mental health diagnosis (F (2/18) = 0.82) However, those with anxiety were shown to have higher depressions scores (M=16.17) than those diagnosed with only depression (M=13.5). Other factors that did not have a significant impact on depression include alcohol, marijuana, other drugs, or overuse of prescription drugs.

Discussion

GenTAC Health-Related Quality of Life

Overall, this study population reported low quality of life scores for physical functioning, role limitations, bodily pain and general health. Two variables were significant across all four domains: education and employment. With the exception of physical functioning, higher education correlated with a higher quality of life. Higher HRQoL tracking with higher education is an expected finding. People with higher education degrees generally have a higher income, which has been shown to increase an individual's general overall health (Feinstein et al., n.d.). People who have higher educations are also more likely to participate in preventative care (Feinstein et al., n.d.). They might know more about their

options and how to navigate through them for the best possible outcome. They may also have better job satisfaction and overall happiness with their profession. While higher education does not necessarily equate with happiness, it can lead to certain advantages that provide individuals with a better chance of having a satisfactory outcome.

The second variable that was significant across all domains was employment. With the exception of physical functioning, individuals that are employed, students and homemakers have a higher HRQoL than individuals that are retired and those who are unemployed. Similar to education, one would expect employment to bring better health outcomes since these individuals are more likely to have a steady income, housing, and access to health insurance. Homemakers are often supported by a partner or may be independently wealthy with the same benefits of full-time employment. Although students widely vary in their individual financial situations, they most likely benefit from financial support from parents or student loans and scholarships. Depending on the institution, some students are also required to have health insurance to attend. Those that are employed, students or homemakers likely do not have the burden of financial strain compared to those who are retired or unemployed, thus improving their HRQoL. Individuals who are retired and over the age of 65 may be on a Medicare plan. Medicare has limitations on the amount services it can cover, for example, occupational and physical therapy (Medicare, n.d.). Also, retirees living on a fixed income may not have the financial mobility to have access to alternative health insurance. Additionally, retirees typically are older individuals and their age can negatively impact their pain levels and general health. The individuals that self-

reported as unemployed also includes individuals that are unemployed due to disability. This group is most likely to be on Medicare, which, as described above, could limit health coverage. Due to their unemployment or inability to work due to a disability, these individuals are more likely to be in a lower socioeconomic class, which could also negatively impact HRQoL (Feinstein et al., n.d.).

Interestingly, for both education and employment, physical functioning showed a statistically significant increase in HRQoL for those of lower education and those who are unemployed. This was not expected based on what was shown in the other domains. Individuals with that are employed or have a higher education may have more active lifestyles or have higher demands placed upon them in the workplace. These individuals would then be impacted more by the symptoms of their aortic disease. This is also supported by the fact that both of these groups scored higher in the role limitation domain. Another reason could be that the study focuses on physical functioning at the moment they take the survey, which can impact the participant in two ways. Firstly, the participant might be further along in their disease course and would have expected their symptoms to improve. If their symptoms did not improve, the participant might be more inclined to negatively assess their quality of life. Secondly, if the participant is early in their disease course, they might rate themselves as being more severely impacted because mentally they are having difficulty adjusting to their diagnosis. Also, those were employed may have worse physical functioning than those were unemployed or retired, as they are exerting themselves much more in the workplace. Individuals with a higher education are less likely to be working jobs

that require tasks involving excess physical function. Thus, they are more likely to be able to maintain working with poor functioning before eventually going on disability. Another possibility for this finding may be that individuals did not answer the HRQoL survey questions completely in this specific category. There are a total of 10 questions, each with varying degrees of physical functioning impairment that could impede completion of the task at hand (ex: lifting a bowl or walking several blocks). Twenty-four individuals left the first question blank, which corresponds with the most severe limitation of physical functioning. Several other questions on the HRQoL survey were left blank by individuals. This ultimately affects the overall average for a specific individual's physical functioning score, skewing it lower for individuals who skipped questions.

Those who were married or did not have a partner had lower physical functioning. This could be due to the inclusion of individuals that were widowed, who typically are individuals of an older age. It could also be that these individuals may take on more physical stress daily since they have no partner or spouse with which to share the burden. Thus, limitations in physical activities become more noticeable.

There were also significant results in physical functioning in regards to an individual's race. Individuals who did not identify as white showed significantly better physical functioning than those who identified as white. The reason for this is thought to be due to sample size. One hundred sixty-nine (89.9%) individuals classified themselves as white, while only 19 (10.1%) of individuals did not. However, in the general health domain, individuals who did not identify as white scored lower than those who did. This could be a

result of other confounding societal factors that have shown poorer health-related outcomes for people of color.

Other significant findings with physical functioning were that individuals that had a primary diagnosis of a genetic syndrome or mutation reported higher scores than individuals without a primary diagnosis of a genetic syndrome of mutation. Additionally, individuals that had a diagnosis of TAAD, rupture or marked tortuosity had lower scores for this domain. It should be marked that both groups overall had generally poor physical function based on their low MOS SF-36 scores in the physical domain. However, it is possible that those who had a known genetic mutation or syndrome may be receiving adequate therapies and interventions that are allowing them to have slightly increased physical functioning. Individuals who have a genetic predisposition to TAA/TAD but no mutation or known syndrome are typically treated purely on symptoms and family history. Preventative care or close surveillance to catch things impacting physical functioning is unlikely for these individuals since many doctors will not know what to specifically look for. Those who had a diagnosis of TAA/TAD, rupture or marked tortuosity scored lower with physical functioning, which could be due to exercise and physical exertion limitations recommended by a medical professional (Halaweh et al., 2015). These individuals may also experience lower physical function due to recovery time post-surgery to correct their TAAD. Additionally, other unadjusted, confounding factors such as unrelated health problems and lifestyle factors may influence the relationship between diagnosis of genetic syndrome or TAA/TAD and physical functioning.

However, this data also showed that in the general health domain, individuals who had a diagnosis of TAA/TAD, rupture, or tortuosity reported higher average scores than those who did not have any of these diagnoses. Separately those who had a diagnosis of Marfan syndrome or other known genetic mutation or syndrome had a lower perception of general health than those who did not have a known genetic mutation or syndrome. Those who had a known genetic mutation or syndrome most likely have multiple health issues other than just physical restriction or surgery recovery related to TAA/TAD that could negatively impact overall perception of general health.

The domains of role limitations and pain had the same variables significantly associated with them. Age is significant factor in both, with older age tracking with poorer scores in role limitations. However, in the domain of pain, the oldest population (54 to 84 years old) scored highest in HRQoL second to only the youngest group (33 years old and younger). Reasons for this could be that those in the elderly population group are people who are not diagnosed with a genetic syndrome or have a milder course of the disease. Other than education and employment, the only other significant variable in both domains was that of insurance. Better HRQoL was associated with private insurance in regards to role limitations and pain. Private insurance offers more coverage and opportunity for preventative therapies and treatments, and ultimately positively impacting role limitation and pain in individuals.

The overlap in questions between role limitation and pain could account for the similarities amongst the variables. One of two questions that indicate pain HRQoL ask if the pain interfered with an individual's normal work – essentially asking if pain caused any role

limitations. While this could be part of the overlap, role limitations did not seem to be limited to just pain. As mentioned before, the overall mean for role limitations is much lower than the overall mean in pain management.

Finally, when reviewing the populations studied by GenTAC, Marfan syndrome is likely the most studied when looking at HRQoL. A large number of those studies utilized the MOS SF-36 survey either alone or in conjunction with other surveys. These studies are relatively consistent that people with Marfan syndrome have a lower HRQoL as compared to the general population. (Fusar-Poli et al., 2008; Rand-Hendriksen et al., 2010). This study also showed that those with a diagnosis of Marfan syndrome had a significantly lower HRQoL score in the general health domain. Both Fusar-Poli and Rand-Hendriksen showed that general health for Marfan syndrome was low, 51.56 (24.89) and 47 (24) respectively, which was slightly higher than this study's results for general health of 44.6 (23.4) (2008; 2010). While not being statistically significant, the HRQoL for role-limitations and physical functioning from GenTAC was lower than both Rand-Hendriksen [role limitations = 43 (42) and physical functioning = 70 (25)], and Fuser-Poli, [role limitations =70.83 (27.56) and physical functioning =77.92 (20.26)] (2008; 2010). Additionally, the GenTAC HRQoL for pain was between Rand-Hendriksen 55 (26) and Fuser-Poli 57.53 (29.79) even though it too was not statistically significant (2008; 2010). The lack of statistical significance is thought to be most likely due to the small sample size of diagnosed individuals.

GenTAC Health-Related Quality of Life Study Limitations

The MOS SF-36 survey itself, while validated, has certain limitations. One of the

known limitations of this survey is that subgroups of older age, Black race, less educated and impoverished individuals have had problematic evaluation for certain criteria (McHorney et al., 1994). The survey did not adequately look at or correct for the fact that these individuals may already have a lower HRQoL before illness based on societal and, in the case of age, physiological complications. Future analysis should adjust for potentially correlated or confounding factors.

Additionally, the GenTAC Consortium only used part of the MOS SF-36 scale. The scale also inquires about role limitations due to emotional problems, emotional well-being, vitality, and social functioning aspects of HRQoL. Because these domains were not assessed, this patient population's social and emotional health were not evaluated through this study. It is also important to note that the survey is self-reported, and temporal effects in relation to diagnosis of a genetic syndrome/mutation or TAA/TAD could have affected how an individual answered questions about physical functioning, pain, etc. The UTH and BCM sites recruited from cardiothoracic services or clinics and so the numbers of patients who recently had surgery and completed the survey are significant, which may have resulted in lower reported scores of physical health.

Self-reported data is also a limitation in itself. More than half of the population had incomplete or missing HRQoL data and were excluded in the analysis. It is possible that the patients who completed these questions and those who did not have different characteristics that may be related to quality of life. Additionally, when initially analyzing the self-reported medical diagnosis against the enrollment diagnosis based on medical records, it was found

that around 50% of the individuals did not report a diagnosis of TAAD, rupture or tortuosity or a diagnosis of Marfan syndrome. It could not be determined whether the missing data was due to patients refusing to self-report a diagnosis or a lack of information or understanding of a diagnosis.

Depression Measurements in AD and AA Survivors

Currently, there are limited studies measuring depression of AD and AA survivors, and to the best of the researchers' knowledge, no study measuring survivors' experiences with genetic and/or mental health services. This study illustrated an overall increase in depression in AD when compared to other studies using the QIDS-16. One large study using 1,500 Sequenced Treatment Alternatives to Relieve Depression (STAR*D) patients. The STAR*D measured which depression treatments are most effective for outpatients with nonpsychotic MDD (Rush et al., 2003).

The average QIDS-16 score for survivors of an AD or AA was 13.05 (Moderate depression) and SD=4.9. Sleep disturbance had the highest score using the QIDS-16, followed by appetite/weight change. This finding correlated with a previous study by Chaddha et al. (2015), which demonstrated anxiety and depression effects on AD survivors' lifestyles and showed that 32% of patients had self-reported depression and 32% of patients had anxiety due to their AD. Physicians treating survivors of an AD or AA should screen for and monitor alterations in sleep and appetite/weight symptoms and work to reduce these depressive symptoms in patients who may be more susceptible.

Another area of this study that had a negative correlation with depression was

employment status ($F(6/63) = 2.94$, $p<0.05$). As seen in other studies, individuals who were employed were more likely to have a steady income, housing, and access to health insurance, thus providing with an overall improved health status. Employment status has been shown to impact quality of life in survivors or AD (Chaddha et al., 2015).

Genetic services were found to correlate with decreased depression.These services were also shown to help the patient understand their condition ($r(16) = 0.46$, $p<0.05$). Decreased depression also correlated with the patient's rating of the genetic services they received providing them with useful resources ($r(16) = 0.45$, $p<0.05$). These correlations suggested that an informative session with a genetic specialist may lead to a decrease in depression. This data supported a meta-analysis that measured the quality of education and the rates of depression in individuals recovering from cardiac surgery (Fredericks & Yau, 2017). Depression scores were not related to having genetic testing for an aortic dissection or an aortic aneurysm ($t(73) = 0.25$), demonstrating that the genetic testing alone was not associated with decreases in depression scores. There was no difference in depression scores for those who were referred to genetic services after surgery ($t(72) = 0.16$).

Study Limitations to Depression Measurements in AD and AA Survivors

While these results are helpful in understanding the importance of genetic professionals in the care of individuals with a history of AD or AA, several factors may have impacted the results of this study. This study may not have shown a significant difference in the variables measured due to the limited sample size. Of these 75 individuals that completed the QIDS-16, only 61 completed the survey in its entirety, including mental health history.

Though this study did not show any significant correlation between these demographic variables and depression, future studies with a larger study population are necessary to support this data.

The final limitation of this study was the lack of diversity in this patient population. Sixty-seven (89.3%) identified as Caucasian, one (1.3%) identified as Black or African American, two (2.7%) identified as Asian, and three (4%) identified as multiple races. Lack of diversity could lead to population bias, as other populations may experience different AA or AD treatments and outcomes when compared to Caucasians. The lack of diversity could also impact these results as job status and access to healthcare such as consultations with genetic professionals may vary among races other than Caucasian. Having a survey in languages other than English would allow for more diverse populations to participate in this study. Publicizing the study from various sources beyond Facebook support groups could recruit a more diverse patient population. Reaching out to multiple patient populations related to other institutions in conjunction with The John Ritter Research Program in Aortic and Vascular Diseases would have also been beneficial in studying a variety of individuals.

One important aspect that this study did not examine was comorbidity between anxiety and depression. Previous diagnosis of anxiety was measured, but no validated anxiety measurement was utilized to screen individuals. All data was self-reported from individuals; therefore, information regarding a person's diagnosis cannot be verified.

Conclusion

HRQoL was shown to be poor in this patient population with TAA and TAD or genetic predisposition to TAA and TAD. Several demographic factors were shown to be significantly associated with physical health, in particular, employment status and education level. Additionally, people who were diagnosed with Marfan or other genetic syndromes or mutations reported significantly lower general health compared to those who did not have diagnosis of a genetic syndrome or mutation. Patients with TAA and TAD have significantly lower physical functioning but interestingly higher perception of general health.

For future studies, it would be beneficial to have the more diverse patient population of the entire GenTAC Consortium. This particular patient population gathered from GenTAC was not representative of all that were enrolled in the consortium and eliminated any individuals under the age of 18. A larger, more diverse patient population could further explore variables such as race and its role in physical functioning. In addition, the questionnaires were self-administered resulting in significant missing data. In the future, study personnel should consider administering these questionnaires over the telephone or in-person to improve data quality.

A complete MOS SF-36 scale should be considered when surveying individuals about HRQoL. Leaving out portions of this survey could prevent a more thorough evaluation of a patient population, as other portions of the survey have been studied in the Marfan syndrome population. For example, when individuals diagnosed with Marfan syndrome were evaluated using the complete MOS SF-36 and compared to the general population, individuals scored

lower on HRQoL in the mental domain (including mental health or emotional well-being, role limitations due to emotional problems, social functioning, and vitality or energy/fatigue) than the general population (Fusar-Poli et al., 2008; Rand-Hendriksen et al., 2010). Additionally, the MOS SF-36 is itself limited as it does not account for older age, race, lower levels of education, and impoverishment in the general population. (McHorney et al., 1994) An HRQoL survey that also accounts for the aforementioned variables would be beneficial in future studies to observe HRQoL in these individuals.

With regards to genetic counseling practice, emphasis should be given to pretest and posttest counseling to facilitate understanding of patient's diagnosis of TAA/TAD or genetic condition. Many of these individuals inaccurately self-reported or did not report their diagnoses or genetic tests that were included in their medical records. Some individuals also mentioned that they were unsure if they even had genetic testing or a diagnosis when their medical records indicated that they did. These discrepancies can be potentially alleviated through patient education, visual aids, and letter writing directly to a patient. Surveys can be distributed post-session to evaluate an individual's understanding of the information they received during the visit or session.

The overall perception of general health was relatively poor 55.0 (SD=25.8). Scores indicated a diagnosis of depression in 30% of the GenTAC study population. Based on the data observed, routine assessment of a patient's physical status, role limitations and adjustment to their lifestyle/activity is recommended in genetic counseling session. An assessment of mental health and subsequent referral to an appropriate provider, if needed,

should also be considered when working with this patient population. Genetic counselors can then adjust the session and help facilitate coping and/or make appropriate referrals if needed.

Depression was demonstrated to increase for survivors of AD and AA, with associations to alterations in sleep and changes in their appetite/weight. A larger and diverse sample size is needed to explore this correlation fully in addition to the possible comorbidity of anxiety and impact of HRQoL. It is vital for researchers to further investigate this finding in hopes of providing more impactful health care to survivors of AD or AA.

Future studies should include scales that measure both depression and anxiety, as these two psychological conditions are comorbid (references). One study surveyed 1,500 individuals to estimate a mean QIDS-16 score of 8.6 with a standard deviation of 8.6 (Mild depression) (Rush et al., 2006). Additionally, an ongoing survey could increase sample size for future studies, reach a much more diverse patient population, and provide more data for analysis of anxiety and depression in this patient population.

Another approach to assessing the impact of an AD or AA would be to measure the HRQoL with a patient survey such as the MOS SF-36. The MOS SF-36 has been utilized in similar patient populations such as with individuals post-cardiac surgery or individuals with Marfan syndrome (Goyal et al., 2005, Ghanta et al., 2016, Rand-Hendriksen et al., 2010). The MOS SF-36 has been used to demonstrate the precise impact the condition had on the individual. Qualitative studies could prove to be beneficial in developing a tailored depression and anxiety scale for these individuals.

Genetic professionals, surgeons, and cardiologists should be aware of the mental

health implications that arise from the experience of an acute aortic dissection or the diagnosis of an aortic aneurysm. Furthermore, data show that interaction with a genetic professional may decrease depressive symptoms. Advocating for this patient population to meet with a genetic professional could positively impact mental health. Additional studies are needed to demonstrate the effects genetic professionals can have on this patient population to support or nullify our claims.

Acknowledgements

We would like to thank the supervisors at the University of Texas Health and Science Center and the John Ritter Research Program for Aortic and Vascular Diseases; especially, Stephanie Wallace for her guidance over the distribution of our survey and Ellen Regalado for her guidance regarding the GenTAC data. We would like to thank Professor Mike Smith of Columbia University for his much appreciated statistical analysis, and the faculty, staff, and classmates at the Joan H. Marks Program in Human Genetics at Sarah Lawrence College, especially Claire Davis for all of her support and wisdom.

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Tables

Table 1. (Demographic and clinical characteristics of GenTAC study population)	
Variable	Summary statistic
Age [1]	43.9 (14.2)
33 years old and younger	48 (25.1%)
34 to 44 years old	49 (25.7%)
45 to 53 years old	49 (25.7%)
54 to 84 years old	45 (23.6%)
Gender [2]	
Male	108 (56.0%)
Female	85 (44.0%)
Race [3]	
White race	169 (89.9%)
Non-White race	19 (10.1%)
Education [4]	
Some college or less	91 (49.2%)
College or post graduate	94 (50.8%)
Marital status [5]	
Married	112 (59.3%)
Not married	77 (40.7%)
Insurance [6]	
Private	129 (73.7%)
Non-private	46 (26.3%)
Income [7]	
<$50,000	65 (39.4%)
$50,000- $100,000	60 (36.4%)
>$100,000	40 (24.2%)
Employment [8]	
Employed, student or homemaker	128 (68.5%)
Unemployed	40 (21.4%)
Retired	19 (10.2%)
Depression [9]	55 (32.2%)
Primary diagnosis of Marfan syndrome [10]	32 (16.5%)
Primary diagnosis of known genetic syndrome or mutation [11]	67 (34.7%)
Approximate age at diagnosis of primary condition [12]	33.1 (18.4)
Diagnosis of thoracic aortic	164 (85.4%)
Ever had vascular or heart surgeries	28 (51.9%)
Number of years after heart or	4.2 (5.4)
1 year	1 (4.4%)
2 years	2 (8.7%)
3 years	2 (8.7%)
4 years	2 (8.7%)
1: missing 3 particpants	9: missing 23 particpants
2: missing 1 particpants	10: missing 0 particpants
3: missing 6 particpants	11: missing 1 particpants
4: missing 9 particpants	12: missing 6 particpants
5: missing 5 particpants	13: missing 2 particpants
6: missing 19 particpants	14: missing 140 particpants
7: missing 29 particpants	15: missing 171 particpants
8: missing 7 particpants	

Table 1: Demographic and clinical characteristics of GenTAC study population:

Demographic and clinical characteristics of a study population from the GenTAC registry are described in this table. This study population includes patients, aged 18 or older, with a genetically triggered thoracic aortic aneurysm and/or dissection. Patients were recruited at the University of Texas Health and Science Center at Houston and Baylor College of Medicine.

Table 2: Health-related quality of life (HrQoL) in 4 major domains as seen in a GenTAC study population

Table 2: Health related quality of life (HrQoL) in four major domains as seen in a GenTAC study population								
Variable	Physical Functioning	p value	Role Limitation	p value	Pain	p value	General Health	p value
Age		0.1217		0.0124		0.0116		0.8910
33 years old and younger	19.2 (17.9)		56.0 (43.8)		74.7 (25.5)		53.9 (20.9)	
34 to 44 years old	27.5 (29.5)		39.9 (44.4)		57.4 (29.8)		55.1 (25.8)	
45 to 53 years old	29.1 (26.2)		38.3 (43.6)		57.2 (31.8)		54.2 (30.6)	
54 to 84 years old	32.0 (30.7)		25.6 (36.5)		59.9 (29.6)		57.8 (26.1)	
Gender		0.0895		0.9603		0.6521		0.0379
Male	23.7 (26.4)		39.9 (42.5)		61.3 (30.1)		58.3 (24.6)	
Female	30.3 (25.9)		40.3 (44.3)		63.3 (29.2)		50.6 (26.7)	
Race		0.0074		0.2404		0.1550		0.0013
White race	24.8 (25.7)		42.0 (43.5)		62.8 (29.8)		57.7 (25.2)	
Non-White race	42.9 (31.2)		28.6 (39.7)		51.9 (32.2)		38.0 (22.1)	
Education		0.0032		0.0007		0.0017		0.0032
Some college or less	32.1 (28.3)		28.7 (38.7)		54.6 (30.9)		49.9 (26.0)	
College or post graduate	20.6 (22.7)		50.5 (44.0)		68.4 (27.1)		61.0 (24.5)	
Marital status		0.0340		0.1675		0.1284		0.3699
Married	30.7 (27.9)		36.0 (43.5)		59.2 (30.8)		56.3 (25.7)	
Not married	22.3 (23.9)		45.1 (42.0)		66.0 (27.4)		52.8 (26.7)	
Insurance		0.0673		0.0160		0.0440		0.0027
Private	25.0 (26.0)		45.6 (43.5)		65.4 (28.9)		59.1 (24.0)	
Non-private	33.5 (28.7)		27.0 (38.5)		55.0 (29.1)		45.4 (30.3)	
Income		0.0671		0.1698		0.0594		0.0008
<$50,000	32.2 (27.3)		34.2 (43.1)		57.1 (29.8)		46.5 (23.9)	
$50,000- $100,000	27.0 (28.2)		40.9 (42.6)		62.8 (29.0)		61.3 (26.7)	
>$100,000	19.8 (21.3)		50.6 (42.5)		71.2 (28.4)		62.4 (22.6)	
Employment		<0.0001		<0.0001		0.0012		<0.0001
Employed, student or	21.6 (24.5)		49.6 (43.8)		66.8 (28.2)		61.5 (23.2)	
Unemployed	43.2 (26.5)		14.2 (30.4)		46.7 (31.0)		32.8 (22.2)	
Retired	31.3 (28.7)		23.6 (37.8)		57.6 (28.8)		60.1 (27.9)	
Depression		0.0613		0.2072		0.6247		0.0187
No	22.3 (25.9)		43.5 (43.6)		64.3 (29.7)		58.6 (26.1)	
Yes	30.4 (25.0)		34.3 (40.9)		61.9 (28.7)		48.6 (24.2)	
Primary diagnosis of Marfan syndrome		0.7071		0.5935		0.9313		0.0124
No	26.5 (26.7)		40.8 (43.7)		61.8 (30.4)		57.1 (25.8)	
Yes	28.4 (25.9)		36.3 (40.7)		62.2 (28.0)		44.6 (23.4)	
Primary diagnosis of known genetic syndrome or mutation		0.0148		0.2513		0.5721		0.0002
No	23.4 (25.3)		42.4 (43.4)		61.0 (30.8)		59.9 (25.5)	
Yes	33.2 (27.7)		34.8 (42.2)		63.6 (28.6)		45.7 (24.1)	
Diagnosis of thoracic aortic aneurysm/dissection, rupture or marked tortuosity		0.0254		0.7943		0.8470		0.0181
No	37.0 (28.3)		38.0 (44.6)		62.9 (26.7)		44.3 (22.8)	
Yes	24.9 (25.8)		40.3 (42.9)		61.7 (20.7)		56.8 (26.0)	

Measurements of Health-Related Quality of Life (HRQoL) in the four major domains of physical functioning, pain, role limitations and general health of a study population from the GenTAC registry are described in this table. Factors such as demographics, genetic and medical diagnoses are correlated with each of the four domains.

Table 3: QIDS-16 Results for Survivors of AD or AA

QIDS-16 Results			
	Frequency (n)	Percent (%)	Cumulative Percent
No Depression	4	5.3	5.3
Mild Depression	23	30.7	36
Moderate Depression	23	30.7	66.7
Severe Depression	19	25.3	92.0
Very severe Depression	6	8.0	100.0
Total	75	100.0	

Measurements of depression is present by the frequency and percent for all the different severities of depression using the QIDS-16.

Table 4: QIDS-16 Means and Standard Deviation

QIDS-SR$_{16}$ item	**Average Response (SD)**
Sleep disturbance	2.49 (0.64)
Sad mood	1.31 (0.97)
Appetite/weight change	2.03 (1.10)
Concentration	1.39 (0.70)
Self-outlook	1.24 (1.22)
Suicidal ideation	0.49 (0.74)
Involvement	1.15 (1.06)
Energy	1.67 (0.89)
Psychomotor change	1.28 (0.98)
Total	13.05 (8.3)

Measurements of depression is present by the mean and standard deviation for all the categories of depression using the QIDS-16.