Research Article

ISSN 2639-8486

Cardiology & Vascular Research

Elevated Cardiopulmonary Complications after Revascularization in Patients with Severe Mental Health Disorders

Leah Gober[1], Adam Brown[2], Avianne P. Bunnell[1,2], Brian E. Bunnell[3,4] and Jean Marie Ruddy[2*]

[1]*School of Medicine, Mercer University School of Medicine, Savannah, GA, USA.*

[2]*Division of Vascular Surgery, Medical University of South Carolina, Charleston, SC, USA.*

[3]*Department of Psychiatry and Behavioral Sciences, Medical University of South Carolina, Charleston, SC, USA.*

[4]*Department of Psychiatry and Behavioral Neurosciences, University of South Florida, Tampa, FL, USA.*

***Correspondence:**
Jean Marie Ruddy, MD FACS, Associate Professor of Surgery, Division of Vascular Surgery, Medical University of South Carolina, 30 Courtenay Drive, MSC 295, Charleston, SC 29425, Tel: 843-876-8568; Fax: 843-876-4413.

Received: 09 September 2021; **Accepted:** 11 October 2021

Citation: Gober L, Brown A, Bunnell AP, et al. Elevated Cardiopulmonary Complications after Revascularization in Patients with Severe Mental Health Disorders. Cardiol Vasc Res. 2021; 5(5): 1-6.

ABSTRACT

Introduction: *Mental health disorders (MHD) are prevalent within surgical patient populations and can be associated with poorer postoperative outcomes, particularly in those with more severe MHD (schizophrenia and bipolar disorder). However, these associations have not been examined in vascular surgery patients. This study investigated patients undergoing lower extremity revascularization, hypothesizing that those with severe MHD would experience worse health and postoperative outcomes.*

Methods: *A retrospective chart review of patients from 2010-2015 with peripheral arterial disease (PAD) requiring revascularization was conducted, with subsequent narrowing to those with concurrent MHD diagnoses, including severe MHD (sMHD) defined as bipolar disorder or schizophrenia and non-severe MHD (nsMHD), defined as anxiety or depression. The primary endpoints were 30-day mortality; Major Adverse Limb Events (MALE) including amputation at the above or below knee level; and Major Adverse Cardiac Events (MACE) including myocardial infarction (MI), congestive heart failure (CHF) exacerbation, and arrhythmia. Secondary endpoints were readmission within 30 days, pulmonary complications, and wound infection. Statistical analyses included Fisher Exact Test and Student's T-test.*

Results: *Eighteen patients with MHD (sMHD, n=10; nsMHD, n=8) were identified and stratified. Twenty-four limbs were revascularized (sMHD, n=13; nsMHD, n=11). Overall incidence of 30-day mortality, MALE, and MACE were 4.2%, 33.3%, and 50.0%, respectively. Readmission rate, pneumonia, and wound infection occurred in 41.7%, 20.8%, and 16.7% of the population. Stratifying by MHD severity, no significant differences were observed for medical comorbidities, MALE, intervention type (open vs. endovascular), or treatment indication (claudication vs. critical limb ischemia). Patients with sMHD had significantly higher rates of MACE compared to patients with nsMHD (30.8% vs. 18.2%, $p<.05$). Pneumonia was also more prevalent in this group (38.5% vs. 0.0%, $p<.05$).*

Conclusion: *While patients with concurrent diagnoses of MHD and PAD presented with similar comorbidities, comparable disease severity, and were equally treated by open versus endovascular techniques, those with severe MHD suffered significantly elevated rates of cardiopulmonary complications, specifically MACE and pneumonia. Further investigation is warranted to identify opportunities to optimize post-operative care for these complex patients.*

Keywords
Peripheral artery disease, Depression, Anxiety, Schizophrenia, Bipolar, Mental health disease.

Abbreviations
PAD: Peripheral artery disease, ABI: Ankle-brachial index, nsMHD: Non-severe mental health disorder, sMHD: Severe mental helath disorder, CVD: Cardiovascular disease, CAD: Coronary artery disease, MALE: Major Adverse Limb Events, MACE: Major Adverse Cardiac Events, MI: Myocardial infarction, CHF: Congestive heart failure, NIMH: National Institutes of Mental Health, APA: American Psychiatric Association, DSMIV: Diagnostic and Statistical Manual of Mental Disorders.

Introduction
Vascular disease and mental health disorders (MHD) share a long history of overlap amongst vulnerable populations, along with other comorbidities including smoking, obesity and sedentary lifestyles [1-2]. In 2019, there were an estimated 51.5 million adults aged 18 or older in the United States with AMI. This number represented 20.6% of all U.S. adults [3]. Some notable populations, including those with prior depressive episodes or complicated health conditions resulting in ICU care, suffer from an increased prevalence of MHD, and in some studies a greater relative potential to develop a psychiatric disorder in the post-operative period [4,5]. For example, through structured pre-operative clinical interviews, approximately 55% of bariatric patients were found to meet criteria for a psychological disorder [6]. Cardiothoracic surgical candidates with diagnosed MHD have additionally been found to have increased mortality, less overall physical and mental health improvement postoperatively, and increased cardiac-related hospitalizations [7-9].

While earlier investigations demonstrated an association between open aortic repair and the development of psychiatric symptoms, the relation between infra-inguinal revascularization and MHD has not been fully explored [10,11]. One of the initial studies linking PAD and mental health was out of the Netherlands and sought to understand the effects of quality of life after infra-inguinal bypass. The authors found that revascularization, whether successful, requiring secondary interventions to maintain patency, or complicated by later amputation, resulted in increased pain and decreased social functioning in PAD patients; with amputees suffering the lowest quality of life scores [12]. Further studies in vascular patients have found that PAD had an equivalent health related quality of life burden as that of cardiac disease [13]. These metrics, including physical functioning, bodily pain, and social and emotional functioning, have been lower in vascular patients compared to the general population, potentially contributing to or exacerbating depression [14]. Additionally, a recent nationwide assessment found that 16% of Veteran patients with PAD suffered from depression [15]. This investigation also demonstrated that depression in PAD was associated with an increased risk of death and amputation, particularly among depressed patients not receiving antidepressant therapy. PAD has also been diagnosed with a higher prevalence among patients with more debilitating MHD and these patients have demonstrated accelerated vascular aging [16,17], but the impact of severe MHD (sMHD) such as bipolar disease and schizophrenia on PAD severity and peri-operative outcomes remains unclear. Therefore, the present study aimed to investigate the hypothesis that patients diagnosed with sMHD (bipolar disease and schizophrenia) would have higher rates of peri-operative complications after undergoing infra-inguinal revascularization compared to those with non-severe MHD (nsMHD; depression and anxiety).

Methods
This single center retrospective chart review of adult patients from 2010-2015 diagnosed with MHD and undergoing lower extremity revascularization was approved by the Institutional Review Board of the Medical University of South Carolina. Included were patients with a diagnosis of PAD, either intermittent claudication or critical limb ischemia, who underwent infra-inguinal revascularization. As defined by National Institutes of Mental Health (NIMH) and the American Psychiatric Association (APA) and published in the DSM-IV-TR [18], bipolar disorder and schizophrenia were categorized as severe mental health diagnoses (sMHD) and anxiety and depression were categorized as non-severe mental health diagnoses (nsMHD). Open, endovascular, and hybrid infra-inguinal revascularizations were considered, but patients who underwent emergent interventions were excluded from this study. All hybrid revascularizations, defined as interventions with both open and endovascular components, were reported along with the open intervention group. A pre-operative ABI threshold of ≤ 0.45 was utilized to establish the diagnosis of critical limb ischemia if rest pain or tissue loss were not clearly stated in the patient chart. Patients were also stratified as non-medicated and medicated. Non-medicated patients were defined as those who did not have daily antidepressant or antipsychotic medications initiated 6 months before or after revascularization whereas medicated patients were actively prescribed one or more of these medications.

The primary endpoints were 30-day mortality, Major Adverse Limb Events (MALE) which includes amputation at the above or below knee level, and Major Adverse Cardiac Events (MACE) including myocardial infarction (MI), congestive heart failure (CHF) exacerbation, and arrhythmia. Secondary endpoints were readmission within 30 days, pulmonary events, and wound infection. Additional outcomes and complications were reported as discovered within patient follow-up documentation. Statistical analyses included Fisher Exact Test and Student's T-test with statistical significance set at $p<0.05$.

Results
Eighteen patients and 24 revascularized limbs were evaluated in this retrospective review. As demonstrated in Table 1, the mean age of the cohort was 63.4 ± 10.7 years, most patients were men (77.8%), and Caucasian (61.1%). Nearly all patients had a history of tobacco use (94.4%). Most patients had associated hypertension (77.8%) and a majority were being treated with aspirin (72.2%) and

a statin (94.4%). Many patients received treatment for their MHD with regimens that included antidepressants (50%), antipsychotics (50%), and/or and benzodiazepines (38.9%). Very few had seen a mental health provider in the 6-months prior to surgery (5.6%). When separated by MHD, there was no significant difference among demographics between the two groups (Table 1).

Procedure specific data and perioperative vascular disease severity is presented in Table 2. Based on the symptoms reported and the surgeon's clinical diagnosis, most interventions were performed for critical limb ischemia (CLI, 70.8%), but pre-operative ABI was more often recorded to be >0.45 (55.6%). Both open/hybrid (41.7%) and endovascular (58.3%) interventions were utilized extensively in this cohort. Intensive Care Unit stay was only required in 25% of patients and 83.3% were able to be discharged to home, but only 37.5% received home health services. Again, when stratifying patients by severity of MHD, there were no significant differences between the groups in these peri-operative metrics.

Regarding the total cohort, the rate of MALE was 33.3% and 30-day mortality was 4.2% (Table 3). MACE occurred at a rate of 50% and 20.8% developed pneumonia. Wound infection occurred in 26.7% and 37.5% required reintervention, both of which likely contributed to the 30-day readmission rate of 41.7% for medical care. Considering the sMHD group, the rate of MACE and pneumonia were significantly higher than in those with nsMHD (p=0.025, p=0.041, respectively). The other post-operative outcomes did not differ between these groups.

Discussion

When treating patients with PAD, consideration and management of comorbidities can significantly influence patient outcomes. This single center retrospective study was conducted to investigate whether severity of MHD can likewise play a role. In this cohort, despite there being no differences in medical comorbidities and peri-operative indications of PAD severity, there was a significantly increased incidence of MACE and pneumonia in those with sMHD.

Table 1: Patient demographics and comorbidities in the cohort undergoing infra-inguinal revascularization with concurrent mental health disorder.

	Total (n=18)	sMHD (n=10)	nsMHD (n=8)	p-value
Age (Mean ± SD)	63.4 ± 10.7	63.6 ± 13.2	63.7 ± 8.3	0.966
BMI (Mean ± SD)	25.5 ± 5.9	26.1 ± 5.1	24.7 ± 7.1	0.653
Sex % (n)				1.000
Male	77.8 (14)	80 (8)	75 (6)	
Female	22.2 (4)	20 (2)	25 (2)	
Race % (n)				0.367
Caucasian	61.1 (11)	50 (5)	75 (6)	
non-Caucasian	38.9 (7)	50 (5)	25 (2)	
Comorbidities % (n)				
Hypertension	77.8 (14)	70 (7)	87.5 (7)	0.588
CAD	50 (9)	30 (3)	75 (6)	0.153
CHF	44.4 (8)	40 (4)	50 (4)	1.000
CVA	5.6 (1)	0 (0)	12.5 (1)	0.444
COPD	38.9 (7)	30 (3)	50 (4)	0.631
DM	33.3 (6)	30 (3)	37.5 (3)	1.000
CKD	27.8 (5)	40 (4)	12.5 (1)	0.314
Dialysis	22.2 (4)	30 (3)	12.5 (1)	0.588
Substance Use % (n)				
Tobacco Use (Current or Former)	94.4 (17)	90 (9)	100 (8)	1.000
Alcohol Use	61.1 (11)	70 (7)	50 (4)	0.631
Illicit Drug Use	16.7 (3)	10 (1)	25 (2)	0.559
Vascular Related Medications % (n)				
Aspirin	72.2 (13)	60 (6)	87.5 (7)	0.314
Statin	94.4 (17)	100 (10)	87.5 (7)	0.444
Dual Antiplatelet	77.8 (14)	70 (7)	87.5 (7)	0.588
Anticoagulant	50 (9)	60 (6)	37.5 (3)	0.637
Psychiatric Medications % (n)				
Antidepressant	50 (9)	40 (4)	62.5 (5)	0.637
Antipsychotic	50 (9)	50 (5)	50 (4)	1.000
Benzodiazepine	38.9 (7)	50 (5)	25 (2)	0.367
Other Sedative	22.2 (4)	10 (1)	37.5 (3)	0.275
Mental Health Provider Visit % (n)				
Within 6-Months Pre-Surgery	5.6 (1)	0 (0)	12.5 (1)	0.444
Within 6-Months Post-Surgery	11.1 (2)	10 (1)	12.5 (1)	1.000

Table 2: Procedure-specific data for this cohort of patients undergoing infra-inguinal revascularization with concurrent mental health disorder.

	Total Limbs (n=24)	sMHD (n=13)	nsMHD (n=11)	p-value
Clinical Indication for Intervention % (n)				0.659
Claudication	29.2 (7)	23.1 (3)	36.4 (4)	
CLI	70.8 (17)	76.9 (10)	63.6 (7)	
Surgery Performed % (n)				1.000
Open/Hybrid	41.7 (10)	38.5 (5)	45.5 (5)	
Endovascular Revascularization	58.3 (14)	61.5 (8)	54.5 (6)	
Pre-Operative Ankle Brachial Index % (n)				0.637
ABI > 0.45	55.6 (10)	44.4 (4)	66.7 (6)	
ABI ≤ 0.45	44.4 (8)	55.6 (5)	33.3 (3)	
Post-Operative Ankle Brachial Index % (n)				1.000
ABI ≥ 0.7	46.2 (6)	44.4 (4)	50 (2)	
ABI < 0.7	53.8 (7)	55.6 (5)	50 (2)	
ICU Stay Associated with Surgery % (n)	25 (6)	38.5 (5)	9.1 (1)	0.179
Discharge Location % (n)				1.000
Home	83.3 (20)	84.6 (11)	81.8 (9)	
Other	16.7 (4)	15.4 (2)	18.2 (2)	
Home Health Resources Established upon Discharge	37.5 (9)	53.8 (7)	18.2 (2)	0.105

Table 3: Post-operative outcomes in this cohort of patients undergoing infra-inguinal revascularization with concurrent mental health disorder.

	Total Limbs (n=24)	sMHD (n=13)	nsMHD (n=11)	p-value
Major Adverse Limb Event % (n)	33.3 (8)	38.5 (5)	27.3 (3)	0.679
Above Knee Amputation	16.7 (4)	23.1 (3)	9.1 (1)	0.596
Below Knee Amputation	20.8 (5)	23.1 (3)	18.2 (2)	1.000
30-Day Mortality % (n)	4.2 (1)	8 (1)	0	1.000
Patent Graft or Stent at Follow-Upn% (n)	50 (12)	66.7 (6)	54.5 (6)	1.000
Wound Infection % (n)	16.7 (4)	15.4 (2)	18.2 (2)	1.000
Reintervention % (n)	37.5 (9)	30.8 (4)	45.5 (50	0.675
Major Adverse Cardiac Event % (n)	50 (12)	30.8 (10)	3 (2)	0.025*
Myocardial Infarction	25 (6)	31 (4)	18 (2)	0.649
CHF Exacerbation	16.7 (4)	31 (4)	0 (0)	0.098
Arrhythmia	8.3 (2)	15 (2)	0 (0)	0.482
Reintubation % (n)	0	0 (0)	0 (0)	1.000
Pneumonia % (n)	20.8 (5)	38.5 (5)	0 (0)	0.041*
30-Day Readmission for Medical Care % (n)	41.7 (10)	54 (7)	27 (3)	0.240
Post-Operative Psychiatric Treatment Admission % (n)	20.8 (5)	15 (2)	27 (3)	0.630

These findings suggest that identifying MHD in patients with PAD may provide opportunities for medical and social interventions to decrease the risk of post-operative complications.

Depression in PAD patients has become increasingly studied in the last decade, suggesting promising action items that may help to identify and target early intervention in this at-risk population [19]. A large study of veterans, an especially vulnerable and well-defined population, demonstrated that depression was directly associated with increased risk of death and amputation. In this study, patients who were properly medicated with antidepressants had a lower risk of amputation [20]. Other studies have focused solely on outlining the differences in sex and development of PAD, determining that depression is the strongest risk factor for PAD in women while smoking and high fibrinogen levels are the strongest risk factors for PAD in men [21]. With respect to severity of depression, studies have found that more numerous and severe depressive symptoms are associated with impaired lower extremity functional performance, including shorter walking distances and lower speeds [15,22]. Anxiety disorders, the most common mental illness in the United States, have been associated with pain at rest and atypical symptoms in patients with PAD. In studies of patients with PAD, the prevalence of anxiety ranges from 25-30% with depression ranging from 27-30% [23,24]. Though the association for these two nsMHD with PAD are strong, implications regarding timing, type, and success of intervention is not yet clear.

It is well established that cardiovascular disease and related-death occurs more commonly in patients with schizophrenia and more recent data from large cohort studies show an increased risk of PAD among this population [16,25]. The mechanism that links this association has been suggested to range from peripheral endothelial dysfunction secondary to metabolic dysfunction at the microvascular level to chronic peripheral inflammation due to elevated C-reactive protein in patients with schizophrenia [26,27]. Further, a study in Taiwan suggested that the use of atypical antipsychotics in patients with schizophrenia may actually play a role in the development of PAD [16]. There is also ample evidence

that persons with bipolar disorder experience accelerated stiffening of the vasculature measured as increased pulse wave velocity and aortic augmentation pressure, independent of BMI [17]. This augmented vascular aging therefore increases the burden and disease of peripheral vessels, contributing to PAD.

Interestingly, the severity of MHD and its independent association with PAD has yet to be fully explored. With many studies focusing on either severe mental health disorders (schizophrenia or bipolar disorder) or non-severe MHD (depression, anxiety), there has been less focus on the stratification between the two groups. With both groups at a defined increased risk for PAD and cardiovascular disease compared to the general population, this investigation sought to identify whether outcomes varied following infra-inguinal intervention and suggests that cardiopulmonary complications were more frequent among those with sMHD. Thus, the potentially increased risk for patients with sMHD to suffer peri-operative MACE or pneumonia may allow vascular specialists to anticipate these issues and engage ancillary as well as subspecialty providers to assist in preventative measures.

Limitations

This retrospective study has several limitations. The use of the electronic medical record may be susceptible to confounding and inaccuracies due to the nature of administrative data recording. For instance, we were unable to account for patients who did not return for follow-up within our system. Additionally, medication compliance could not be assessed. Also, the retrospective nature of the study allows for identification of trends in patients with sMHD but cannot provide causality. Finally, the small sample size limits the depth and application of statistical analysis.

Conclusions

In a single center retrospective review of patients undergoing infra-inguinal revascularization, there was no increased rate of mortality or MALE in patients with sMHD. However, a significantly increased incidence of MACE and pneumonia was identified. Further investigation may confirm this association between MHD severity and cardiopulmonary outcomes as well as identify potential causes and opportunities for prevention. Overall, these findings suggest the importance of vascular specialists taking a holistic approach to treating PAD by including treatment, education, and resources for patients with comorbid MHD to reduce the risk of post-operative complications after revascularization.

References

1. Simon GE, von Korff M, Saunders K, et al. Association Between Obesity and Psychiatric Disorders in the US Adult Population. Archives of General Psychiatry. 2006; 63: 824-830.
2. Breslau N. Psychiatric comorbidity of smoking and nicotine dependence. Behavior Genetics. 1995; 25: 95-101.
3. https://www.samhsa.gov/data/sites/default/files/reports/rpt29393/2019NSDUHFFRPDFWHTML/2019NSDUHFFR1PDFW090120.pdf
4. Yen YC, Huang CK, Tai CM. Psychiatric aspects of bariatric surgery. Current Opinion in Psychiatry. 2014; 27: 374-379.
5. Ghoneim MM, O'Hara MW. Depression and postoperative complications: an overview. BMC Surgery. 2016; 16: 5.
6. Mühlhans B, Horbach T, de Zwaan M. Psychiatric disorders in bariatric surgery candidates: a review of the literature and results of a German prebariatric surgery sample. General Hospital Psychiatry. 2009; 31: 414-421.
7. Perrotti A, Mariet AS, Durst C, et al. Relationship between depression and health-related quality of life in patients undergoing coronary artery bypass grafting: a MOTIV-CABG substudy. Quality of Life Research. 2016; 25: 1433-1440.
8. Blumenthal JA, Lett HS, Babyak MA, et al. Depression as a risk factor for mortality after coronary artery bypass surgery. The Lancet. 2003; 362: 604-609.
9. Connerney I, Shapiro PA, McLaughlin JS, et al. Relation between depression after coronary artery bypass surgery and 12-month outcome: a prospective study. The Lancet. 2001; 358: 1766-1771.
10. Liberzon I, Abelson JL, Amdur RL, et al. Increased psychiatric morbidity after abdominal aortic surgery: Risk factors for stress-related disorders. Journal of Vascular Surgery. 2006; 43: 929-934.
11. King AP, Abelson JL, Gholami B, et al. Presurgical Psychological and Neuroendocrine Predictors of Psychiatric Morbidity After Major Vascular Surgery. Psychosomatic Medicine. 2015; 77: 993-1005.
12. Tangelder MJD, McDonnel J, van Busschbach JJ, et al. Quality of life after infrainguinal bypass grafting surgery. Journal of Vascular Surgery. 1999; 29: 913-919.
13. Regensteiner JG, Hiatt WR, Coll JR, et al. The impact of peripheral arterial disease on health-related quality of life in the Peripheral Arterial Disease Awareness, Risk, and Treatment: New Resources for Survival (PARTNERS) Program. Vascular Medicine. 2008; 13: 15-24.
14. Maksimovic M, Vlajinac H, Marinkovic J, et al. Health-Related Quality of Life Among Patients with Peripheral Arterial Disease. Angiology. 2014; 65: 501-506.
15. Arya S, Lee S, Zahner GJ, et al. The association of comorbid depression with mortality and amputation in veterans with peripheral artery disease. Journal of Vascular Surgery. 2018; 68: 536-545.
16. Hsu WY, Lin CL, Kao CH. A Population-Based Cohort Study on Peripheral Arterial Disease in Patients with Schizophrenia. PLOS ONE. 2016; 11: e0148759.
17. Sodhi SK, Linder J, Chenard CA, et al. Evidence for accelerated vascular aging in bipolar disorder. Journal of Psychosomatic Research. 2012; 73: 175-179.
18. American Psychiatric Association. Diagnostic Criteria from DSM-IV-TR.; 2000.
19. Ramirez JL, Grenon SM. Depression and peripheral artery disease: why we should care and what we can do. CVIR Endovascular. 2018; 1: 14.

20. Grenon SM, Vittinghoff E, Owens CD, et al. Peripheral artery disease and risk of cardiovascular events in patients with coronary artery disease: Insights from the Heart and Soul Study. Vascular Medicine. 2013; 18: 176-184.

21. Grenon SM, Cohen BE, Smolderen K, et al. Peripheral arterial disease, gender, and depression in the Heart and Soul Study. Journal of Vascular Surgery. 2014; 60: 396-403.

22. Ruo B, Liu K, Tian L, et al. Persistent Depressive Symptoms and Functional Decline Among Patients with Peripheral Arterial Disease. Psychosomatic Medicine. 2007; 69: 415-424.

23. Smolderen KG, Hoeks SE, Pedersen SS, et al. Lower-leg symptoms in peripheral arterial disease are associated with anxiety, depression, and anhedonia. Vascular Medicine. 2009; 14: 297-304.

24. Aragão JA, Andrade LGR de, Neves OMG, et al. Anxiety and depression in patients with peripheral arterial disease admitted to a tertiary hospital. Jornal Vascular Brasileiro. 2019; 18: e20190002.

25. Osborn DPJ, Levy G, Nazareth I, et al. Relative Risk of Cardiovascular and Cancer Mortality in People with Severe Mental Illness from the United Kingdom's General Practice Research Database. Archives of General Psychiatry. 2007; 64: 242-249.

26. Israel AK, Seeck A, Boettger MK, et al. Peripheral endothelial dysfunction in patients suffering from acute schizophrenia: A potential marker for cardiovascular morbidity?. Schizophrenia Research. 2011; 128: 44-50.

27. Sicras-Mainar A, Rejas-Gutiérrez J, Navarro-Artieda R, et al. C-reactive protein as a marker of cardiovascular disease in patients with a schizophrenia spectrum disorder treated in routine medical practice. European Psychiatry. 2013; 28: 161-167.