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Prevalence and Risk Factors Associated With Hypertension in von Willebrand Disease

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Abstract

Background: von Willebrand factor (VWF) is a biomarker for endothelial damage. Increased VWF levels are observed in hypertension (HTN) and disorders of endothelial dysfunction, for example, atherosclerotic heart disease (ASHD) and diabetes. Whether low VWF protects against HTN is unknown. **Methods:** To determine prevalence and risk factors for HTN in patients with von Willebrand disease (VWD), we conducted a cross-sectional analysis of discharge data from the National Inpatient Sample, 2009 to 2011. Group comparisons were performed by Rao-Scott χ^2 test. Odds of HTN and HTN outcomes in VWD were estimated by weighted multivariable logistic regression. **Results:** The prevalence of hypertension in patients with VWD (N = 7556), 37.35%, was significantly lower than that in non-VWD patients (N = 19 918 970), 49.40%, $P < .0001$. Hypertension risk factors (hyperlipidemia, diabetes, smoking, hepatitis C, and HIV) and HTN outcomes (ASHD, myocardial infarction [MI], ischemic stroke, and renal failure) were less common in patients with VWD than in non-VWD patients, all $P \leq .0001$. Patients with VWD were younger, 49.67 versus 57.30 years, Caucasian, 82.23% versus 68.35%, and female, 75.44% versus 59.61%, $P < .0001$. Patients with HTN were older, 67.55 versus 47.29 years, male, 45.99% versus 34.90%, and had more HTN risk factors and HTN outcomes than those without HTN, all $P < .0001$, including male and female subgroups, each $P < .0001$. The unadjusted odds of HTN in patients with VWD (odds ratio [OR] = 0.611, $P < .0001$) and of HTN outcomes in patients with VWD (ASHD, OR = 0.509; MI, OR = 0.422; ischemic stroke, OR = 0.521; renal failure, OR = 0.420, all $P < .0001$) became insignificant after adjustment for HTN risk factors plus demographics (age/race/gender), OR = 1.035, $P = .260$. **Conclusion:** The risk of HTN is reduced in patients with VWD, but not after adjustment for HTN risk factors plus demographics, as patients with VWD not having HTN are also typically young, Caucasian, and female.

Keywords

atherosclerosis, cardiovascular disease, endothelial damage, essential hypertension, von Willebrand disease; von Willebrand factor

Introduction

It is estimated that approximately 30% of adults in the United States are diagnosed with hypertension (HTN) or are taking antihypertensive medications.[1] The risk factors associated with HTN have been well established—obesity, insulin resistance, smoking, diabetes, hyperlipidemia, primary renal disease, and aging. Alternatively, HTN remains a major modifiable risk factor for cardiovascular disease (CVD) and atherosclerotic heart disease (ASHD). As the population ages and the rate of obesity increases, the number of patients with HTN will likely grow. Among those with congenital bleeding disorders, the availability of better treatment options has resulted in a life expectancy similar to that of the general population. Not surprisingly, we and others are increasingly recognizing HTN in such patients,[2,3] including those with von Willebrand disease (VWD), the most common bleeding disorder. Yet, whether low von Willebrand factor (VWF) protects against HTN remains unknown.

Although the exact pathogenesis of primary HTN is unknown, it is considered a disorder of endothelial cell dysfunction and injury. von Willebrand factor, which is deficient or defective in VWD, is released from endothelial cells during endothelial inflammation and injury, and elevated VWF levels are associated with increased systemic blood pressure, left atrial diameter, left atrial volume, and left atrial volume

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index.[4-12] Thus, while VWF is essential for physiologic platelet adhesion and aggregation, it is widely accepted as a marker of pathologic endothelial cell damage. Although endothelial damage can occur as a result of HTN, some authors speculate that endothelial damage may actually promote HTN.[8,10,12] The observation that VWF antigen levels are increased in patients with HTN,[8,10,12] but decreased in patients with HTN who have been successfully treated,[8,10,11] supports this concept.

Patients with HTN having target organ damage are at high risk of cardiovascular morbidity and mortality. Elevated VWF levels are associated with the development of target organ damage due to HTN.[10,11] Elevated VWF is not only a risk factor for CVD but also an established major risk factor for stroke.[5,6,10,13] Hypertension induces remodeling of vascular endothelium in response to changes in pressure. It is speculated that low VWF levels protect against arterial thrombosis, consistent with animal models of VWD in which development of coronary artery disease (CAD) is decreased.[14] In fact, atherosclerosis is present in patients with VWD at autopsy,[15] suggesting an occlusive clot may not form. Further, a cross-sectional study of over 600 European patients with VWD indicated only 3% of those with type 1 or 2 VWD and none of those with type 3 VWD had thrombosis,[5] although whether low VWF levels protect against HTN, stroke, ASHD, or CVD remains controversial.[3,6,10,13,16-18] To study this question, we determined the prevalence of and risk factors for HTN in individuals with VWD.

Materials and Methods

This was a cross-sectional analysis of discharge data from the National Inpatient Sample (NIS) during the most recent 3-year period available, between January 1, 2009, and December 31, 2011. The NIS represents a 20% sample of US discharges from all community hospitals participating in the Healthcare Cost and Utilization project. It includes patients covered by Medicare, Medicaid, private insurance, and uninsured.

Discharges among adults (18 years and older) with and without VWD were evaluated by age, race, gender, primary and secondary diagnoses, demographics, and length of stay. Deidentified discharge data were classified by *International Classification of Diseases, Ninth Revision* (*ICD-9*) diagnostic codes for HTN (401-405). Comorbidities were also assessed, including ASHD (414), diabetes (250), obesity (278), smoking (V15.82), hyperlipidemia (272.0, 272.4), myocardial infarction (MI; 412), angina (413), renal failure (403, 404, 585, 586), hematuria (599.7, 599.71, 599.72), proteinuria (791), stroke (430-434), HIV infection (042, 079.53, 795.71, V08), liver disease (571.8, 571.9, 572.8), and hepatitis C virus (HCV) infection (070.41, 070.44, 070.51, 070.54, 070.70, 070.71). This was an exempt study, approved by the institutional review board of the University of Pittsburgh.

Discharge weights from the NIS database were used to produce discharge-level estimates for all community hospitals in the United States. The prevalence of HTN was estimated among patients with and without VWD, as were demographics (age, race, and gender), length of stay, inpatient mortality, risk factors for HTN (ASHD, MI, ischemic stroke, hyperlipidemia, diabetes mellitus, obesity, smoking, HCV, and HIV), and HTN-associated outcomes (ASHD, angina, MI, ischemic stroke, hemorrhagic stroke, hematuria, proteinuria, and renal failure), using all discharges, and separately among males and females. These variables were also compared between those with and without HTN. Continuous data (eg, age, length of stay) were compared by weighted simple linear regression, and categorical data (eg, race, risk factors) were compared across groups by the Rao-Scott χ^2 test.[19] The odds ratio of HTN in patients with VWD compared to patients without VWD was estimated by weighted univariate logistic regression and by 2-weighted multivariable logistic regression models—model 1: adjusting for HTN risk factors (hyperlipidemia, diabetes mellitus, obesity, smoking, hepatitis C, liver disease, HIV) and model 2: adjusting for HTN risk factors in model 1 plus demographics (age, race, and gender). We tested for VWD $\times$ gender interaction effect to determine whether separate models among males and females were necessary, but this was not significant ($P = .08$). Weighted univariate and multivariate logistic models were also fitted for HTN outcomes using the same modeling strategy employed for HTN.

Results

Prevalence of HTN in Patients With VWD

During the 3-year period between January 1, 2009, and December 31, 2011, the prevalence of HTN in patients with VWD (N = 7556), 37.35%, was significantly lower than that in non-VWD patients (N = 19 918 970), 49.40%, $P < .0001$ (Table 1). Individuals with VWD were more likely to be younger, 49.67 versus 57.30 years, Caucasian, 82.23% versus 68.35%, and female, 75.44% versus 59.61%, as compared with patients without VWD, all $P < .0001$. The most common admission diagnoses overall were delivery without cesarean section (6.66%), delivery with cesarean section (3.18%), pneumonia (2.37%), conductive hearing loss (1.59%), CAD (1.48%), obstructive bronchitis (1.35%), delivery with previous cesarean section (1.33%), osteoarthritis (1.17%), urinary tract infection (1.14%), and atrial fibrillation (1.13%). Those with VWD were also less likely to be admitted with CVD or chronic kidney disease (CKD) and had shorter lengths of stay and lower inpatient mortality than those without VWD, all $P < .0001$. Similar findings regarding HTN prevalence, age, race, and length of stay were observed separately, among males and females.

Overall, HTN risk factors, including hyperlipidemia, diabetes mellitus, smoking, and HIV, were significantly less common in those with VWD than in those without VWD, all $P < .0001$, as was obesity, $P = .028$ (Table 1). Hepatitis C was more common in VWD than those without VWD, $P < .0001$, as was liver disease, $P = .046$, and both findings were likely transfusion related. Hypertension-associated outcomes, including ASHD, MI, ischemic stroke, and renal failure, all $P < .0001$, and angina, $P = .0031$, were also less common in individuals

Table 1. Prevalence of HTN and HTN Outcomes by Gender in Adults With and Without VWD.

	All Adult Discharges			Adult Male Discharges			Adult Female Discharges		
	VWD	No VWD		VWD	No VWD		VWD	No VWD	
	Percent or Mean (SE)	Percent or Mean (SE)	*P* Value[a]	Percent or Mean (SE)	Percent or Mean (SE)	*P* Value[a]	Percent or Mean (SE)	Percent or Mean (SE)	*P* Value[a]
No. of adult admissions, raw (weighted)	7556 (37 415)	19 918 970 (98 686 824)	–	1857 (9187)	8 026 805 (39 817 077)	–	5697 (28 220)	11 870 458 (58 764 092)	–
No. HTN, raw (weighted)	2823 (13 974)	9 844 345 (48 751 806)	–	882 (4364)	4 527 975 (22 422 452)	–	1940 (9606)	5 315 113 (26 323 356)	–
% HTN	37.35	49.4	<.0001	47.5	56.31	<.0001	34.04	44.79	<.0001
Age (years)	49.67 (0.23)	57.30 (0.005)	<.0001	54.88 (0.48)	60.37 (0.01)	<.0001	47.97 (0.26)	55.24 (0.01)	<.0001
Sex (male)	24.56	40.39	<.0001	–	–	–	–	–	–
Race/ethnicity									
White	82.23	68.35	<.0001	82.44	70.75	<.0001	82.16	66.72	<.0001
Black	6.79	15.03		6.76	14.59		6.8	15.33	
Hispanic	6.42	10.57		6.78	9.05		6.3	11.6	
Asian	1.64	2.27		1.20	1.9		1.79	2.52	
Native American	0.47	0.68		0.44	0.65		0.48	0.7	
Other	2.44	3.11		2.38	3.07		2.46	3.13	
Admission for HTN	0.37	0.93	<.0001	0.54	1.05	.0344	0.31	0.85	<.0001
Admission for CVD	1.40	2.19	<.0001	2.83	3.45	.1427	0.94	1.34	.0081
Admission for CKD	0.20	0.51	.0001	0.44	0.67	.2446	0.12	0.41	.0004
Length of stay (days)	4.60 (0.07)	4.77 (0.001)	<.0001	5.43 (0.17)	5.22 (0.003)	<.0001	4.34 (0.07)	4.47 (0.002)	<.0001
Inpatient mortality	1.34	2.20	<.0001	2.40	2.75	.3597	0.99	1.82	<.0001
HTN risk factors									
Hyperlipidemia	17.27	25.59	<.0001	25.22	30.94	<.0001	14.69	22.01	<.0001
Diabetes	13.50	23.41	<.0001	17.92	27.65	<.0001	12.06	20.58	<.0001
Obesity	9.22	9.98	.028	7.13	8.96	.0057	9.89	10.69	.0518
Smoke	6.42	8.38	<.0001	9.47	11.45	.0074	5.43	6.3	.007
Hepatitis C	3.75	1.79	<.0001	6.24	2.78	<.0001	2.94	1.13	<.0001
Liver Disease	1.00	0.79	.0458	1.37	0.93	.0528	0.87	0.7	.1077
HIV	0.39	0.76	.0001	1.16	1.25	.7209	0.14	0.44	.0005
HTN-associated outcomes									
ASHD	10.92	19.52	<.0001	19.37	27.72	<.0001	8.18	14	<.0001
Angina	0.50	0.80	.0031	0.85	1.07	.3524	0.38	0.62	.0241
MI	1.99	4.58	<.0001	2.70	6.68	<.0001	1.76	3.17	<.0001
Ischemic stroke	1.55	2.97	<.0001	1.87	3.62	<.0001	1.45	2.54	<.0001
Hemorrhagic stroke	0.60	0.57	.6705	1.23	0.72	.0094	0.39	0.46	.3926
Renal failure	5.57	12.32	<.0001	9.42	16.08	<.0001	4.32	9.8	<.0001
Hematuria	1.34	1.07	.0298	2.70	1.76	.0024	0.89	0.61	.0074
Proteinuria	0.20	0.31	.0861	0.06	0.31	.0754	0.24	0.31	.3632

Abbreviations: ASHD, atherosclerotic heart disease; CKD, chronic kidney disease; CVD, cardiovascular disease; HTN, hypertension; MI, myocardial infarction; SE, standard error; VWD, von Willebrand disease.
[a]Rao-Scott χ^2 test.

with VWD than in non-VWD individuals. The exceptions were hemorrhagic stroke ($P = .6705$) and hematuria ($P = .0298$; Table 1).

Prevalence of VWD in Patients With HTN

The prevalence of VWD in patients with HTN (N = 9 847 168), 0.03%, was significantly lower than that in non-HTN patients (N = 10 079 358), 0.05%, $P < .0001$ (Table 2). Patients with VWD having HTN were more likely to be older, 67.55 versus 47.29 years, Caucasian, 69.76% versus 66.96%, and male, 45.99% versus 34.90%, as compared with patients with VWD not having HTN, all $P < .0001$.

Those patients with VWD having HTN were also more likely to be admitted with CVD or CKD and had longer lengths of stay and higher inpatient mortality than those with VWD not having HTN, all $P < .0001$. Patients with HTN were more likely than those without HTN to have HTN-associated risk factors, including hyperlipidemia, diabetes, obesity, smoking, and liver disease, all $P < .0001$ (Table 2). The exceptions were hepatitis C and HIV, which were less common in VWD with HTN, $P < .0001$. Patients with VWD having HTN were also more likely than those without HTN to have HTN-associated outcomes, including ASHD, angina, MI, ischemic stroke, hemorrhagic stroke, renal failure, hematuria, and proteinuria, all $P < .0001$ (Table 2). Similar findings in age and race were observed separately, among males and females.

Univariate and Multivariate Analyses of HTN and HTN Outcomes

In univariate logistic regression analysis, the odds of HTN were significantly lower in patients with VWD than those without VWD, OR = 0.611 (confidence interval [CI] 0.583-0.640), $P < .0001$, and of HTN outcomes (ASHD, OR = 0.509; MI, OR = 0.422; ischemic stroke, OR = 0.521; renal failure, OR = 0.420), all $P < .0001$ (Table 1). In multivariate logistic regression, these findings persisted after adjustment for HTN risk factors (hyperlipidemia, diabetes, obesity, smoking, hepatitis C, HIV; model 1), $P < .0001$. However, after adjustment for HTN risk factors and demographics (age, race, gender; model 2), the odds ratio for HTN was no longer significant, OR = 1.035 (0.975-1.100), $P = .264$ (Table 3). We also show the unadjusted prevalence of HTN in males (56.3%) was significantly different from that in females (44.8%), $P < .0001$, which was no longer significant after adjustment for the prevalence of HTN and HTN risk factors (hyperlipidemia, diabetes, obesity, smoking, hepatitis C, and HIV) and demographics (age, race, gender; Table 4).

Discussion

This cross-sectional study of the NIS cohort based on *ICD* codes and representing a 20% sample of inpatient discharges in the United States shows a 24% lower prevalence of HTN in those with VWD than in those without VWD, which is associated with a significantly lower risk of HTN risk factors (hyperlipidemia, diabetes, obesity, smoking, and HIV) and a significantly lower risk of HTN outcomes (ASHD, angina, MI, ischemic stroke, and renal failure) than those without VWD (Table 1). Although these findings suggest VWD may protect against HTN, the difference that we found does not necessarily allow a conclusion of association between VWD and HTN for several reasons. First, the apparent difference in the frequency of HTN is due to the differences in age, race, gender, and race/ethnicity. For example, HTN is more common in older people and the individuals with VWD having HTN are on average older, 67.55 years, than those without HTN, 47.29 years. Second, this study was a comparison between discharged patients with VWD and discharged patients with other diagnoses, the latter of whom may not have been a random sample from the population. Third, since blood pressure is unlikely to have contributed to admission for patients with VWD, causality cannot be established.

Although studies have shown a low risk of HTN and cardiovascular risk in animals with VWD,[14] the few published clinical studies to date are potentially biased by small sample size and lack of adjustment for HTN-associated risk factors. As HTN is unlikely to be an admitting diagnosis, an inpatient sample analysis may not necessarily resolve this problem. Optimally, an outpatient sample if rigorously collected might help in this analysis, but, unfortunately, with the recognized age-associated increase in VWF,[20,21] it is possible that older patients with VWD, in whom HTN might be expected, might not be identified.

Although HTN and HTN-associated outcomes may be lower in those with VWD than the general population without VWD, it remains unknown whether a certain VWF level, genotype, or VWD subtype is protective. Future studies are needed to determine the degree, if any, to which VWF protects against HTN and associated outcomes, and to consider, if findings confirm VWF protection, the potential utility of reducing VWF to help control HTN and associated cardiovascular morbidity.

There are several other limitations to this study. First, the use of inpatient discharge data may miss patients who are healthier and have not required admission. Secondly, the NIS represents only 20% of the total inpatient population, but the use of discharge-level weights allowed the determination of nationally representative estimates. Third, discharge diagnoses require coding, which is limited by coding accuracy. As this is a cross-sectional study, it is subject to potential bias and not able to determine causality. Fourth, the NIS database contains no laboratory variables and, thus, it was not possible to determine whether a specific VWF level, genotype, or VWD subtype is protective against HTN or CVD. Finally, because VWD is a rare disease, the pool of patients is limited, and outcomes might be biased; however, the large sample size of this NIS database is a major strength enabling analyses of rare diseases such as VWD.

In summary, the findings of this study of the NIS sample indicate that while the prevalence and risk of HTN are decreased in patients with VWD in unadjusted analysis and after adjustment for HTN risk factors (hyperlipidemia, diabetes, obesity, smoking, hepatitis C, HIV), when the analyses

Table 2. Prevalence of Risk Factors for HTN in Patients With VWD.

	All Discharges			Adult Male Discharges			Adult Female Discharges		
	HTN	No HTN		HTN	No HTN		HTN	No HTN	
	Percent or Mean (SE)	Percent or Mean (SE)	*P* Value[a]	Percent or Mean (SE)	Percent or Mean (SE)	*P* Value[a]	Percent or Mean (SE)	Percent or Mean (SE)	*P* Value[a]
No. of admissions (weighted)	9 847 168 (48 765 780)	10 079 358 (49 958 459)	–	4 528 857 (22 426 816)	3 499 805 (17 399 448)	–	5 317 053 (26 332 962)	6 559 102 (32 459 349)	–
No. VWD, raw (weighted)	2823 (13 974)	4733 (23 440)	–	882 (4364)	975 (4823)	–	1940 (9606)	3757 (18 613)	–
% VWD	0.03	0.05	<.0001	0.02	0.03	<.0001	0.04	0.06	<.0001
Age (years)	67.55 (0.005)	47.29 (0.01)	<.0001	65.59 (0.01)	53.65 (0.01)	<.0001	69.22 (0.01)	43.90 (0.01)	<.0001
Sex (male)	45.99	34.9	<.0001						
Race/ethnicity									
White	69.76	66.96	<.0001	70.36	71.25	<.0001	69.25	64.67	<.0001
Black	16.94	13.14		16.04	12.70		17.7	13.38	
Hispanic	8.12	12.99		8.21	10.15		8.04	14.51	
Asian	1.95	2.58		1.99	1.77		1.91	3.01	
Native American	0.60	0.76		0.60	0.71		0.6	0.79	
Other	2.64	3.56		2.80	3.42		2.5	3.64	
Admission for CVD	3.52	0.90	<.0001	4.80	1.72	<.0001	2.43	0.46	<.0001
Admission for CKD	1.01	0.03	<.0001	1.15	0.05	<.0001	0.89	0.02	<.0001
Length of stay (days)	5.12 (0.002)	4.42 (0.002)	<.0001	5.17 (0.003)	5.29 (0.004)	<.0001	5.08 (0.003)	3.97 (0.002)	<.0001
Inpatient mortality	2.38	2.02	<.0001	2.51	3.06	<.0001	2.27	1.46	<.0001
HTN risk factors									
Hyperlipidemia	41.53	10.02	<.0001	43.82	14.32	<.0001	39.58	7.75	<.0001
Diabetes	36.45	10.68	<.0001	37.72	14.67	<.0001	35.37	8.57	<.0001
Obesity	13.44	6.60	<.0001	11.74	5.38	<.0001	14.89	7.28	<.0001
Smoke	11.31	5.51	<.0001	14.05	8.11	<.0001	8.98	4.13	<.0001
Hepatitis C	1.74	1.85	<.0001	2.42	3.24	<.0001	1.16	1.11	<.0001
Liver disease	0.85	0.73	<.0001	0.88	1.00	<.0001	0.82	0.59	<.0001
HIV	0.59	0.93	<.0001	0.84	1.77	<.0001	0.38	0.48	<.0001
HTN outcomes									
ASHD	30.82	8.49	<.0001	37.59	15.00	<.0001	25.06	5.03	<.0001
Angina	1.27	0.34	<.0001	1.48	0.55	<.0001	1.1	0.22	<.0001
MI	7.25	1.97	<.0001	9.14	3.50	<.0001	5.64	1.16	<.0001
Ischemic stroke	4.73	1.25	<.0001	4.98	1.86	<.0001	4.52	0.93	<.0001
Hemorrhagic stroke	0.81	0.33	<.0001	0.90	0.49	<.0001	0.73	0.25	<.0001
Renal failure	21.75	3.12	<.0001	24.63	5.05	<.0001	19.3	2.09	<.0001
Hematuria	1.31	0.84	<.0001	1.96	1.50	<.0001	0.76	0.49	<.0001
Proteinuria	0.40	0.23	<.0001	0.37	0.25	<.0001	0.43	0.22	<.0001

Abbreviations: ASHD, atherosclerotic heart disease; CKD, chronic kidney disease; CVD, cardiovascular disease; HTN, hypertension; MI, myocardial infarction; SE, standard error; VWD, von Willebrand disease.
[a]Rao-Scott χ^2 test.

Table 3. Unadjusted and Adjusted Odds for HTN and HTN Outcomes in Adults With and Without VWD.

	Unadjusted		Adjusted			
			Model 1[a]		Model 2[b]	
Outcome	OR (95% CI)	*P* Value	aOR (95% CI)	*P* Value	aOR (95% CI)	*P* Value
Hypertension	0.611 (0.583-0.64)	<.0001	0.737 (0.7-0.776)	<.0001	1.035 (0.975-1.1)	.2604
ASHD	0.509 (0.473-0.547)	<.0001	0.616 (0.571-0.664)	<.0001	0.846 (0.777-0.921)	.0001
Angina	0.623 (0.453-0.856)	.0036	0.763 (0.554-1.052)	.0985	0.894 (0.637-1.255)	.5186
MI	0.422 (0.359-0.497)	<.0001	0.512 (0.435-0.603)	<.0001	0.64 (0.538-0.761)	<.0001
Ischemic stroke	0.521 (0.435-0.623)	<.0001	0.599 (0.499-0.719)	<.0001	0.708 (0.579-0.865)	.0007
Hemorrhagic stroke	1.067 (0.798-1.427)	.6601	1.087 (0.813-1.454)	.5732	1.124 (0.793-1.594)	.5102
Renal failure	0.42 (0.38-0.463)	<.0001	0.499 (0.452-0.551)	<.0001	0.709 (0.637-0.789)	<.0001
Hematuria	1.248 (1.022-1.524)	.0299	1.291 (1.058-1.577)	.0121	1.844 (1.5-2.267)	<.0001
Proteinuria	0.635 (0.376-1.074)	.0904	0.695 (0.41-1.177)	.1757	0.761 (0.44-1.316)	.3289

Abbreviations: aOR, adjusted odds ratio; ASHD, atherosclerotic heart disease; CI, confidence interval; HTN, hypertension; MI, myocardial infarction; OR, odds ratio; VWD, von Willebrand disease.
[a]Adjusted for HTN risk factors: hyperlipidemia, diabetes, obesity, smoking, hepatitis C, HIV.
[b]Adjusted for HTN risk factors (model 1) and demographics (age, sex, race).

Table 4. Unadjusted and Adjusted Prevalence of HTN in Adults With and Without VWD.[a]

	Unadjusted	Adjusted (Model 2)[b]
Overall	49.4%	49.1%
Female	44.8%	47.0%
Male	56.3%	52.4%

Abbreviations: HTN, hypertension; VWD, von Willebrand disease.
[a]The unadjusted prevalence was significantly different by gender, $P < .0001$. This was no longer significant after adjustment.
[b]In the multivariable logistic model with VWD, HTN risk factors (hyperlipidemia, diabetes, obesity, smoking, hepatitis C, HIV), and demographics (age, race, gender) as independent variables.

were adjusted for demographics (age, race, gender), the prevalence and risk of HTN in patients with VWD were not different from those without VWD. The large size of this cross-sectional database analysis was critical in determining these findings. Whether a certain VWF level is protective against HTN and associated comorbidities must await future prospective study.

Authors' Note

M. Apostolova and M. Ragni contributed to the study design, acquisition of data, interpreted the data, and wrote the manuscript. C. Seaman contributed to the study design, interpreted the data, and critically reviewed the manuscript. D. Comer contributed to the acquisition of data, performed the data analysis, and critically reviewed the manuscript. J. Yabes contributed to the study design, acquisition of data, performed the data analysis, and critically reviewed the manuscript. The data set and analysis of the selected years from the NIS can be obtained by contacting the corresponding author, Dr Margaret V. Ragni, ragni@pitt.edu.

Declaration of Conflicting Interests

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