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Effect of Endovascular Treatment on Quality of Life in Patients with Recurrent Symptoms Associated with Vertebral, Subclavian, or Innominate Arterial Stenosis

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Abstract

Background—Patients with vertebral, subclavian, or innominate arterial stenosis can present with recurrent symptoms that can adversely affect the quality of life (QOL). We aimed at determining the short-term effects of endovascular treatment (ET) on QOL in these patients.

Methods—European Quality of Life Five Dimension Scale (EQ-5D) utility index and visual analog scale (VAS) were ascertained before and within one month of ET in patients with vertebral, subclavian, or innominate arterial stenosis with recurrent episodes of vertigo, near syncope, and/or ataxia. The EQ-5D utility scores were derived from responses to five questions on EQ-5D questionnaire (–0.109 for the least to 1 for most favorable). The EQ-5D VAS score was obtained by subject's indication of his/her health state on a scale of 0 (worst) to 100 (best).

Results—Angioplasty and/or stent placement was performed in 10 patients for stenosis in extracranial vertebral ($n = 6$), intracranial vertebral ($n = 1$), subclavian ($n = 2$), or innominate artery ($n = 1$). There was a significant reduction in preprocedure severity [mean ± standard deviation (SD)] of stenosis compared with postprocedure severity (79.9 ± 14.05% vs. 26.4 ± 37.7%, $p < 0.001$). There was a significant improvement in mean values of EQ-5D VAS postprocedure compared with preprocedure values (72 vs. 57.5, $p = 0.018$). Minimal important difference (improvement of at least 0.074) on EQ-5D utility index and on VAS (improvement ≥ 10 points) was reported by five and six of 10 patients, respectively.

Conclusions—Improvement in QOL appears to be an important measure of effectiveness of ET in patients with vertebral, subclavian, or innominate arterial stenosis with recurrent episodes of vertigo, near syncope, and/or ataxia.

Keywords

Vertebral artery stenosis; subclavian artery stenosis; innominate artery stenosis; vertigo; quality of life

INTRODUCTION

Recurrent positional vertigo and dizziness have been identified as a manifestation of steno-occlusive disease of vertebral and subclavian arteries although it may not meet the criteria of transient ischemic attack or minor stroke [1]. Previous studies have identified that recurrent vertigo related to vestibular dysfunction can negatively impact the patient's quality of life (QOL) [2] and reduction in symptoms can results in prominent improvement in psychological, emotional, and functional components of patient's QOL [3]. The American College of Cardiology Foundation/American Heart Association Task Force on Practice identified huge gaps in knowledge of vertebral arterial disease and recommended registries to ascertain data about prevalence, pathophysiology, natu-

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ral history, and prognosis [4]. The Task Force recommended that symptomatic patients should be considered for subclavian revascularization by use of endovascular or surgical techniques. No specific recommendations were made regarding treatment of extracranial vertebral artery stenosis. The American Heart Association/American Stroke Association guidelines consider stent placement as a treatment option for patients with extracranial vertebral artery stenosis when patients are having symptoms despite optimal medical treatment (Class IIb; Level of Evidence C) [5]. Class II recommendations are based on conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a treatment. Class IIb recommendation also highlights the need for additional studies with broad objectives. Treatment may be considered. There is inconclusive evidence that revascularization of extracranial vertebral or subclavian artery stenosis reduces the risk of ischemic stroke in affected distribution [6]. Another measure that has not been evaluated is improvement in QOL in patients with vertebral or subclavian artery stenosis after revascularization who present with recurrent symptoms that do not meet the definition of ischemic stroke. We performed this study to determine the short-term effects of endovascular treatment (ET) on QOL in patients with extracranial vertebral or subclavian artery stenosis, and to address some of the knowledge gaps identified in the current guidelines.

METHODS

The patients who underwent ET for extracranial vertebral, subclavian, or innominate artery stenosis at Mercyhealth Rockford hospital between May 2016 and June 2017 were included. The protocol for data collection as part of a standard database was approved by the local Institutional Review Board. Each patient had recurrent episodes of vertigo, near syncope, and/or ataxia. Patients in whom the presenting symptom was only ischemic stroke or transient ischemic attack were excluded.

ET was performed for stenosis of 70% or greater (including complete occlusions) and/or pressure gradient of 15 mm of greater between intraarterial pressures measured before and after stenotic segment. The severity of extracranial vertebral artery stenosis was quantitated by expressing the minimum lumen diameter as a fraction of reference normal distal vertebral artery as described previously [7]. The nondiseased portion of the sixth segment which extends classically from the subclavian artery to the transverse foramen of sixth cervical vertebrae was used as the reference artery for quantifying the stenosis. The severity of stenosis in subclavian and innominate arteries was measured by expressing the minimum lumen diameter as a fraction of diameter of reference nondiseased distal artery. The proximal nondiseased segment was used as a reference artery if no clear nondiseased segment in the distal portion could be identified as reference (in patients with innominate stenosis).

All patients provided written informed consent prior to the procedure. Patients with any of the following characteristics or conditions were not treated: (1) history of bleeding diathesis, including disorders treated with warfarin therapy (however, patients who had been administered warfarin but had stopped taking the medication three days before the procedure and had an international normalized ratio of less than 1.2 were eligible for treatment) and (2) patients undergone major surgery, with previous hemorrhagic stroke, pregnancy or lactation, or gastrointestinal or genitourinary bleeding within the previous 30 days. Patients were administered aspirin (325 mg daily) and clopidogrel (75 mg daily) orally starting at least three days before the procedure. If clopidogrel could not be initiated three days before the procedure, a loading dose of 300 mg was administered.

All procedures were performed with conscious sedation using a combination of intravenous midalozam and fentanyl. Arterial access was established from either the femoral or radial arterial approach using a 6 to 8 F introducer sheath. Intravenous heparin bolus of 50 U per kilogram was administered. A balloon expandable stent was placed using standard techniques. Primary angioplasty and pre- and post-stent placement angioplasty were performed as required. All patients underwent a neurological examination before 24 hours postprocedure, and at 1–3 months follow-up clinic visit by a board-certified neurologist.

Each patient was retrospectively asked at follow-up postprocedure visit to complete the European Quality of Life Five Dimension Five Level Scale (EQ-5D-5L) [8] questionnaire regarding five questions on mobility, self-care, usual activities, pain/discomfort, and anxiety/depression). Each patient completed two questionnaires to represent assessment before and within one month of the procedure. The patients were asked to choose one response (no problems, slight problems, moderate problems, severe problems, or extreme problems) for each of the five domains. The resulting response was a 1-digit number expressing the level selected for that dimension. Levels 1, 2, 3, 4, and 5 of increasing severity were coded as a "1," "2," "3," "4," and "5". The responses for the five dimensions were combined in a five-digit number describing the respondent's health state (from "11111"

meaning no problems at all to "55555" meaning extreme problems in all five dimensions) [9]. These 3125 possible health states, as defined by the EQ-5D-5L descriptive system, were converted into a corresponding single country specific index value. The EQ-5D utility index [10] ranges from –0.109 for the least favorable health state to 1 for most favorable state. Currently, the value sets for directly deriving index values from EQ-5D-5L health states are not available. The index value sets were derived models generated from the EuroQol Group coordinated study across six countries (Denmark, England, Italy, Netherlands, Poland, and Scotland). The models convert response patterns of EQ-5D health states into a single summary index by applying a formula that attaches weights to each of the response levels in each dimension as described by Shaw et al. [8].

We also determined the European QOL Visual Analog Scale (VAS) [11] before and within one month of the procedure. The EQ-5D VAS score was obtained by requesting the subject to indicate their own perception of his/her health state on a scale of 0 (worst) to 100 (best) labeled as endpoints labeled "the best health you can imagine" and "the worst health you can imagine" [11–13].

The analysis was predominantly descriptive with continuous variable and categorical variables expressed as either mean with SD and frequencies, respectively. We compared mean values using paired sample *t*-test using IBM SPSS statistical software (IBM Corp., Armonk, NY, USA) Version 20. The mean values of EQ-5D utility index and VAS were compared before and after the procedure. The primary outcome for analysis was a minimal important difference or more in the EQ-5D utility index defined as an improvement of at least 0.074 [14,15] compared with the preprocedure EQ utility index value. We also ascertained the minimal clinically significant difference in EQ-VAS, defined by an improvement of 10 points or greater, as used in the previous studies [16].

RESULTS

Angioplasty and stent placement were attempted in 12 patients (mean age 61.9 years; six were men) with extracranial or intracranial vertebral, subclavian, or innominate artery stenosis. In two patients, one with complete occlusion of left subclavian artery and another with occlusion of right extracranial vertebral artery, revascularization was unsuccessful. In a total of 10 patients, angioplasty and/or stent placement was performed for stenosis located in extracranial vertebral (n = 6), intracranial vertebral (n = 1), subclavian (n = 2), or innominate artery (n = 1). Table 1 provides the clinical and procedural characteristics of the patients. The procedure was performed from femoral, radial accesses, and with both femoral and radial access in 9, 1, and 2 patients, respectively. The mean preprocedure stenosis (±SD) was 79.9% (±14.05%) and postprocedure stenosis was 26.4% (±37.7) ($p < 0.001$). Eight patients were treated with balloon expandable stents and two patients underwent primary angioplasty. Pre- or post-stent angioplasty was performed in one of the eight patients. In one patient with extracranial vertebral artery occlusion which extended into the intracranial segment, primary angioplasty was performed. The total days of hospitalization ranged from 0–3 days with seven of 12 patients being discharged to home on the day of the procedure.

The pre- and post-procedure EQ-5D utility index and VAS scores for each of the patient are presented in Table 2. Among the 10 patients with successful revascularization, eight reported improvement in EQ-5D utility index and six reported improvement in VAS. There was a non-significantly higher mean value for EQ-5D utility index postprocedure (mean ± SD) (0.777 ± 0.11) compared with preprocedure values (0.733 ± 0.15, p = 0.3) in 10 patients with successful revascularization. There was a significant improvement in mean values of EQ-5D VAS postprocedure (mean ± SD) (72 ± 15.31) compared with preprocedure values (57.5 ± 21.51, p = 0.018). Minimal important difference on EQ-5D utility index was reported by five of 10 patients and minimal important difference on VAS was reported by six of 10 patients who underwent ET. One patient reported no change in either EQ-5D utility index or VAS postprocedure and one reported no chance in the VAS score, however, reported minimal important difference in EQ-5D utility index.

The individual change in each of the components of EQ-5D utility index is provided in Table 2. Patients who reported an improvement in EQ-5D utility index postprocedure reported improvement in mobility (n = 7), selfcare (n = 3), usual activities (n = 3), pain/discomfort (n = 5), and anxiety/depression (n = 6). Two patients reported worsening in EQ-5D utility index postprocedure. One patient who underwent right extracranial vertebral artery stent placement and did not report improvement had a large thrombosed basilar artery aneurysm with basilar artery occlusion. Therefore, the component of patient's symptoms related to local aneurysmal mass effect and basilar artery occlusion and not amenable to revascularization was not clear.

There was no difference in mean value of VAS postprocedure compared with preprocedure values in two

Table 1. Baseline and clinical characteristics and procedure details of patients

	Age/ gender	Cardiovascular risk factors	Recurrent symptoms	Additional symptoms	Location of the lesion	Preprocedure stenosis	Stent/balloon used	Postprocedure stenosis	Duration of hospitalization (days)
1	59/M	HTN	Ataxia	Dysarthria, right hemiparesis, hemisensory deficits	Right vertebral artery	65%	RX Herculink Elite Renal and Biliary Stent System 6.0 × 15 mm Abbott Vascular, CA, USA	0%	2
2	76/F	HTN, HLD, DM	Ataxia	Left hemiparesis	Right subclavian artery	80%	Omnilink Elite Vascular Balloon Expandable Stent System 7.0 mm × 59 mm (OTW) Abbott Vascular, CA, USA	0%	3
3	66/M	HTN, HLD, DM, CS	Vertigo and ataxia	Dysarthria	Right vertebral artery	65%	RX Herculink Elite Renal and Biliary Stent System 6.0 × 15 mm × 135cm Abbott Vascular, CA, USA	0%	3
4	56/M	HTN, CS	Vertigo and ataxia	Dysarthria	Left vertebral artery	60%	RX Herculink Elite Renal and Biliary Stent System 6.0 × 15 mm Abbott Vascular, CA, USA	0%	1
5	45/M	HTN, CS	Vertigo and ataxia	Dysarthria	Right innominate artery	80%	Omnilink Elite Vascular Balloon Expandable Stent System 7.0 mm × 59 mm (OTW) Abbott Vascular, CA, USA	0%	0
6	81/F	HLD	Ataxia	Visual obscuration	Left vertebral artery (intracranial)	84%	Boston Scientific Gateway (OTW) PTA Balloon Catheter 2.5 mm × 15 mm Legal Manufacturer, MA, USA	36%	0
7	83/F	HTN	Ataxia	None	Left vertebral artery	75%	RX Herculink Elite Renal and Biliary Stent System (Cobalt Chromium) 6.0 × 15mm Abbott Vascular, CA, USA	10%	1
8	51/M	HTN, CS	Vertigo and ataxia	Right hemiparesis and hemisensory loss	Left vertebral artery	79%	Multilink Mini vision Coronary Stent System 3.5 mm × 15 mm Abbott Vascular, Ireland.	28%	0
9	76/F	None	Vertigo and ataxia	Nausea and vomiting	Right subclavian artery	71%	Omnilink Elite Vascular Balloon Expandable Stent System 9 mm × 29 mm (OTW) Abbott Vascular, CA, USA	0%	0
10	52/M	HTN HLD, DM	Vertigo and ataxia	Visual obscuration	Right vertebral artery (distal cervical segment)	100%	TREK Coronary Dilatation Catheter 3.0 mm × 20 mm, Abbott Vascular, El Coyol Alajuila, Costa Rica.	43%	0
11	50/F	CS	Vertigo and ataxia	Diplopia	Right vertebral artery	100%	NA	100%	0
12	48/F	HTN, HLD, CS	Vertigo and ataxia	Intermitted left upper extremity ischemic symptoms and horizontal diplopia	Left subclavian artery	100%	NA	100%	0

Abbreviations: HTN, hypertension; HLD, hyperlipidemia; CS, current cigarette smoker; DM, diabetes mellitus; NA, not applicable.

Table 2. The pre- and post-procedure EQ-5D utility index and VAS scores for each of the patients

Pt. no.	Procedural status	Mobility	Self care	Usual activities	Pain/ discomfort	Anxiety/ depression	VAS score	EQ-5D-5L 5L-profile	EQ-5D-5L index
1	Pre	Moderate	No	Slight	Slight	Moderate	70	31,223	0.735
	Post	Moderate	No	Slight	Slight	Slightly	80	31,222	0.748
2	Pre	Severe	No	No	No	Moderate	60–70	41,113	0.798
	Post	No	No	No	No	No	60–70	11,111	1.0
3	Pre	No	No	No	No	No	75	11,111	1.0
	Post	Slight	No	No	Moderate	No	75	21,131	0.813
4	Pre	Slight	No	Slight	Moderate	No	75	21,231	0.790
	Post	No	No	Severe	Slight	No	100	11,221	0.832
5	Pre	Slight	No	No	Moderate	Moderate	70	21,133	0.768
	Post	No	No	No	No	Slight	85	11,112	0.876
6	Pre	Moderate	Slight	No	Moderate	Moderate	50	32,133	0.627
	Post	Slight	No	Slight	Slight	Moderate	65	21,223	0.744
7	Pre	Severe	Slight	Moderate	Severe	Moderate	35	42,343	0.477
	Post	Moderate	No	Slight	Severe	Slightly	75	31,242	0.604
8	Pre	No	No	No	Severe	Moderate	75	11,143	0.659
	Post	No	No	No	Severe	Moderate	75	11,143	0.659
9	Pre	Moderate	Moderate	Moderate	Moderate	Moderate	10	33,333	0.597
	Post	Slight	Slight	Slight	Slight	No	50	22,221	0.738
10	Pre	Slight	No	No	No	No	50	21,111	0.880
	Post	Slight	Slight	Slight	No	Slight	50	22,212	0.751
11	Pre	Moderate	No	Moderate	Moderate	Moderate	50	31,333	0.708
	Post	No	No	No	No	No	100	11,111	1.0
12	Pre	Slight	No	Slight	Slight	Slight	70	21,222	0.708
	Post	Slight	No	Slight	No	Slight	70	21,212	0.794

Abbreviations: VAS, visual analog scale.

patients in whom ET was unsuccessful. However, one of two patients reported improvement in pain/discomfort with a minimal important difference in the EQ-5D utility index of 0.086.

DISCUSSION

We identified short-term improvement in QOL measures in patients who had recurrent episodes of vertigo, near syncope, and/or ataxia and underwent ET for vertebral, subclavian, or innominate artery stenosis. Such measures have not been investigated in previous studies in this patient population [6,17,18]. Previous studies have focused on ascertaining vascular death, myocardial infarction, stroke in the supply territory of the symptomatic vertebral artery, or any stroke [6,17,18]. The number of events in both patients were treated with stent and those treated with medical treatment have been small to determine any conclusive benefit of ET in the previous studies [6,17]. The patient population in our study could be different from patients recruited in the previous clinical trials because each patient had recurrent episodes of vertigo, near syncope, and/or ataxia, symptoms which may or may not meet the inclusion criteria of minor ischemic stroke or transient ischemic attack required in the previous trials. Therefore, the selected patient population may be more likely to demonstrate a benefit in QOL measures rather than reduction in rate of recurrent ischemic stroke.

QOL assessment has gained more importance in recent years due to relative insensitivity of other existing scales to detect smaller changes with direct relevance to patient's psychosocial and physical well-being [19,20]. Any intervention with beneficial effects on patients' daily functioning, subjective health, and well-being independent of prevention of new events is still highly relevant [16,21,22]. QOL has been integrated in cost effectiveness study pertaining to stroke and stroke-related interventions due to such importance [23–25]. Previous studies have assessed the QOL in patients undergoing carotid enarterectomy and carotid stent placement [26]. An analysis of 12 studies (4224 patients) identified a decline in QOL measures followed by return to pre-

treatment values 1 year after carotid endarterectomy [26]. A smaller analysis of patients undergoing carotid stent placement demonstrated no initial decline in QOL measures, but no difference at 1 year in a comparison between carotid endarterctomy and carotid stent placement. The comparison of health-related QOL measures in the Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy trial demonstrated that patients treated with carotid stent placement (compared with carotid endarterectomy) had better scores at two weeks, but there were no differences at 1-month follow-up assessment [27].

We used EQ-5D utility index and VAS for assessment of QOL, both of which have been extensively evaluated in stroke survivors[28,29]. The three-level version (now called EQ-5D-3L) was initially introduced [30] followed by a 5-level version of the EQ-5D-5L to improve the sensitivity and other psychometric properties of the EQ-5D-3L [31]. A previous study demonstrated a low level of missing values, establishing known-groups validity of EQ-5D-5L and also, improved discriminatory power and improved convergent validity when compared with EQ-5D-3L [32]. Responsive, defined as ability to detect clinically important changes within individuals before and after a therapeutic intervention, has been validated for both EQ-5D-5L and VAS in a previous study [33]. All the patients in our study completed their own assessment which limited the bias introduced by proxy assessment identified in the previous studies [34].

The results of our study should be interpreted with certain considerations. The number of patients was small and therefore, a larger number will be required for a definitive assessment. The EQ-5D utility index and VAS were assessed at one month postprocedure; and thus, are not representative of long term outcomes. Since the EQ-5D utility index and VAS were ascertained retrospectively, the ascertainment are subject to recall bias meaning that patients remember their former state as better or worse than it actually was and thus, confound the magnitude of change [35,36]. The influence of current state (whether patient feels well at time of assessment) may lead the patient to magnify the magnitude of change by negatively rating the retrospective assessment of preprocedure state. There was no control population and the magnitude of benefit with medical treatment alone is not quantified. Another issue that should be recognized that vertigo, near syncope, and/or ataxia can occur from multiple and overlapping etiologies and therefore, may not always be responsive to ET and subsequent improvement in regional cerebral blood flow.

Therefore, the data is preliminary but supports the ascertainment of QOL measures in addition to the previously used clinical endpoints in patients who had recurrent episodes of vertigo, near syncope, and/or ataxia and underwent ET for vertebral, subclavian, or innominate artery stenosis.

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