Clinical Profile and Management Outcomes among Patients with Carotid-Cavernous Fistula

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ABSTRACT

Background. A carotid-cavernous sinus fistula (CCF) is an abnormal communication between the internal carotid artery and/or the external carotid artery and the cavernous sinus. There is a paucity of information on the ophthalmic outcomes of endovascular treatment for CCF in the Philippines.

Objectives. This study aimed to describe the clinical experience of CCF in our institution in order to further our understanding of the disease. This study described the demographic profile, risk factors, and clinical features of patients with CCF, and compared the data of patients according to the type of CCF. The study discussed the changes in clinical features over time in CCF patients who chose not to undergo endovascular treatment. The study also discussed the clinical outcomes of CCF patients who underwent endovascular treatment and compared the clinical outcomes to CCF patients who did not undergo endovascular treatment.

Methods. A retrospective cohort study design was performed using a medical record review of patients clinically diagnosed with CCF from January 2011 to June 2019.

Results. One hundred twenty medical records of patients diagnosed with CCF were included. Based on angiographic findings, patients were grouped according to type of CCF, with 86 patients in Group 1 or Direct CCF, 23 patients in Group 2 or Indirect CCF, and 11 patients in Group 3 or Mixed type of CCF. The patients were also grouped according to treatment, with 109 patients in Group A, or patients who did not undergo endovascular treatment, and 11 patients in Group B, or patients who underwent endovascular treatment. There was a male predominance in CCF, most occurring in the age range of 26 to 35 years. Risk factors for CCF were trauma and hypertension. Clinical features included the presence of blurring of vision, proptosis, corkscrewing of conjunctival vessels, extraocular movement limitation, diplopia, audible bruit, elevated intraocular pressure, and pulsation. Findings on Computed Tomography scan included dilated superior ophthalmic vein, proptosis, and enlarged extraocular muscles. Direct CCF (Group 1) occurred mostly in males, with mean age of 39.1 years, and with trauma as the major risk factor. Indirect CCF (Group 2) occurred mostly in females, with mean age of 52.1 years, and with hypertension as the major risk factor. Regardless of the type of CCF, patients who did not undergo endovascular treatment can exhibit spontaneous improvement or worsening of clinical features. Patients who underwent endovascular treatment generally had favorable clinical outcomes, manifesting as either improvement or no worsening of features. There were minimal ophthalmic complications associated with treatment.

Conclusion. Endovascular treatment is safe and effective in the improvement of visual acuity, corkscrewing of conjunctival vessels, amount of proptosis, extraocular movement limitation, diplopia, and presence of audible bruit.

Keywords: carotid-cavernous fistula, direct carotid-cavernous fistula, indirect carotid-cavernous fistula, treatment outcomes in carotid-cavernous fistula

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INTRODUCTION

A carotid-cavernous sinus fistula (CCF) is an abnormal communication between the internal carotid artery (ICA) and/or the external carotid artery (ECA) and the cavernous sinus. Classification is based on etiology (spontaneous or traumatic), hemodynamic characteristics (high- or low-flow), and anatomic characteristics (direct or indirect).[1-3]

Direct CCFs are high-flow shunts with direct connections between the ICA and the cavernous sinus.[4] Common causes include blunt trauma, ruptured ICA aneurysm, Ehlers-Danlos Syndrome, and iatrogenic interventions.[5,6]

Indirect CCFs are low-flow shunts with connections between the cavernous arterial branches of the ICA and/or the ECA and the cavernous sinus. Hypertension, Ehlers-Danlos Type IV, fibromuscular dysplasia, dissection of the ICA and a post-menopause state are known risk factors for indirect fistulas.[1]

Dandy's triad of bruit, proptosis, and conjunctival chemosis are the most common signs of direct and indirect CCF. Patients with CCF can also experience diplopia, headache, and blurring of vision, caused by the increase in intra-cavernous pressure.[1,3,7] Other findings on physical examination include: corkscrewing of conjunctival vessels, extraocular movement limitation, color deficit, relative afferent pupillary defect, optic nerve anatomical changes, fundus changes, pulsatile bruit, and elevated intraocular pressure (IOP).[3,5,8,9] The clinical presentation of direct fistulas appears more acutely, compared to the indolent presentation of indirect fistulas.[3]

Radiologic imaging is essential in correctly diagnosing CCF and in recommending the appropriate treatment.[10] Radiologic findings of CCF on both computed tomography (CT) and magnetic resonance imaging (MRI) include superior ophthalmic vein dilation, cavernous sinus enlargement, proptosis, and extraocular muscle enlargement.[10-12] The gold-standard imaging modality in the diagnosis of CCF is cerebral angiography.[10]

Treatment options for CCF include manual external carotid compression (MECC), endovascular treatment, and surgery. Ophthalmic indications for recommending treatment include glaucoma, diplopia, intolerable bruit or headache, retinal ischemia, progressive loss of vision, and severe proptosis causing exposure keratopathy.[8]

The role of ophthalmologists in the management of CCF is vital to avoid irreversible complications of visual loss, such as in secondary glaucoma when topical anti-glaucoma medications should be promptly initiated.[3] Ophthalmologists also monitor the status of proptosis, corneal surface exposure, optic nerve damage, and retinal damage.[3]

This study described the clinical experience of CCF in the Philippine General Hospital Department of Ophthalmology and Visual Sciences (PGH DOVS) in order to further our understanding of the disease. Many of subjects in this study chose not to undergo endovascular treatment due to financial reasons. This study described the demographic profile, risk factors, and clinical features of patients with CCF, and compared the data of patients according to the type of CCF. The study discussed the changes in clinical features over time in CCF patients who chose not to undergo endovascular treatment. The study also discussed the clinical outcomes of CCF patients who underwent endovascular treatment and compared the clinical outcomes to CCF patients who did not undergo endovascular treatment.

METHODS

Study Design

The study was conducted in full conformance with the principles of the Declaration of Helsinki and Good Clinical Practice. The research protocol was reviewed and approved by the ethics board of the study site. Identities and information of patients were kept anonymized and confidential. A waiver of informed consent was approved by the ethics board because the research presented no more than minimal risk and does not involve interventions for which informed consent is required. The investigators declared no conflicts of interests.

A retrospective cohort study design was used by conducting a medical record review of patients who were initially seen in PGH DOVS Orbit Clinic from January 2011 to June 2019, diagnosed clinically with CCF, and had not undergone treatment on initial consult. The diagnosis of CCF was confirmed by imaging and angiographic studies. Subjects with angiographically confirmed CCF were referred to the PGH Department of Radiology for possible endovascular treatment. Subjects who did not receive endovascular treatment were followed up at least once over a period of 3 to 6 months. Subjects who received endovascular treatment were followed up 1 week, 1 month, 3 months, and 6 months after treatment. A patient data sheet was accomplished for each patient by one of the investigators.

Classifications

Patients were divided into two groups, namely: Group A for those who did not receive endovascular treatment for CCF, and Group B for those who received endovascular treatment for CCF. As part of the standard management of CCF in the Orbit Clinic, all patients were assumed to have been instructed to do manual external carotid compression.

Groups A and B were further subdivided into three groups, based on the affected vessels on cerebral angiography, and on the anatomic classification of Barrow.[2] Group 1 subjects were Direct CCF or Type A fistulas that arise directly from the ICA. Group 2 subjects were Indirect CCF, either Type B fistulas involving meningeal branches of the ICA or Type C fistulas involving meningeal branches of the ECA. Group 3 subjects were Indirect CCF with Type D fistulas involving meningeal branches of both ICA and ECA.

On each consult, patient data were tabulated into 6 groups. Group A-1 included patients with Direct CCF who did not undergo endovascular treatment. Group A-2

included patients with Indirect CCF who did not undergo endovascular treatment. Group A-3 included patients with Mixed type of CCF who did not undergo endovascular treatment. Group B-1 included patients with Direct CCF who underwent endovascular treatment. Group B-2 included patients with Indirect CCF who underwent endovascular treatment. Group B-3 included patients with Mixed type CCF who underwent endovascular treatment.

Characteristics

A patient data sheet was used to record the age, gender, laterality, chief complaint, and risk factors, like hypertension, diabetes mellitus, pregnancy, and trauma. Information on radiologic imaging was retrieved from the radiology reports found in the medical case records.

Clinical Features and Outcome Measures

CCF can present with various clinical features in the eye that reflect the impact of abnormal blood flow and venous congestion in the orbit. Monitoring changes in these clinical features is crucial for timely diagnosis, assessment, and management of disease progression, and assessment of clinical outcomes and treatment efficacy.

Visual acuity

Visual acuity refers to the clarity or sharpness of vision. CCF can cause changes in visual acuity and lead to visual impairment. The level of visual impairment can vary among patients with CCF.

All 120 patients underwent reading of a Snellen chart to report distance vision on each day of consult. The visual acuity for the affected eye or the worse eye (for bilateral cases) was assigned an equivalent logMAR score. In the patient data sheet, the best corrected visual acuity was classified as Good if vision was better than 0.5 logMar, Low if vision was equal to or between 0.5 logMar and 1.3 logMar, Blurring of Vision if vision was worse than 1.3 but equal to or better than light perception, and Loss of Vision if there was no light perception.

For statistical analysis, visual acuity was classified into two, namely: VA >0.4, indicating absence of good vision, and VA ≤0.4, indicating presence of good vision.

Corkscrewing of conjunctival vessels

The presence of corkscrewing conjunctival vessels gives the appearance of conjunctival hyperemia, and results from arterialization of the conjunctival and episcleral vessels. The abnormal flow of blood into the veins of the orbit leads to venous congestion and subsequent conjunctival vascular engorgement. The corkscrew appearance is due to the tortuosity and dilation of conjunctival vessels that extend to the limbus.

In the patient data sheet, corkscrewing of the conjunctival vessels was classified as Present if there were prominent, tortuous conjunctival vessels seen on gross eye examination, and classified as Absent if there were none.

Proptosis

Proptosis in CCF refers to the abnormal anterior displacement of the eye caused by congestion of orbital tissues due to dilation of the venous drainage of the orbit.

In the patient data sheet, proptosis was classified as Present if the measurement on Hertel exophthalmometer was more than 20 mm, or a difference of more than 2 mm between eyes (for bilateral cases), and classified as Absent if the measurement was equal to or less than 20 mm. The amount of proptosis was recorded as the difference in millimeters between eyes or the amount over 20 mm on the worse side for bilateral cases.

Elevated intraocular pressure

Elevated intraocular pressure (IOP) in CCF is the result of increased venous congestion in the orbit due to abnormal blood flow in the cavernous sinus. The arterialization of the conjunctival and episcleral vessels disrupts the normal balance of intraocular fluid dynamics, leading to elevated IOP.

Elevated IOP was defined as more than 21 mmHg measured on Goldmann applanation tonometry. All patients with elevated IOP on Initial Consult were started on anti-glaucoma medication. In the patient data sheet, the IOP was classified as Normal if measurement was equal to or less than 21 mmHg and not on anti-glaucoma medication, Controlled if measurement was equal to or less than 21 mmHg while on anti-glaucoma medication, Uncontrolled if measurement was more than 21 mmHg while on anti-glaucoma medication, and Untreated if measurement was more than 21 mmHg and not on anti-glaucoma medication.

For statistical analysis, intraocular pressure was classified into IOP <21 mmHg and IOP ≥21 mmHg, regardless of whether patients were on anti-glaucoma medication or not.

Extraocular movement limitation

Extraocular movement limitation in CCF results from mechanical compression or stretching of the oculomotor and abducens cranial nerves due to increased pressure in the cavernous sinus. The extent and pattern of extraocular movement limitation can vary and can manifest as limited eye abduction, elevation, or depression. Relieving mechanical compression on the cranial nerves can potentially improve extraocular movement limitation.

In the patient data sheet, extraocular movement limitation was classified as Present if there were abnormal findings on extraocular muscle function test, and classified as Absent if extraocular movement was full on all directions of gaze.

Diplopia

Diplopia in CCF is primarily attributed to extraocular movement limitation and misalignment of the eyes. Relieving mechanical compression on the cranial nerves and improving extraocular movement limitation can alleviate diplopia.

In the patient data sheet, diplopia was classified as Present if double vision on primary gaze was reported by the

subjects on extraocular muscle function test, and classified as Absent if double vision was not reported by the patient.

Audible bruit

Bruit refers to an abnormal whooshing or buzzing sound that occurs in synchrony with the pulse rate. Bruits can be heard by the patient or by the examiner during auscultation of periorbital blood vessels with a stethoscope. Bruit is caused by the turbulent blood flow within the abnormal communication between the carotid artery, or its branches, and the cavernous sinus.

In the patient data sheet, bruit was classified as Present if a vascular sound associated with turbulent blood flow was audible to the patient or heard by the examiner using a stethoscope, and classified as Absent if there was no vascular sound appreciated.

Pulsation

Pulsation in CCF refers to a pulsating rhythmic sensation that can be felt or observed in the periorbital area, and occurs in synchrony with the pulse rate, Pulsation results from the turbulence caused when the high-pressure arterial blood is shunted into the low-pressure venous system, producing pulsatile flow dynamics within the cavernous sinus that is transmitted to various structures in the orbit.

In the patient data sheet, pulsation was classified as Present when a thrill was palpable in the periorbital area, and was classified as Absent if there was no palpable thrill.

Statistical Analysis

The demographics, risk factors, clinical features, types of CCF, management options, and outcomes of treatment were organized in Table 1 and reported through descriptive statistics.

Data from the patient data sheet was organized into tables and categorized based on angiographic type and treatment type, specifically Groups A-1, A-2, A-3, B-1, B-2, and B-3. Clinical features and outcomes corresponding to the mentioned classification were recorded and summarized in Tables 2 to 11.

Tables 2-A to 10-A included data of the clinical features in Group A, who were patients who did not undergo endovascular treatment, on Initial Consult, 3 months Follow-up Consult, and 6 months Follow-up Consult. Because of the large drop-out rate in the 6 months Follow-up Consult, comparison of clinical features on Initial Consult and 3 months Follow-up Consult was done. The 2-tailed Mid-P Exact Test ($\alpha<0.05$) of openepi.com was used in Group A to determine improvement or worsening of clinical features during the 3 months Follow-up Consult.

Tables 2-B to 10-B included data of the clinical outcomes in Group B, who were patients who underwent endovascular treatment, on Initial Consult, 1 week Follow-up Consult, 1 month Follow-up Consult, 3 months Follow-up Consult, and 6 months Follow-up Consult. Results on 3 months Follow-up of patients in Group A, which served as the control, were compared to patients in Group B, and were tallied in

Table 1. Characteristics for CCFs

	Group A: Without treatment			Group B: With treatment		
	Group A-1 Direct	Group A-2 Indirect	Group A-3 Mixed	Group B-1 Direct	Group B-2 Indirect	Group B-3 Mixed
Number of subjects	82	19	8	4	4	3
***Average age** (years)*	39.5	50.7	33.5	31.8	58.5	51.3
Gender						
Male	51	3	6	2	0	1
Female	31	16	2	2	4	2
Laterality						
Right	34	6	3	3	1	2
Left	34	10	4	1	2	0
Bilateral	14	3	1	0	1	1
Risk factors						
None	7	1	1	0	0	1
Trauma	63	4	6	4	2	1
Hypertension	14	14	2	0	4	1
Pregnancy	1	1	1	0	0	0
Diabetes mellitus	5	4	0	0	2	0
Chief complaint						
Proptosis	47	8	6	2	1	1
Eye redness	20	5	1	1	3	0
Diplopia	6	2	0	1	0	1
Blurring of vision	3	1	1	0	0	1
Eyelid swelling	3	2	0	0	0	0
Eye pain	3	0	0	0	0	0
Upper lid mass	0	1	0	0	0	0

Table 2A. Visual Acuity in CCF without Endovascular Treatment

Visual Acuity in Group A	Initial Consult	Follow-up Consults		*p* (2-tail, α<0.05)
		3 months	6 months	
Group A-1: Direct	n = 82	n = 80	n = 49	0.7847
Good vision	56 (68.3%)	53 (66.2%)	34 (69.4%)	
Low vision	12 (14.6%)	15 (18.3%)	7 (14.3%)	
Blurring of vision	9 (11.0%)	6 (7.5%)	4 (8.2%)	
Loss of vision	5 (6.1%)	6 (7.5%)	4 (8.2%)	
Group A-2: Indirect	n = 19	n = 18	n = 17	0.5117
Good vision	14 (73.7%)	15 (83.3%)	15 (88.2%)	
Low vision	1 (5.3%)	0	1 (5.9%)	
Blurring of vision	3 (15.8%)	1 (5.6%)	0	
Loss of vision	1 (5.3%)	2 (1.1%)	1 (5.9%)	
Group A-3: Mixed	n = 8	n = 8	n = 5	0.6000
Good vision	7 (87.5%)	6 (75%)	4 (80%)	
Low vision	0	1 (12.5%)	1 (20%)	
Blurring of vision	0	0	0	
Loss of vision	1 (12.5%)	1 (12.5%)	0	

p-Value based on Mid-P Exact Test of initial consult and 3 months follow-up consult.

Table 2B. Visual Acuity in CCF with Endovascular Treatment

Visual Acuity in Group B	Before Treatment	After Treatment			
	Initial	1 week	1 month	3 months	6 months
Group B-1: Direct	n = 4	n = 4	n = 4	n = 4	n = 4
Good vision	3 (75%)	3 (75%)	3 (75%)	3 (75%)	3 (75%)
Low vision	1 (25%)	1 (25%)	1 (25%)	1 (25%)	1 (25%)
Blurring of vision	0	0	0	0	0
Loss of vision	0	0	0	0	0
Group B-2: Indirect	n = 4	n = 4	n = 4	n = 4	n = 4
Good vision	4 (100%)	4 (100%)	4 (100%)	4 (100%)	4 (100%)
Low vision	0	0	0	0	0
Blurring of vision	0	0	0	0	0
Loss of vision	0	0	0	0	0
Group B-3: Mixed	n = 3	n = 3	n = 3	n = 3	n = 3
Good vision	2 (66.7%)	2 (66.7%)	2 (66.7%)	2 (66.7%)	3 (100%)
Low vision	1 (33.33%)	0	0	0	0
Blurring of vision	0	1 (33.33%)	1 (33.33%)	1 (33.33%)	0
Loss of vision	0	0	0	0	0

Table 3A. Corkscrewing of Conjunctival Vessels in CCF without Endovascular Treatment

Corkscrewing of conjunctival vessels in Group A	Initial Consult	Follow-up Consults		*p* (2-tail, α<0.05)
		3 months	6 months	
Group A-1: Direct	n = 82	n = 80	n = 49	0.05721
Present	82 (100%)	76 (95%)	42 (85.7%)	
Absent	0	4 (5%)	7 (14.3%)	
Group A-2: Indirect	n = 19	n = 18	n = 17	0.9730
Present	18 (94.7%)	17 (94.4%)	15 (88.2%)	
Absent	1 (5.3%)	1 (5.6%)	2 (11.8%)	
Group A-3: Mixed	n = 8	n = 8	n = 5	0.5000
Present	8 (100%)	7 (87.5%)	5 (100%)	
Absent	0	1 (12.5%)	0	

p-Value based on Mid-P Exact Test of initial consult and 3 months follow-up consult.

Table 3B. Corkscrewing of Conjunctival Vessels in CCF with Endovascular Treatment

Corkscrewing of conjunctival vessels in Group B	Before Treatment	After Treatment			
	Initial	1 week	1 month	3 months	6 months
Group B-1: Direct	n = 4	n = 4	n = 4	n = 4	n = 4
Present	4 (100%)	4 (100%)	4 (100%)	4 (100%)	4 (100%)
Absent	0	0	0	0	0
Group B-2: Indirect	n = 4	n = 4	n = 4	n = 4	n = 4
Present	4 (100%)	2 (50%)	2 (50%)	2 (50%)	2 (50%)
Absent	0	2 (50%)	2 (50%)	2 (50%)	2 (50%)
Group B-3: Mixed	n = 3	n = 3	n = 3	n = 3	n = 3
Present	2 (66.7%)	2 (66.7%)	2 (66.7%)	2 (66.7%)	2 (66.7%)
Absent	1 (33.3%)	1 (33.3%)	1 (33.3%)	1 (33.3%)	1 (33.3%)

Table 4A. Proptosis in CCF without Endovascular Treatment

Proptosis in Group A	Initial Consult	Follow-up Consults		*p* (2-tail, α<0.05)
		3 months	6 months	
Group A-1: Direct	n = 82	n = 80	n = 49	**0.007881**
Present	70 (85.4%)	54 (67.5%)	31 (63.3%)	
Absent	12 (15%)	26 (32.5%)	18 (36.73%)	
Mean amount of proptosis (mm)	4.61	3.88	4.06	
Group A-2: Indirect	n = 19	n = 18	n = 17	0.2462
Present	16 (82.2%)	12 (66.7%)	11 (64.7%)	
Absent	3 (15.8%)	6 (33.3%)	6 (35.3%)	
Mean amount of proptosis (mm)	4.4	3.3	3.1	
Group A-3: Mixed	n = 8	n = 8	n = 5	0.5000
Present	8 (100%)	7 (87.5%)	4 (80%)	
Absent	0	1 (12.5%)	1 (20%)	
Mean amount of proptosis (mm)	5.9	4.4	6.2	

p-Value based on Mid-P Exact Test of initial consult and 3 months follow-up consult. Statistically significant p-values <0.05 in bold.

Table 4B. Proptosis in CCF with Endovascular Treatment

Proptosis in Group B	Before Treatment	After Treatment			
	Initial	1 week	1 month	3 months	6 months
Group B-1: Direct	n = 4	n = 4	n = 4	n = 4	n = 4
Present	4 (100%)	4 (100%)	3 (75%)	3 (75%)	3 (75%)
Absent	0	0	1 (25%)	1 (25%)	1 (25%)
Mean amount of proptosis (mm)	5.5	2.8	2	2	1.8
Group B-2: Indirect	n = 4	n = 4	n = 4	n = 4	n = 4
Present	4 (100%)	0	0	0	0
Absent	0	4 (100%)	4 (100%)	4 (100%)	4 (100%)
Mean amount of proptosis (mm)	3.8	0	0	0	0
Group B-3: Mixed	n = 3	n = 3	n = 3	n = 3	n = 3
Present	3 (100%)	1 (33.33%)	1 (33.33%)	1 (33.33%)	1 (33.33%)
Absent	0	2 (66.67%)	2 (66.67%)	2 (66.67%)	2 (66.67%)
Mean amount of proptosis (mm)	5.3	4	2	2	1.7

Table 5A. Elevated Intraocular Pressure in CCF without Endovascular Treatment

Elevated intraocular pressure in Group A	Initial Consult	Follow-up Consults		*p* (2-tail, α<0.05)
		3 months	6 months	
Group A-1: Direct	n = 82	n = 80	n = 49	**0.00005507**
Normal	19 (23.2%)	22 (27.5%)	18 (36.7%)	
Controlled	23 (28.0%)	43 (53.8%)	20 (40.8%)	
Uncontrolled	27 (32.2%)	12 (15%)	10 (20.4%)	
Untreated	13 (15.8%)	3 (3.8%)	1 (2.0%)	
Group A-2: Indirect	n = 19	n = 18	n = 17	0.6375
Normal	5 (26.3%)	3 (16.7%)	4 (23.5%)	
Controlled	4 (21.0%)	7 (38.9%)	7 (14.3%)	
Uncontrolled	9 (47.4%)	5 (27.8%)	5 (29.4%)	
Untreated	1 (5.26%)	3 (16.7%)	1 (5.9%)	
Group A-3: Mixed	n = 8	n = 8	n = 5	0.1000
Normal	3 (37.5%)	5 (62.5%)	2 (40%)	
Controlled	2 (25%)	3 (37.5%)	2 (40%)	
Uncontrolled	2 (25%)	0	0	
Untreated	1 (12.5%)	0	1 (20%)	

p-Value based on Mid-P Exact Test of initial consult and 3 months follow-up consult.
Statistically significant p-values <0.05 in bold.

Table 5B. Elevated Intraocular Pressure in CCF with Endovascular Treatment

Elevated intraocular pressure in Group B	Before Treatment	After Treatment			
	Initial	1 week	1 month	3 months	6 months
Group B-1: Direct	n = 4	n = 4	n = 4	n = 4	n = 4
Normal	0	1 (25%)	1 (25%)	2 (50%)	1 (25%)
Controlled	3 (75%)	3 (75%)	2 (50%)	2 (50%)	3 (75%)
Uncontrolled	1 (25%)	0	1 (25%)	0	0
Untreated	0	0	0	0	0
Group B-2: Indirect	n = 4	n = 4	n = 4	n = 4	n = 4
Normal	0	1 (25%)	1 (25%)	1 (25%)	1 (25%)
Controlled	2 (50%)	2 (50%)	3 (75%)	3 (75%)	2 (50%)
Uncontrolled	1 (25%)	1 (25%)	0	0	1 (25%)
Untreated	1 (25%)	0	0	0	0
Group B-3: Mixed	n = 3	n = 3	n = 3	n = 3	n = 3
Normal	3 (75%)	1 (33.3%)	1 (33.3%)	1 (33.3%)	2 (66.7%)
Controlled	1 (25%)	2 (66.7%)	2 (66.7%)	2 (66.7%)	1 (33.3%)
Uncontrolled	1 (25%)	0	0	0	0
Untreated	0	0	0	0	0

Table 6A. Extraocular Movement Limitation in CCF without Endovascular Treatment

Extraocular movement limitation in Group A	Initial Consult	Follow-up Consults		*p* (2-tail, α<0.05)
		3 months	6 months	
Group A-1: Direct	n = 82	n = 80	n = 49	**0.07197**
Present	63 (76.8%)	51 (63.8%)	23 (47.0%)	
Absent	19 (23.2%)	29 (36.2%)	26 (53.1%)	
Group A-2: Indirect	n = 19	n = 18	n = 17	0.2451
Present	9 (47.4%)	5 (27.8%)	4 (23.5%)	
Absent	10 (52.6%)	13 (72.2%)	13 (76.5%)	
Group A-3: Mixed	n = 8	n = 8	n = 5	0.6573
Present	4 (50%)	3 (37.5%)	1 (20%)	
Absent	4 (50%)	5 (62.5%)	4 (80%)	

p-Value based on Mid-P Exact Test of initial consult and 3 months follow-up consult.

Table 6B. Extraocular Movement Limitation in CCF with Endovascular Treatment

Extraocular movement limitation in Group B	Before Treatment	After Treatment			
	Initial	1 week	1 month	3 months	6 months
Group B-1: Direct	n = 4	n = 4	n = 4	n = 4	n = 4
Present	3 (75%)	1 (25%)	1 (25%)	1 (25%)	1 (25%)
Absent	1 (25%)	3 (75%)	3 (75%)	3 (75%)	3 (75%)
Group B-2: Indirect	n = 4	n = 4	n = 4	n = 4	n = 4
Present	4 (100%)	0	0	0	0
Absent	0	4 (100%)	4 (100%)	4 (100%)	4 (100%)
Group B-3: Mixed	n = 3	n = 3	n = 3	n = 3	n = 3
Present	3 (100%)	2 (66.7%)	2 (66.7%)	2 (66.7%)	2 (66.7%)
Absent	0	1 (33.3%)	1 (33.3%)	1 (33.3%)	1 (33.3%)

Table 7A. Diplopia in CCF without Endovascular Treatment

Diplopia in Group A	Initial Consult	Follow-up Consults		*p* (2-tail, α<0.05)
		3 months	6 months	
Group A-1: Direct	n = 82	n = 80	n = 49	0.05882
Present	32 (39.0%)	20 (25%)	10 (20.41%)	
Absent	50 (61.0%)	60 (75%)	39 (79.6%)	
Group A-2: Indirect	n = 19	n = 18	n = 17	**0.0006733**
Present	5 (26.3%)	3 (16.7%)	2 (11.8%)	
Absent	14 (73.7%)	15 (83.3%)	15 (88.24%)	
Group A-3: Mixed	n = 8	n = 8	n = 5	0.6573
Present	4 (50%)	3 (37.5%)	1 (20%)	
Absent	4 (50%)	5 (62.5%)	4 (80%)	

p-Value based on Mid-P Exact Test of initial consult and 3 months follow-up consult. Statistically significant p-values <0.05 in bold.

Table 7B. Diplopia in CCF with Endovascular Treatment

Diplopia in Group B	Before Treatment	After Treatment			
	Initial	1 week	1 month	3 months	6 months
Group B-1: Direct	n = 4	n = 4	n = 4	n = 4	n = 4
Present	3 (75%)	1 (25%)	1 (25%)	1 (25%)	1 (25%)
Absent	1 (25%)	3 (75%)	3 (75%)	3 (75%)	3 (75%)
Group B-2: Indirect	n = 4	n = 4	n = 4	n = 4	n = 4
Present	1 (25%)	0	0	0	0
Absent	3 (75%)	4 (100%)	4 (100%)	4 (100%)	4 (100%)
Group B-3: Mixed	n = 3	n = 3	n = 3	n = 3	n = 3
Present	2 (66.7%)	2 (66.7%)	2 (66.7%)	2 (66.7%)	2 (66.7%)
Absent	1 (33.3%)	1 (33.3%)	1 (33.3%)	1 (33.3%)	1 (33.3%)

Table 8A. Bruit Audible by Patient in CCF without Endovascular Treatment

Bruit audible by patient in Group A	Initial Consult	Follow-up Consults		*p* (2-tail, α<0.05)
		3 months	6 months	
Group A-1: Direct	n = 82	n = 80	n = 49	0.1101
Present	29 (35.4%)	19 (23.8%)	8 (16.3%)	
Absent	53 (64.6%)	61 (76.2%)	41 (83.7%)	
Group A-2: Indirect	n = 19	n = 18	n = 17	0.5117
Present	5 (26.3%)	3 (16.7%)	2 (11.8%)	
Absent	14 (73.7%)	15 (83.3%)	15 (88.2%)	
Group A-3: Mixed	n = 8	n = 8	n = 5	>0.9999999
Present	2 (25%)	2 (25%)	1 (20%)	
Absent	6 (75%)	6 (75%)	4 (80%)	

p-Value based on Mid-P Exact Test of initial consult and 3 months follow-up consult.

Table 8B. Bruit Audible by Patient in CCF with Endovascular Treatment

Bruit audible by patient in Group B	Before Treatment	After Treatment			
	Initial	1 week	1 month	3 months	6 months
Group B-1: Direct	n = 4	n = 4	n = 4	n = 4	n = 4
Present	2 (50%)	0	0	0	0
Absent	2 (50%)	4 (100%)	4 (100%)	4 (100%)	4 (100%)
Group B-2: Indirect	n = 4	n = 4	n = 4	n = 4	n = 4
Present	0	0	0	0	0
Absent	4 (100%)	4 (100%)	4 (100%)	4 (100%)	4 (100%)
Group B-3: Mixed	n = 3	n = 3	n = 3	n = 3	n = 3
Present	1 (33.3%)	0	0	0	0
Absent	2 (66.7%)	3 (100%)	3 (100%)	3 (100%)	3 (100%)

Table 9A. Bruit Audible by Examiner in CCF without Endovascular Treatment

Bruit audible by examiner in Group A	Initial Consult	Follow-up Consults		*p* (2-tail, α<0.05)
		3 months	6 months	
Group A-1: Direct	n = 82	n = 80	n = 49	**0.001816**
Present	55 (67.1%)	34 (42.5%)	15 (30.6%)	
Absent	27 (32.9%)	46 (57.5%)	34 (69.4%)	
Group A-2: Indirect	n = 19	n = 18	n = 17	0.1093
Present	8 (42.1%)	3 (16.7%)	3 (17.6%)	
Absent	11 (57.9%)	15 (83.3%)	14 (82.4%)	
Group A-3: Mixed	n = 8	n = 8	n = 5	0.3231
Present	3 (37.5%)	1 (12.5%)	1 (20%)	
Absent	5 (62.5%)	7 (87.5%)	4 (80%)	

p-Value based on Mid-P Exact Test of initial consult and 3 months follow-up consult. Statistically significant p-values <0.05 in bold.

Table 9B. Bruit Audible by Examiner in CCF with Endovascular Treatment

Bruit audible by examiner in Group B	Before Treatment	After Treatment			
	Initial	1 week	1 month	3 months	6 months
Group B-1: Direct	n = 4	n = 4	n = 4	n = 4	n = 4
Present	3 (75%)	0	0	0	0
Absent	1 (25%)	4 (100%)	4 (100%)	4 (100%)	4 (100%)
Group B-2: Indirect	n = 4	n = 4	n = 4	n = 4	n = 4
Present	2 (50%)	0	0	0	0
Absent	2 (50%)	4 (100%)	4 (100%)	4 (100%)	4 (100%)
Group B-3: Mixed	n = 3	n = 3	n = 3	n = 3	n = 3
Present	2 (66.7%)	0	0	0	0
Absent	1 (33.3%)	3 (100%)	3 (100%)	3 (100%)	3 (100%)

Table 10A. Pulsation in CCF without Endovascular Treatment

Pulsation in Group A	Initial Consult	Follow-up Consults		*p* (2-tail, α<0.05)
		3 months	6 months	
Group A-1: Direct	n = 82	n = 80	n = 49	**0.04640**
Present	23 (28.0%)	12 (15%)	8 (16.3%)	
Absent	59 (72.0%)	68 (85%)	41 (83.7%)	
Group A-2: Indirect	n = 19	n = 18	n = 17	0.5117
Present	5 (26.3%)	3 (16.7%)	2 (11.8%)	
Absent	14 (73.7%)	15 (83.3%)	15 (88.2%)	
Group A-3: Mixed	n = 8	n = 8	n = 5	>0.9999999
Present	1 (12.5%)	1 (12.5%)	1 (20%)	
Absent	7 (87.5%)	7 (87.5%)	4 (80%)	

p-Value based on Mid-P Exact Test of initial consult and 3 months follow-up consult. Statistically significant p-values <0.05 in bold.

Table 11. The Odds Ratio was the statistical measure used to quantify the association between endovascular treatment and clinical outcomes.

RESULTS

Demographics

The 120 medical records of CCF, diagnosed clinically by the presence of proptosis, corkscrewing of the conjunctival vessels, and bruit, were included in the study. Table 1 summarizes the characteristics of the subjects. Diagnosis by cerebral angiography showed 86 patients (71.7%) to have Direct CCF (Group 1), 23 patients (19.2%) had Indirect CCF (Group 2), and 11 (9.2%) had Mixed Type of CCF (Group 3). There were 109 (91.8%) patients who did not undergo endovascular treatment (Group A), and 11 (9.2%) patients who underwent endovascular treatment (Group B).

The mean age of patients with Direct CCF (Group 1) was 39 years, while the mean age of patients with Indirect CCF (Group 2) was 52 years.

Table 10B. Pulsation in CCF with Endovascular Treatment

Pulsation in Group B	Before Treatment	After Treatment			
	Initial	1 week	1 month	3 months	6 months
Group B-1: Direct	n = 4	n = 4	n = 4	n = 4	n = 4
Present	1 (25%)	1 (25%)	1 (25%)	1 (25%)	1 (25%)
Absent	3 (75%)	3 (75%)	3 (75%)	3 (75%)	3 (75%)
Group B-2: Indirect	n = 4	n = 4	n = 4	n = 4	n = 4
Present	0	0	0	0	0
Absent	4 (100%)	4 (100%)	4 (100%)	4 (100%)	4 (100%)
Group B-3: Mixed	n = 3	n = 3	n = 3	n = 3	n = 3
Present	0	0	0	0	0
Absent	3 (100%)	3 (100%)	3 (100%)	3 (100%)	3 (100%)

Table 11. Comparison of Clinical Outcomes between CCF without treatment and CCF with Endovascular Treatment

Clinical Outcomes	Without Treatment	With Endovascular Treatment	Odds Ratio	95% CI
Visual Acuity (VA)			**1.95**	(0.40, 9.52)
VA >0.4	32	2		
VA ≤0.4	74	9		
Corkscrewing of conjunctival vessels			**6.25**	(1.31, 29.80)
Present	100	8		
Absent	6	3		
Proptosis			**3.87**	(1.06, 14.14)
Present	73	4		
Absent	33	7		
Intraocular Pressure (IOP)			Not statistically significant	
IOP ≥21 mmHg	23	0		
IOP <21 mmHg	83	11		
Extraocular movement limitation			**3.35**	(0.84, 13.32)
Present	59	3		
Absent	47	8		
Diplopia			**0.87**	(0.21, 3.51)
Present	26	3		
Absent	80	8		
Bruit audible by patient			Not statistically significant	
Present	24	0		
Absent	82	11		
Bruit audible by examiner			Not statistically significant	
Present	38	0		
Absent	68	11		
Pulsation			**1.78**	(0.21, 14.86)
Present	16	1		
Absent	90	10		

Odds ratio at 3 months follow-up consult. Statistically significant odds ratio in bold.

Overall, there was a slight male predominance, with 63 of the 120 patients (52.5%) being male, and 57 of the 120 patients (47.5%) being female. There were more males (53 of 86 patients or 61.6%) in Direct CCF (Group 1), showing a male predominance. There were more females (20 of 23 patients or 87.0%) in Indirect CCF (Group 2), showing a female predominance.

Of the 120 patients, CCF occurred unilaterally in 100 (83.3%) and bilaterally in 20 (16.7%). The occurrence of CCF did not show a preference for laterality, as 49 patients presented on the right and 51 patients presented on the left.

Risk factors for CCF were trauma, hypertension, diabetes mellitus, and pregnancy. In the 86 patients with Direct CCF (Group 1), the most common risk factor was trauma (67 patients or 77.9%). In the 23 patients with Indirect CCF (Group 2), the most common risk factor was hypertension (18 patients or 78.3%).

Chief complaints were similar for all types, Direct CCF (Group 1), Indirect CCF (Group 2), and Mixed type of CCF (Group 3), namely: proptosis in 65 patients (54.2%), eye redness in 30 patients (25%), diplopia in 10 patients (8.3%), blurring of vision in 6 patients (5%), eyelid swelling in 5 patients (4.2%), eye pain in 3 patients (2.5%), and upper eyelid mass in 1 patient (0.8%).

Data on radiologic findings were gathered from radiologic reports found in the medical case records of patients. There were 94 patients (78.3%) with Computed Tomography scans and 10 patients (8.3%) with Magnetic Resonance Imaging. There were 16 medical case records that did not include information on radiologic imaging. The most common findings were dilated superior ophthalmic vein (SOV) in 103 patients (99.0%), proptosis in 80 patients (76.9%), and extraocular muscle enlargement in 65 patients (62.5%).

Clinical Features and Clinical Outcomes

All groups of patients were followed up for 6 months, however, Group A showed a drop out of 33 (40.2%) patients. The 3 months Follow-up Consults were therefore used for statistical analysis of data. Tables 2A to 10A showed the clinical features of patients who did not undergo endovascular treatment and documented the progression or worsening of features over time. Tables 2B to 10B showed the clinical features of patients before and after endovascular treatment. Table 11 compared the clinical features of patients who did not undergo endovascular treatment 3 months after initial consult with the clinical outcome of patients 3 months after endovascular treatment.

The visual acuity results were shown in Tables 2A (Group A) and 2B (Group B). The mean logMAR score for visual acuity in CCF on Initial Consult was 0.13. Majority of patients in all Groups had Good Vision. For Group A, the 2-tailed Mid-P exact test yielded p-values of 0.7847 for Group A-1, 0.5117 for Group A-2, and 0.6000 for Group A-3. All the p-values indicated that there was no statistically significant difference in visual acuity on Initial Consult and on 3 months Follow-up Consult. There was no statistically significant worsening or improvement in visual acuity over a period of 3 months in patients who had Direct CCF, Indirect CCF, and Mixed Type CCF who did not undergo endovascular treatment. On inspection of visual acuity results on Initial Consult and on 3 months Follow-up Consult in Group A data, there were 10 patients with improvement in visual acuity and 7 patients with worsening of vision. Of the 10 patients with improvement in visual acuity on 3 months Follow-up Consult compared to Initial Consult, 5 patients with Direct CCF improved from low vision to good vision, 3 patients with Direct CCF improved from blurring of vision to low vision, 1 patient with Indirect CCF had improvement from blurring of vision to low vision, and 1 patient with Indirect CCF improved from blurring of vision to good vision. Of the 7 patients with worsening of vision, 3 patients with Direct CCF worsened from good vision to low vision, 1 patient with Direct CCF worsened from low vision to blurring of vision, 1 patient with Direct CCF worsened from low vision to loss of vision, 1 patient with Indirect CCF worsened from blurring of vision to loss of vision, and 1 patient with Mixed Type CCF worsened from good vision to low vision. For Group B, Table 11 showed the odds ratio for the association between visual acuity and endovascular treatment to be 1.95 (95% CI: 0.40-9.52), which indicated that endovascular treatment had 1.95 higher odds of having good vision compared to no endovascular treatment. However, the 95% Confidence Interval showed that this association was not statistically significant.

For corkscrewing of conjunctival vessels, almost all patients in all Groups presented with corkscrewing of the conjunctival vessels on Initial Consult, as seen in Tables 3A (Group A) and 3B (Group B). In Table 3A, although there were a few patients in Group A that showed resolution of corkscrewing of conjunctival vessels, the 2-tailed Mid-P exact test yielded p-values of 0.05721 for Group A-1, 0.9730 for Group A-2, and 0.5000 for Group A-3. All the p-values indicated that there was no statistically significant difference in the number of patients with corkscrewing of conjunctival vessels on Initial Consult and on 3 months Follow-up Consult. There was no statistically significant difference in the number of patients with Direct CCF, Indirect CCF, and Mixed Type CCF who did not undergo endovascular treatment that showed the presence or absence of corkscrewing of conjunctival vessels over a period of 3 months. For Group B, Table 11 showed the odds ratio for the association between corkscrewing of the conjunctival vessels and endovascular treatment to be 6.25 (95% CI: 1.31-29.80), which indicated that endovascular treatment had 6.25 higher odds of not having corkscrewing of the conjunctival vessels compared to no endovascular treatment. The 95% Confidence Interval showed that this association was statistically significant. On inspection of the results for corkscrewing of the conjunctival vessels Before Treatment and on 3 months After Treatment in Group B data, Table

3B showed that patients who manifested resolution of the corkscrewing of conjunctival vessels belonged to Indirect CCF and Mixed Type CCF. None of the patients with Direct CCF manifested resolution of corkscrewing of conjunctival vessels 3 months after endovascular treatment.

Proptosis was shown in Tables 4A (Group A) and 4B (Group B). The mean amount of proptosis in CCF on Initial Consult was 4.66 mm, and proptosis was present in majority of patients in all Groups. For Group A, Table 2-A showed that the 2-tailed Mid-P exact test yielded p-values of 0.007881 for Group A-1, 0.2462 for Group A-2, and 0.5000 for Group A-3. These p-values indicated that there was no statistically significant difference in amount of proptosis on Initial Consult and on 3 months Follow-up Consult in Groups A-2 and A-3. For patients with Indirect CCF and Mixed Type CCF, there was no statistically significant increase or decrease in the amount of proptosis over a period of 3 months. The Mid-P value was statistically significant in Group A-1, indicating that there was a statistically significant decrease in the amount of proptosis of 0.73 mm in patients with Direct CCF who did not undergo endovascular treatment from Initial Consult to 3 months Follow-up Consult. For Group B, Table 4B showed that all patients had proptosis before endovascular treatment, with a mean amount of proptosis of 5.67 mm. On 3 months Follow-up Consult after endovascular treatment, 100% of patients in Groups B-2 and B-3 and 25% of patients in Group B-1 showed resolution of proptosis. The mean amount of proptosis on 3 months Follow-up Consult after endovascular treatment was 1.27 mm, showing a decrease of 4.4 mm. Table 11 showed the odds ratio for the association between proptosis and endovascular treatment to be 3.87 (95% CI: 1.06-14.14), which indicated that endovascular treatment had 3.87 higher odds of having a no proptosis compared to no endovascular treatment. The 95% Confidence Interval showed that this association was statistically significant.

The results for elevated IOP were shown in Tables 5A (Group A) and 5B (Group B). The mean IOP on Initial Consult was 22.63 mmHg for all patients, 22.82 mmHg for Group A, and 20.82 mm for Group B. For Group A, Groups A-1, A-2, and A-3 had almost equal number of patients with elevated IOP and not elevated IOP on Initial Consult. Since all patients with elevated IOP were managed with anti-glaucoma medication, there was a decrease in the number of patients with elevated IOP on 3 months Follow-up Consult. The mean IOP for Group A on 3 months Follow-up Consult was 19.038. For Group A, the 2-tailed Mid-P exact test yielded p-values of 0.00005507 for Group A-1, 0.6375 for Group A-2, and 0.1000 for Group A-3. These p-values indicated that there was no statistically significant difference in IOP on Initial Consult and on 3 months Follow-up Consult in patients with Indirect CCF and Mixed Type CCF who did not undergo endovascular treatment. There was a statistically significant improvement in IOP control over a period of 3 months in patients with Direct CCF who did not undergo endovascular treatment. For Group B, Table 11 showed the odds ratio for the association between elevated IOP and endovascular treatment not to be statistically significant. There was no association between endovascular treatment and resolution of elevated IOP. On inspection of Group B data on elevated IOP in Table 5B, however, there were no patients with Direct CCF, Indirect CCF, and Mixed Type CCF who had elevated IOP at the 3 months Follow-up Consult after endovascular treatment. All patients who initially presented with elevated IOP on Initial Consult either had normal IOP or controlled IOP with anti-glaucoma medication 3 months after endovascular treatment.

Results of extraocular movement were shown in Tables 6A (Group A) and 6B (Group B). For Group A, comparing the number of patients with extraocular movement limitation on Initial Consult and on 3 months Follow-up Consult, Groups A-1, A-2, and A-3 all showed a decrease in the number of patients with extraocular movement limitation. However, for Group A, the 2-tailed Mid-P exact test yielded p-values of 0.07197 for Group A-1, 0.5117 for Group A-2, and 0.6573 for Group A-3. All p-values indicated that there was no statistically significant difference in presence of extraocular muscle limitation on Initial Consult and on 3 months Follow-up Consult. There was no statistically significant improvement or worsening in the number of patients with Direct CCF, Indirect CCF, and Mixed Type CCF who did not undergo endovascular treatment and that did not have extraocular muscle limitation over a period of 3 months. For Group B, Table 11 showed the odds ratio for the association between extraocular movement limitation and endovascular treatment to be 3.35 (95% CI: 0.84-13.32), which indicated that endovascular treatment had 3.35 higher odds of not having extraocular movement limitation compared to no endovascular treatment. However, the 95% Confidence Interval showed that this association was not statistically significant. On inspection of Group B data in Table 6B, for patients with Direct CCF, Indirect CCF, and Mixed Type CCF, there was an increase in the number of patients without extraocular movement limitation on the 3 months Follow-up consult after endovascular treatment.

The diplopia results were shown in Tables 7A (Group A) and 7B (Group B). For Group A, comparing the number of patients with diplopia on Initial Consult and on 3 months Follow-up Consult, Groups A-1, A-2, and A-3 all showed a decrease in the number of patients with diplopia. For Group A, the 2-tailed Mid-P exact test yielded p-values of 0.05882 for Group A-1, 0.0006733 for Group A-2, and 0.6573 for Group A-3. The p-values indicated no statistically significant difference in visual acuity on Initial Consult and on 3 months Follow-up Consult for patients with Direct CCF and Mixed Type CCF who did not undergo endovascular treatment. There was a statistically significant decrease in the number of patients with diplopia over a period of 3 months only in patients with Indirect CCF who did not undergo endovascular treatment. For Group B, Table 11 showed the odds ratio

for the association between visual acuity and endovascular treatment to be 0.87 (95% CI: 0.40-9.52), which indicated that endovascular treatment had 0.87 higher odds of not having diplopia compared to no endovascular treatment. However, the 95% Confidence Interval showed that this association was not statistically significant.

The results for audible bruit by patient were shown in Tables 8A (Group A) and 8B (Group B). For Group A, comparing the number of patients reporting bruit on Initial Consult and on 3 months Follow-up Consult, Groups A-1 and A-2 showed a decrease in the number of patients with audible bruit, while Group A-3 showed no change. For Group A, the 2-tailed Mid-P exact test yielded p-values of 0.1101 for Group A-1, 0.5117 for Group A-2, and >0.9999999 for Group A-3. The p-values indicated that there was no statistically significant difference in the number of patients reporting bruit on Initial Consult and on 3 months Follow-up Consult in patients with Direct CCF, Indirect CCF, and Mixed Type CCF who did not undergo endovascular treatment. For Group B, Table 11 showed the odds ratio for the association between bruit reported by the patient and endovascular treatment not to be statistically significant. On inspection of Group B data on bruit reported by the patient in Table 8B, however, there were no patients with Direct CCF, Indirect CCF, and Mixed Type CCF who reported the presence of bruit on the 3 months Follow-up Consult after endovascular treatment.

The results for audible bruit by examiner were shown in Tables 9A (Group A) and 9B (Group B). In Group A, comparing the number of examiners reporting bruit on Initial Consult and on 3 months Follow-up Consult, Groups A-1, A-2 and A-3 showed a decrease in the number of examiners reporting audible bruit. For Group A, the 2-tailed Mid-P exact test yielded p-values of 0.001816 for Group A-1, 0.1093 for Group A-2, and 0.3231 for Group A-3. The p-values indicated a statistically significant decrease in the number of examiners reporting bruit on 3 months Follow-up Consult, compared to Initial Consult, only in patients with Direct CCF who did not undergo endovascular treatment. The decrease in the number of examiners not reporting bruit in patients with Indirect CCF and Mixed Type CCF who did not undergo endovascular treatment were not statistically significant. For Group B, Table 11 showed the odds ratio for the association between bruit reported by the examiner and endovascular treatment not to be statistically significant. On inspection of Group B data on bruit reported by the examiner in Table 9B, there were no patients with Direct CCF, Indirect CCF, and Mixed Type CCF who were reported by the examiner to have bruit on the 3 months Follow-up Consult after endovascular treatment.

The pulsation results were shown in Tables 10A (Group A) and 10B (Group B). In Group A, comparing the number of patients with pulsation on Initial Consult and on 3 months Follow-up Consult, Groups A-1 and A-2 showed a decrease in the number of patients with pulsation, while there was no change in Group A-3. For Group A, the 2-tailed Mid-P exact test yielded p-values of 0.04640 for Group A-1, 0.5117 in Group A-2, and >0.9999999 in Group A-3. The p-values indicated a statistically significant decrease in the number of patients with pulsation on 3 months Follow-up Consult, compared to Initial Consult, only in patients with Direct CCF who did not undergo endovascular treatment. The decrease in the number of patients with pulsation and with Indirect CCF who did not undergo endovascular treatment was not statistically significant. For Group B, Table 11 showed the odds ratio for the association between pulsation and endovascular treatment to be 1.78 (95% CI: 0.21-14.86), which indicated that endovascular treatment had 1.78 higher odds of not having pulsation compared to no endovascular treatment. The 95% Confidence Interval showed that this association was not statistically significant. On inspection of Group B data on pulsation in Table 10B, pulsation was only seen in 1 of the 4 patients with Direct CCF and pulsation persisted after endovascular treatment. Indirect CCF and Mixed Type CCF did not present with pulsation before treatment, and there was no change after treatment.

Data from Tables 2B to 10B generally showed a favorable clinical outcome in patients who underwent endovascular treatment. There was either improvement or no worsening of clinical features after treatment. There was only 1 patient with Mixed Type CCF who had worsening of vision from low vision to blurring of vision after endovascular treatment. This showed that there was minimal ophthalmic complications associated with endovascular treatment.

DISCUSSION

Carotid cavernous fistula (CCF) is an increasingly common disease in the Philippines with significant ophthalmic consequences. Yet, there still remains a paucity of data and published research on CCF in the Philippines. This study contributes to the existing available data and experience in the management of CCF and in the sequelae of CCF when managed conservatively without endovascular intervention.

In the Philippine General Hospital (PGH), Sotalbo et al. documented 156 cases of CCF diagnosed using cerebral angiogram, with some undergoing endovascular intervention, performed in the Department of Radiology from 2006-2016.[13] Concepcion et al. in the PGH Department of Ophthalmology and Visual Sciences (DOVS) examined the incidence of increased IOP in CCF patients, and the IOP outcomes after endovascular treatment.[14]

Several findings in this study are consistent with previous published research in existing literature. Direct CCF has a male predominance and more commonly occurs in younger individuals.[12,15,16] Indirect CCF has a female predominance and more commonly occurs in older patients.[17] Trauma was the most common risk factor in direct CCF, and hypertension was the most common risk factor in indirect CCF.[3,5,6,8,12,16]

The clinical features of CCF are characterized by Dandy's triad of bruit, proptosis, and chemosis.[18] Other clinical features that were documented in this study were blurring of vision, proptosis, corkscrewing of vessels, relative afferent pupillary defect, extraocular muscle limitation, diplopia, pulsation, audible bruit, optic nerve anatomical changes, and fundus changes.[3,5,8,9,12] The clinical presentation of CCF, however, depends on the angiographic type, in which highly pressurized blood is transmitted to the cavernous sinus from abnormal connections.[7] Direct CCF usually has a more dramatic and rapid clinical presentation.[3,12]

Radiologic imaging, like plain CT scan and MRI, can be used to confirm the diagnosis of CCF.[5,10-12,16] Plain CT scan has been found to be the preferred imaging in the PGH DOVS Orbit Clinic in confirming the presence of CCF. Radiologic features of CCF include the presence of dilated superior ophthalmic vein (SOV), proptosis, and enlarged EOM. Dilated SOV has been seen to be the most common radiologic feature of CCF, and highly correlated with the diagnosis of CCF on cerebral angiography. Cerebral angiography is considered the gold standard in the diagnosis of CCF.[10,12,16]

Various ocular manifestations occur in CCF as a result of abnormal blood flow between the carotid artery and the cavernous sinus. Previous studies have described the ocular presentation of CCF and treatment outcome.

Tan et al.[19] compared the clinical outcomes in 8 cases of Direct CCF and 37 cases of Indirect CCF, of which 7 cases of Direct CCF and 29 cases of Indirect CCF underwent treatment. McNemar's Test was not able to show any statistically significant difference between treated and untreated CCF in terms of visual acuity, intraocular pressure, proptosis, and diplopia. The study by Tan, et al. failed to establish an association between treatment and clinical improvement, and attributed the lack of statistical significance to the small sample size of Direct CCF.

Another study by Rahmatian et al.[20] reported a systematic review of 36 studies discussing endovascular treatment of CCF published through March 2023. The pooled percentages of the pre-treatment clinical findings were reported, and its possible causes were discussed. The study mentioned that the visual outcome of endovascular treatment was difficult to predict, but reported that Direct CCF manifested with poorer vision and endovascular treatment resulted in greater vision recovery. The meta-analysis in the study was not able to provide relevant evidence on endovascular treatment outcomes, but concluded that majority of endovascular treatments resulted in improvement of clinical symptoms.

In this current study, data from Group A, who were patients managed conservatively without endovascular treatment, showed statistically significant improvement in some clinical features, including proptosis, elevated IOP, diplopia, bruit reported by examiner, and pulsation. Spontaneous improvement in clinical features had been reported in previous studies with cases of spontaneous resolution of CCFs that resulted from the thrombosis of the feeder vessels.[19] Tables 9A and 10A showed that the spontaneous resolution of bruit and pulsation, respectively, was demonstrated in Direct CCF, a high flow type of CCF that arises directly from the ICA. Also in this current study, data from Group B, who were patients who underwent endovascular treatment, showed an improvement in all clinical outcomes after treatment, similar to what had been reported in previous studies. This current study, however, was only able to show statistically significant association between endovascular treatment and improvement in corkscrewing of the conjunctival vessels and resolution of proptosis. The obtained result emphasized the necessity of employing diverse treatment approaches, and not just endovascular treatment, to address the ophthalmic manifestations associated with CCF.

In Group A, the percentage of patients with good vision in Direct CCF, in Indirect CCF, and in Mixed Type CCF did not appear markedly different. Table 2A showed that Direct CCF did not manifest with poorer vision, as reported by previous studies. The visual acuity in patients who did not undergo endovascular treatment was shown to improve in 10 patients after 3 months from initial consult, and 8 out of the 10 patients had Direct CCF. The visual acuity in patients who did not undergo endovascular treatment was also shown to worsen in 7 patients after 3 months from initial consult, and 5 out of 7 had Direct CCF, 1 out of 7 had Indirect CCF, and 1 out of 7 had Mixed Type CCF. Visual acuity on initial consult could be affected by other factors like eye trauma and other pre-existing conditions. It was notable that none of the patients with blurring of vision or loss of vision underwent endovascular treatment. Prevention of worsening of good vision was an indication for undergoing endovascular treatment. The poorer vision on Initial Consult of Group A, compared to Group B, gave Group A an expected disadvantage in statistical analysis. In Group B, who were patients who underwent endovascular treatment, Table 2B showed the visual acuity in Direct CCF, Indirect CCF, and Mixed Type CCF to be either good vision or low vision before treatment. After treatment, visual acuity did not change, except in 1 case of worsening of vision in Mixed Type CCF.

For proptosis, although there was a decrease in the mean amount of proptosis in Group A (Table 4A), this decrease was notably smaller than that in Group B, and amounted only to about 1 mm, which could be caused by interobserver difference. Although proptosis was shown to decrease in patients who did not undergo endovascular treatment, the mean decrease in proptosis was higher in patients who underwent endovascular treatment. Despite the failure to show by statistical analysis an association between endovascular treatment and resolution of proptosis, Table 4B showed that all 4 patients with Indirect CCF presented with proptosis before treatment had complete resolution of proptosis after treatment.

In the control of elevated IOP, although the odds ratio failed to show a statistically significant association between control of elevated IOP and endovascular treatment, it can be

noted that patients who underwent endovascular treatment (Table 5B) had better control of IOP, with no patients manifesting with elevated IOP after endovascular treatment and anti-glaucoma medication. In patients who did not undergo endovascular treatment (Table 5A), some patients continued to manifest elevated IOP despite anti-glaucoma medication. It can be assumed that endovascular treatment resulted in control of elevated IOP by addressing the abnormal blood flow to the cavernous sinus that caused arterialization of conjunctival and episcleral vessels and then disruption of the normal balance of intraocular fluid dynamics.

Ophthalmologists play a vital role in the management of patients with CCF. After making the initial diagnosis, ophthalmologists monitor the progression of the clinical signs and symptoms to prevent devastating sight-threatening sequalae, like loss of vision, exposure keratopathy, glaucoma, and stasis retinopathy. After the diagnosis of CCF through cerebral angiography, patients are referred to Interventional Radiology for endovascular treatment as the definitive management. Supportive treatment should be continued to improve treatment outcomes.

This study is the first research to document in detail the result of untreated CCF and the outcome of endovascular treatment, as well as statistically compare the clinical features of untreated and treated CCF. This study also shows the progression and spontaneous resolution of clinical findings, such as visual acuity, proptosis, corkscrewing of conjunctival vessels, extraocular movement limitation, diplopia, audible bruit, and elevated IOP, when patients with CCF do not undergo endovascular treatment.

Endovascular treatment is considered the first line of treatment in the management of CCF.[5,6,12,15,18] Complete resolution of clinical signs and symptoms are seen within hours to days in 80% to 90% of patients with CCF after successful endovascular treatment.[5,10,12,15,21] Patients with residual signs and symptoms after endovascular treatment can still show a significant improvement up to the 6-month follow-up.[9,20,22] This study shows that an improvement in visual acuity, corkscrewing of conjunctival vessels, amount of proptosis, extraocular movement limitation, presence of audible bruit, and pulsation can possibly be attributed to a successful endovascular treatment, but other factors, including supportive treatment can lead to favorable treatment outcome.

CONCLUSION

CCF requires proper multispecialty management in its diagnosis and treatment in order to prevent significant visual impairment and ocular disfigurement. Endovascular treatment is safe and effective in managing ophthalmic signs and symptoms. Endovascular treatment is effective in the improvement and in the prevention of worsening of visual acuity, corkscrewing of conjunctival vessels, amount of proptosis, IOP control, extraocular movement limitation, diplopia, and presence of audible bruit.

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Author Disclosure

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