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Original Article

Surgical Strategy to Reduce the Recurrence of Adventitial Cystic Disease after Treatment

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Purpose: Adventitial cystic disease (ACD) is a rare condition that causes intermittent claudication and non-atherosclerotic disease without cardiovascular risk factors. The etiology and optimal treatment of ACD remain controversial. The purpose of this study was to analyze surgical treatment results for ACD and to elucidate optimal treatment options.

Materials and Methods: We retrospectively reviewed 30 patients with ACD who underwent surgery from 2006 to 2018. Twenty-two patients had arterial ACD, six had venous ACD, and two had combined venous and arterial ACD. We reviewed demographic and clinical characteristics, treatment details, and procedure outcomes.

Results: Recurrence occurred in 6 cases either after cyst excision alone (4/17) or patch angioplasty (2/2). There was no recurrence after vessel excision with interposition grafting (0/7). Therefore, vessel excision was a statistically significant factor in recurrence prevention (P=0.026). Among the six recurrences, joint connections of the cystic lesions were found in four of the six (66.7%).

Conclusion: As a curative surgery for ACD, vessel excision with interposition grafting is a better strategy to prevent recurrence than simple cyst excision alone.

Key Words: Adventitia, Cysts, Excision, Joint

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INTRODUCTION

Adventitial cystic disease (ACD) is a rare non-atherosclerotic disease that causes intermittent claudication without any cardiovascular risk factors. The most commonly involved vessels are the popliteal arteries [1]. If the arterial cyst compresses the arterial lumen, it can cause claudication in the affected limb [2]. Due to the scarcity of ACD, it is sometimes misdiagnosed as atherosclerotic occlusive disease.

The pathogenesis of ACD involves the formation of mucinous cysts within the adventitia of arteries and veins [3]. The cause of ACD is still unclear, so the optimal treatment is also controversial; no definite therapeutic guidelines exist at the moment. Currently, treatment options for ACD include image-guided percutaneous aspiration; angioplasty; complete cyst excision; vascular excision and reconstruction with allograft, autograft, or synthetic graft; and bypass [4].

The purpose of this study was to analyze the rate of ACD recurrence after various surgical treatments and to elucidate the ideal treatment option to reduce recurrence.

MATERIALS AND METHODS

This study was a retrospective review of data collected prospectively at a tertiary hospital between November 2006 and August 2018. A total of 30 patients who were diagnosed with ACD through imaging studies and who underwent surgery were included in this study. We obtained approval from the Institutional Review Board of Samsung Medical Center (SMC 2019-05-041). Written informed consents were waived because of retrospective design of this study. Diagnostic imaging included duplex ultrasonography (DUS), computed tomography (CT), or magnetic resonance imaging (MRI). Postoperative follow-up was performed with DUS or CT.

Continuous variables are presented as means±standard deviations, while categorical variables are presented as numbers of cases with percentages (%). We classified the recurrence rate according to the type of surgical treatment, vessels involved (artery, vein, or combined), affected vessels (e.g., popliteal, femoral, iliac), and presence or absence of joint connection. The connection between the joint and cyst was identified in preoperative CT/MRI or intraoperatively. Due to the small number of cases, we did not perform a multivariate analysis using logistic regression. Kaplan–Meier curves were used to determine the freedom from stenosis or occlusion of the involved vessels.

RESULTS

1) Patient demographic and clinical characteristics

Arterial cysts were most common (n=22, 73.3%), followed by venous cysts (n=6, 20.0%), and combined cysts (n=2, 6.7%). Twenty-two patients were male (73.3%) and the median age was 50.5 years. Fig. 1 represents an arterial ACD case and Fig. 2, a venous ACD case.

In this review, all cases were in the lower extremity and the popliteal vessels were the most common segment involved (n=22, 73.3%; 19 arteries, 1 vein, and 2 combined). The other vessels involved were the femoral vessels (n=6, 20.0%; 3 arteries and 3 veins) and the iliac vein (n=2, 6.7%). The left side was more frequently affected than the right (66.7% vs. 33.3%, respectively).

The symptoms varied depending on whether the lesion

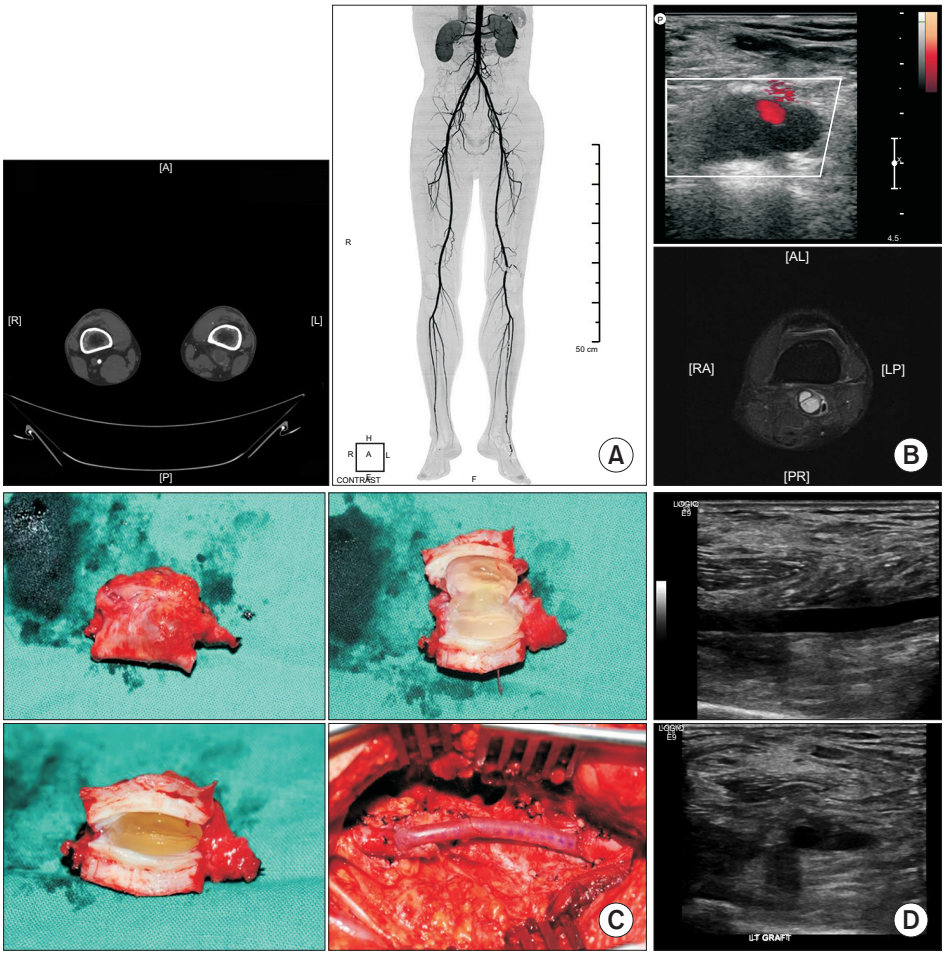

Fig. 1. A 44-year-old male patient who was suffering from left leg claudication was diagnosed with left popliteal artery adventitial cystic disease and underwent left distal superficial femoral artery-popliteal artery interposition with ipsilateral great saphenous vein. (A) Preoperative computed tomography angiography, (B) preoperative duplex ultrasonography (DUS) and magnetic resonance imaging, (C) operative sample and field photograph after interposition, (D) postoperative follow-up DUS.

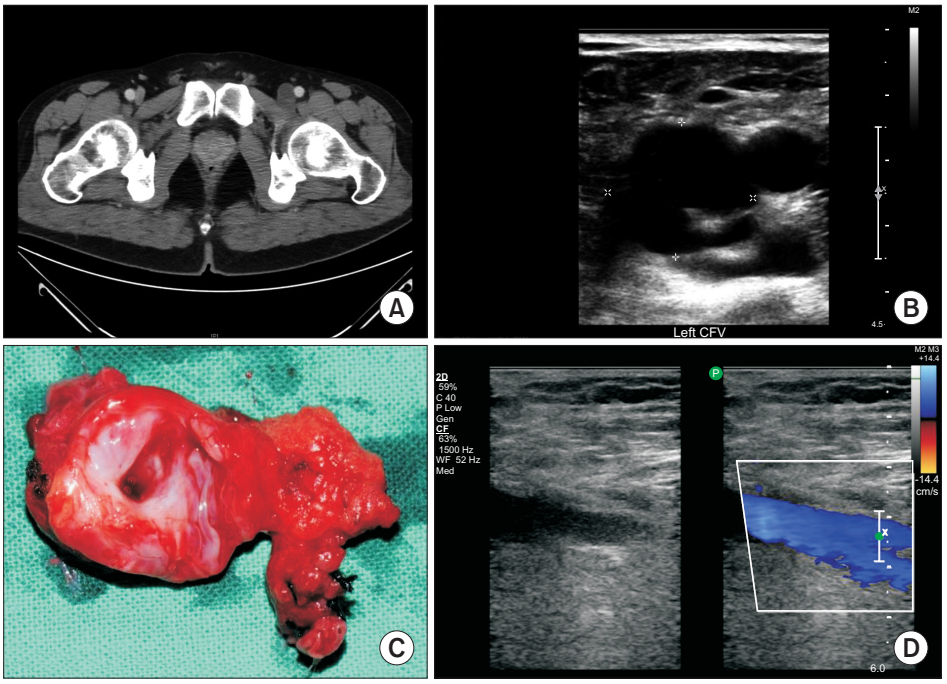

Fig. 2. 39-year-old male patient who suffered from left leg swelling was diagnosed with left femoral vein adventitial cystic disease and underwent left femoral vein cyst excision. (A) Preoperative computed tomography, (B) Preoperative duplex ultrasonography (DUS), (C) operative sampling photograph, (D) postoperative follow-up DUS.

Table 1. Patient demographic and clinical characteristics

Characteristic	Total (n=30)	Arterial (n=22)	Venous (n=6)	Combined (n=2)[a]
Median age (y)	50.5 (32-77)	53.5 (33-77)	39 (32-55)	52 (45-59)
Gender (male)	22 (73.3)	21 (95.5)	1 (16.7)	0 (0.0)
Limb side				
Right	10 (33.3)	9 (40.9)	1 (16.7)	0 (0.0)
Left	20 (66.7)	13 (59.1)	5 (83.3)	2 (100.0)
History of trauma	1 (3.3)	1 (4.5)	0 (0.0)	0 (0.0)
Deep vein thrombosis	2 (6.7)	0 (0.0)	2 (33.3)	0 (0.0)
Symptoms				
Leg claudication	24 (80.0)	22 (100.0)	0 (0.0)	2 (100.0)
Leg swelling	6 (20.0)	0 (0.0)	6 (100.0)	0 (0.0)
Symptom onset time (mo)	3.4 (1-85)	2.9 (1-24)	4.3 (1-12)	45.2 (5-85)
De novo lesion	26 (86.7)	20 (90.9)	4 (66.7)	2 (100.0)
Affected vessel				
Popliteal	22 (73.3)	19 (86.4)	1 (16.7)	2 (100.0)
Femoral	6 (20.0)	3 (13.6)	3 (50.0)	0 (0.0)
Iliac	2 (6.7)	0 (0.0)	2 (33.3)	0 (0.0)
Joint connection	15 (50.0)	10 (45.5)	5 (83.3)	0 (0.0)
Cyst diameter (cm)	1.5 (0.4-3.7)	1.2 (0.4-3.7)	2.3 (1.2-3.7)	1.9 (1.3-2.4)

Values are presented as median (range) or number (%).
[a]Combined cyst=combination of arterial and venous cyst.

was in the arteries or the veins. All arterial cysts presented with leg claudication, while all venous cysts presented with leg swelling. Combined cysts presented with leg claudication. Only one patient had a history of trauma.

A joint connection with the cyst was detected preoperatively in 15 patients (50.0%). The median cyst diameter was 1.5 cm, and venous cysts had larger diameters than arterial cysts (2.3 cm vs. 1.4 cm, respectively; Table 1).

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2) Operative procedures and postoperative antithrombotic management

Among the 30 patients, 17 (56.7%) were treated with cyst excision alone, 11 (36.7%) underwent vessel excision and interposition grafting, and two patients with venous cysts (6.7%) underwent cyst excision with patch angioplasty. Among the 22 patients with arterial cysts, 11 patients (50.0%) underwent cyst excision only, while seven (31.8%) underwent vessel excision and interposition grafting and four patients (18.2%) underwent bypass surgery, leaving the cyst in situ. The conduit for interposition was the great saphenous vein (GSV) in 6 patients, and an expanded polytetrafluoroethylene (ePTFE) graft in 1 patient. For the four bypass surgeries, 3 GSV grafts and 1 ePTFE graft were used. Among the 6 patients with venous cysts, four (66.7%) were treated with cyst excision alone and two underwent cyst excision with bovine patch angioplasty (Table 2).

Postoperative antithrombotic therapy was determined by the type of operation. For arterial cysts treated with cyst excision alone, no antithrombotics were used. In cases of bypass or interposition grafting, aspirin only or aspirin with clopidogrel was administered. For venous cysts treated by cyst excision alone, no antithrombotics were used. In the two patients who underwent cyst excision with patch angioplasty, low molecular weight heparin was used postoperatively. In one case of a preoperative deep vein thrombosis, warfarin was continued after discharge.

3) Follow-up outcomes and recurrence rates

Follow-up imaging studies were done using DUS and/or CT angiography at 1 month, 6 months, and annually. Freedom curves from stenosis and occlusions of the involved vessel are presented in Fig. 3. Arterial cysts showed less stenosis or occlusion at one year without statistical significance (P=0.447). Six patients (20.0%) developed recurrences, including three arterial and three venous ACDs, but arterial ACDs had a lower recurrence rate (50.0% vs. 13.6%, respectively). Median time to recurrence was 14.2 months (21.9 months for arterial cysts and 6.4 months for venous cysts; Table 2). The follow-up data for patients who developed recurrence are described in detail in Table 3.

Recurrence occurred in 6 cases after either cyst excision alone (4/17) or patch angioplasty (2/2) (Table 4). The 3 arterial cyst recurrences developed after cyst excision alone (Supplementary Table 1). There was no recurrence after vessel excision with interposition grafting (0/7) or bypass (0/4). Vessel excision was a statistically significant factor for recurrence prevention (P=0.026). Among the six recurrences, joint connections of the cystic lesions were found in 4 patients (66.7%) without statistical significance (P=0.651).

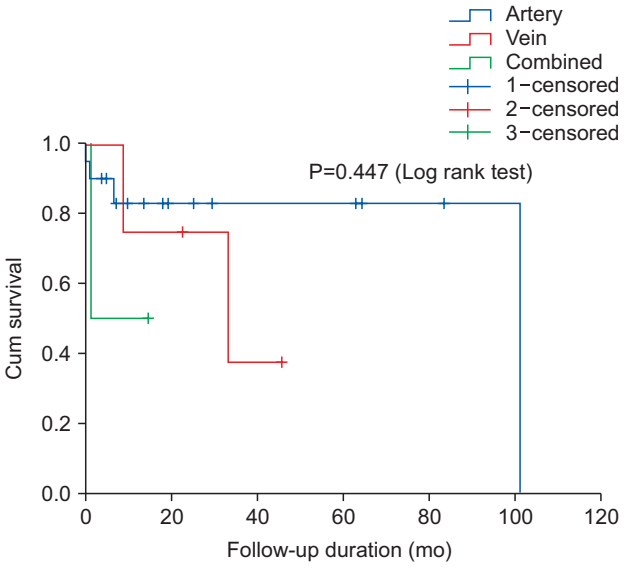

Fig. 3. Freedom curve from stenosis or occlusion according to the vessels involved.

Table 2. Operative procedure and results

Variable	Total (n=30)	Arterial (n=22)	Venous (n=6)	Combined (n=2)
Operative procedures				
Cyst excision only	17 (56.7)	11 (50.0)	4 (66.7)	2 (100.0)
Vessel excision and interposition	7 (23.3)	7 (31.8)	0 (0.0)	0 (0.0)
Bypass	4 (13.3)	4 (18.2)	0 (0.0)	0 (0.0)
Cyst excision with patch angioplasty	2 (6.7)	0 (0.0)	2 (33.3)	0 (0.0)
Results				
Recurrence	6 (20.0)	3 (13.6)	3 (50.0)	0 (0.0)
Median recurred time (mo)	14.2 (1-95)	21.9 (1-95)	6.4 (2.3-33.2)	-

Values are presented as number (%) or median (range).

Table 3. Information on patients with recurrence

Variable	Age (y)/sex					
	51/male	65/male	58/male	32/female	39/female	39/female
Involved vessel	Popliteal artery	Popliteal artery	Popliteal artery	Iliac vein	Femoral vein	Femoral vein
Interval to recurrence (mo)	94.97	0.17	21.9	2.3	33.17	6.4
Operation	Cyst excision	Cyst excision	Cyst excision	Cyst excision & patch angioplasty	Cyst excision	Cyst excision & patch angioplasty
Symptoms after recurrence	Leg claudication	Operation site pain, coldness	No symptom	No symptom	Leg swelling	No symptom
Redo operation	No redo operation	Bypass with GSV graft	No redo operation	Recurrent cyst excision	Recurrent cyst excision	Recurrent cyst excision
Follow-up (mo)	100.97	38.27	38.9	10.87	38.4	22.47
Current status	Patent	Patent	Patent	Recurred	Stenosis	Patent

GSV, great saphenous vein.

Table 4. Recurrence among subgroups

Variable	No recurrence (n=24)	Recurrence (n=6)	P-value
Involved vessel			0.109
Artery	19 (79.2)	3 (50.0)	0.300
Vein	3 (12.5)	3 (50.0)	0.075
Combined	2 (8.3)	0 (0.0)	1.000
Operative procedures			0.026
Cyst excision only	13 (54.2)	4 (66.7)	0.672
Vessel excision and interposition	7 (29.2)	0 (0.0)	0.290
Bypass	4 (16.7)	0 (0.0)	0.557
Cyst excision with patch angioplasty	0 (0.0)	2 (33.3)	0.034
Operative procedures			0.007
Cyst excision only	13 (54.2)	4 (66.7)	0.672
Interposition or bypass	11 (45.8)	0 (0.0)	0.061
Cyst excision with patch angioplasty	0 (0.0)	2 (33.3)	0.034
Affected vessel			0.187
Popliteal	19 (79.2)	3 (50)	0.300
Femoral	4 (16.7)	2 (33.3)	0.571
Iliac	1 (4.2)	1 (16.7)	0.366
Joint connection(+)	11 (45.8)	4 (66.7)	0.651

Values are presented as number (%).

DISCUSSION

ACD is a rare condition that consists of cysts containing mucin that arise in the adventitial layers of vessels. When the cysts compress the artery, causing stenosis or occlusion, claudication symptoms can develop that are similar to other atherosclerotic diseases. It is estimated that 1 out of every 1,200 individuals suffer from claudication [5]. When cysts compress the vein, swelling can develop. However, because of the scarcity of ACD, there are no definitive treatment guidelines and many options without verified efficacy exist.

Since the first case of ACD was published in 1947 [6], many cases have been reported. However, the etiology and optimal treatment of ACD is still contested. There are several theories about the etiology, including repetitive trauma theory, ganglion theory, systemic disorder theory, and developmental theory [7].

Trauma theory asserts that the repetition of trauma causes chronic degeneration of the adventitia, affecting cyst generation [8,9]. However, only 4% of patients had a

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history of trauma [4], and the disease incidence was not correlated with age or more a more active athletic lifestyle. These results were therefore insufficient to support the trauma theory. We consequently found the ganglion theory to be more convincing. Ganglion theory or synovial theory states that synovial cysts enlarge and track along arterial branches and implant themselves in the vessel adventitia. Connections between joint capsules and adjacent vessels have been frequently observed in ACDs. We identified joint connections using preoperative CT, MRI, or intraoperative findings. MRI seemed to be a more effective modality for discovering joint connections, so we proposed the use of an MRI as a diagnostic tool for identifying joint connections [3,4]. Desy and Spinner [4] reported that joint connections were observed in 17% of the patients. In this study, however, we identified joint connections in 50% of the patients. In particular, five out of the six patients with venous cysts (83.3%) had joint connections. Thus, we surmised that joint connection was associated with the development of ACD, especially in those with venous cysts. Furthermore, we suspected that joint connections were deeply related to disease recurrence. In our study, four out of the six recurrence cases had joint connections (66.7%). Due to the small number of subjects, however, no statistical significance was observed (P=0.651).

The treatment of ACD is controversial and there are no clear treatment guidelines available at this time. Percutaneous cyst aspiration, cyst excision, vessel excision with interposition grafting, or bypass are possible options. Interestingly, there are some cases that report spontaneous regression of ACD [10-16]. Zhang et al. [11] have suggested that the regression of ACD is related to the connection between the cyst and the synovium, but this has not been applicable in all cases. We also had two cases of spontaneous regression. First, a 42-year-old male with claudication underwent bypass surgery without cyst excision. Initially after surgery the cyst continued to grow, but after five years the cyst regressed spontaneously (Supplementary Fig. 1). Secondly, a 58-year-old male had recurrent ACD after cyst excision alone and he refused reoperation. Fortunately, after one year, the recurred cyst regressed spontaneously (Supplementary Fig. 2). However, despite these instances of spontaneous regression, long-term follow-up remains mandatory in the majority of patients.

Since spontaneous regression is unpredictable, most patients are treated surgically. In our center, the surgical procedure was selected based on the extent of cyst involvement. For arterial cysts without severe stenosis, cyst excision alone was performed. In cases of total occlusion or severe stenosis, bypass surgery or vessel excision and interposition grafting was done. Bypass was chosen especially when the involved artery segment was long. For venous cysts, cyst excision was considered first, but if severe stricture was expected after excision, patch angioplasty was preferred.

Another treatment option is cyst aspiration. Rosiak et al. [17] reported two cases of popliteal ACD treated by percutaneous aspiration. Even after follow-up monitoring for five years, there was no recurrence. Van Rutte et al. [18] performed a literature review of 68 case reports and found eight cases of exarterectomy with no recurrence and another eight cases of needle aspiration with only one recurrence. An exarterectomy is a circumferential resection of the involved adventitia. The authors concluded that surgical exarterectomy and percutaneous needle aspiration could be alternatives to bypass surgery due to their high success rate and lower degree of invasiveness. However, the authors also recommended that bypass surgery be performed when the artery is completely occluded. In a multi-institutional retrospective study [19], vessel excision with reconstruction was associated with a resolution of symptoms and a reduction in interventional requirements, while cyst drainage alone could result in recurrence and re-intervention.

In this study, recurrence developed in 6 cases after either cyst excision alone (4/17) or patch angioplasty (2/2). There was no recurrence after vessel excision with interposition grafting (0/7). Vessel excision was a statistically significant factor in recurrence prevention (P=0.026). Based on this result, we can conclude that cyst excision alone and patch angioplasty are not effective, and undergoing vessel excision and interposition should be considered to reduce or prevent disease recurrence.

Considering that ganglion theory is the most convincing etiology of ACD, removing the joint connection seems to be necessary to reduce recurrence. During surgery, we attempted to find any joint connection and ligate it. However, in this study there were two recurrences after joint connection ligation. Possible explanations for this are that we did not properly ligate the connection, that there were other communications that we missed, or that joint connectivity was not related to recurrence. A large study is necessary to further determine the association between joint connection and ACD recurrence.

Based on this study and literature review, our center established a treatment strategy for ACDs. If patients have tolerable symptoms, we suggest waiting around one month for possible regression of the cyst. If the symptoms get worse or remain the same, we suggest considering percutaneous cyst aspiration. Due to the possibility of recurrence and re-intervention, continuous short-term follow-up is necessary. After recurrence is detected, surgical treatment, involving vessel excision and interposition or bypass should

be performed along with every effort to identify and ligate any joint connection. If patients present with severe symptoms and total occlusion, we recommend direct surgical treatment with vessel excision and interposition grafting or bypass.

There are several limitations to highlight in this study. First, owing to the small sample size and single-center design, this study is inherently biased and may lack statistical power. Second, as the rate of loss to follow-up was quite high and long-term follow-up was difficult, the recurrence rate may have been underestimated. Third, as only ACD in the lower extremities was collected and reviewed, we cannot directly apply these results to the upper extremity or trunk vessels. Finally, several studies have investigated popliteal arterial ACD, yet the question of whether it is appropriate to expand the treatment options to other arteries and veins remains unclear.

Additionally, although only 30 patients were included in this study, this is still a large cohort of the literature. Also, many surgical options were attempted and reviewed to find a meaningful difference in recurrence rates.

CONCLUSION

Vessel excision and interposition grafting is a better surgical strategy to prevent the recurrence of ACD than simple excision of the cyst. A multicenter study with more patients should be conducted to further test these results. Additionally, the optimal treatment for venous ACD needs to be determined in future studies specifically targeting venous ACDs.

SUPPLEMENTARY MATERIALS

Supplementary data can be found via https://doi.org/10.5758/vsi.2019.35.4.217.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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AUTHOR CONTRIBUTIONS

Concept and design: JHL, YJP. Analysis and interpretation: JHL, YJP. Data collection: JHL, BHC, SHH, DIK, YWK, YJP. Writing the article: JHL, BHC, JHK, YJP. Critical revision of the article: JHL, BHC, YJP. Final approval of the article: JHL, YJP. Statistical analysis: JHL, BHC, YJP. Obtained funding: none. Overall responsibility: JHL, YJP.

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