



Acellular dermal matrix as an alternative to autologous fascia lata for skull base repair following extended endoscopic endonasal approaches

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Abstract

Background Skull base reconstruction after extended endoscopic endonasal approaches (EEAs) can be challenging. In addition to the nasoseptal flap, which has been adopted by most centers, autologous fascia lata is also often utilized. Harvesting of fascia lata requires a separate thigh incision, may prolong recovery, and results in a visible scar. In principal, the use of non-autologous materials would be preferable to avoid a second incision and maintain the minimally invasive nature of the approach, assuming the CSF leak rate is not compromised.

Objective To assess the efficacy of acellular dermal matrix (ADM) as a non-autologous alternative to autologous fascia lata graft for watertight closure of the cranial base following EEAs.

Methods A retrospective chart review of extended EEAs performed before and after the transition from fascia lata to ADM was performed. Cases were frequency matched for approach, pathology, BMI, use of lumbar drainage, and tumor volume. Power analysis was performed to estimate the sample size needed to demonstrate non-inferiority.

Results ADM was used for watertight closure of the cranial base in 19 consecutive extended endoscopic endonasal approaches (16 gasket-seals and 3 buttons) with 1 postoperative CSF leak at the last follow-up (median 5.3, range 1.0–12.6 months). All patients had high-flow intraoperative leaks. The cohort included 8 meningiomas, 8 craniopharyngiomas, 2 chordomas, and 1 pituitaryoma ranging in size from 0.2 to 37.2 cm³ (median 5.5, IQR 2.8–13.3 cm³). In 19 historical controls who received fascia lata, there were 2 postoperative CSF leaks.

Conclusions Preliminary results suggest that ADM provides a non-inferior non-autologous alternative to fascia lata for watertight gasket-seal and button closures following extended EEAs, potentially reducing or eliminating the need to harvest autologous tissue.

Keywords Acellular dermal matrix · Cerebrospinal fluid leak · Chordoma · Craniopharyngioma · Endoscopic endonasal approach · Fascia lata · Meningioma

This work has not previously been published or presented in whole or in part.

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Introduction

Extended endonasal approaches (EEAs) offer an advantageous and increasingly popular route to a variety of anterior skull base pathologies including suprasellar meningiomas, craniopharyngiomas, and clival chordomas [55]. Effective watertight reconstruction of the ventral cranial defect is critical and presented a challenge in the development of these techniques [31, 47, 55]. Inadequate closure can lead to cerebrospinal fluid (CSF) leak, meningitis, pneumocephalus, and death [31, 45, 47]. Multiple closure techniques have been introduced to reduce the rate of postoperative CSF leak. Whereas early series reported leak rates from approximately 20 to 50% for the most complex cases [9, 13, 17, 26, 28, 46, 48, 49], more recent publications have demonstrated that rates between 0 and 10% can be achieved in large series [4, 5, 8, 16, 37, 39, 42, 52, 57].

While CSF leak rates have declined, the ideal closure technique and material for each case remain uncertain. Success rates vary based on pathology, size of the cranial base defect, and experience [55]. A wide variety of techniques have been reported, mostly using multilayer constructs of autologous or non-autologous materials, along with bone and free or vascularized mucosal flaps [11, 12, 15, 28, 42, 48, 50]. We have previously reported a comprehensive closure algorithm which achieved sustained low rates of CSF leak in a large series [42]. For large defects with high-flow intraoperative CSF leaks, the protocol employs a multilayer closure with either a gasket-seal [16, 33], when the bony defect permits, or a button-seal [35], when it does not, followed by a nasoseptal flap. However, in the past, both approaches relied on an autologous fascia lata. The graft must be surgically harvested from the lateral thigh, which can significantly increase postoperative pain, result in a disfiguring and uncomfortable defect, and risks additional complications including infection, seroma, and bleeding [20, 36, 54].

We present our initial experience using an acellular dermal matrix (ADM) allograft in lieu of fascia lata as part of our established protocol for anterior skull base repair following extended endonasal approaches and compare the results with a matched series of cases in which fascia lata was used.

Methods

Study design

A single, established closure algorithm for endonasal endoscopic skull base surgeries has been implemented at Weill Cornell Medical Center since January of 2010 [42]. For extended approaches, defined as those for intradural non-sellar lesions in which portions of the tuberculum, planum sphenoidale, olfactory groove, or clivus were removed and a

high-flow CSF leak was encountered, a gasket-seal or button closure is used. Beginning August 2018, ADM was substituted for fascia lata in both gasket-seal and button closures. We reviewed a prospectively acquired database of all such surgeries performed by the senior author (THS). All cases in which ADM was used as part of a gasket-seal or button closure were identified along with a frequency-matched historical cohort of patients receiving fascia lata. Fascia lata patients were matched on the basis of pathology and location (suprasellar meningioma, clival chordoma, or parasellar craniopharyngioma) in reverse chronological order until a matched cohort was obtained (Table 1). The database and medical records were then reviewed for patient and surgical characteristics as well as outcomes including CSF leaks and other potential complications of closure and CSF management. The study was approved by the Weill Cornell Institutional Review Board with a waiver of informed consent.

Surgical technique

All defects were closed in accordance with the previously described algorithm [42], with the exception of the transition from fascia lata to ADM (AlloMAX, Davol Inc., Warwick, RI, USA), an acellular dermal matrix made of collagen and elastin that is fabricated from human cadaver skin. Like other ADM products, AlloMAX is classified as banked human tissue, which does not require US Food and Drug Administration (FDA) approval and is regulated by the American Association of Tissue Banks (AATB) and the FDA guidelines for banked human tissue.

All intradural non-sellar defects with high-flow CSF leaks were preferentially closed first with an inlay of collagen-based dural substitute (Duraform, Natus Medical Inc., Pleasanton, CA, USA), followed by the gasket-seal closure when feasible [16, 33]. For the gasket-seal to be effective, the defect in the skull base must be surrounded by a rim of bone on at least three sides that lie in a single plane. The vertical and horizontal diameters of the defect are measured with either a ruler or cotton patty. A piece of porous polyethylene implant (MEDPOR, Porex Corp., Newnan, GA, USA) is cut to the same size as the defect. The harvested fascia lata or the ADM is then cut to the shape of the defect and porous polyethylene but with an additional 1 cm beyond the edge circumferentially. The porous polyethylene is placed over the ADM and countersunk into the defect so that the edges of the porous polyethylene are wedged just deep to the bony edges of the defect, holding it in place and serving as a rigid buttress. The center of the ADM sits intracranially while the edges remain in the sinus. The ADM is circumferentially wedged between the MEDPOR and the bony edge of the cranial defect creating the watertight gasket-seal.

In cases where there was an inadequate rim of bone or lack of a single plane in which to wedge the MEDPOR for a

Table 1 Comparison of acellular dermal matrix (ADM) and fascia lata cohorts

	ADM	Fascia lata	<i>p</i>
<i>n</i>	19	19	
Age, years, median (IQR)	49.5 (28.8–65.2)	56.5 (35.9–66.3)	0.64
Sex, F, <i>n</i> (%)	11 (58%)	11 (58%)	1.00
BMI, kg/m ² , median (IQR)	27.3 (22.7–31.3)	26.9 (24.2–32.6)	0.67
Obese, <i>n</i> (%)	7 (36%)	8 (42%)	1.00
Tumor type, <i>n</i> (%)			
Meningioma (SS)	8 (42%)	8 (42%)	1.00
Craniopharyngioma (SS)	8 (42%)	9 (47%)	1.00
Pituitocytoma (SS)	1 (5.3%)	0 (0%)	1.00
Chordoma (clival)	2 (11%)	2 (11%)	1.00
Primary vs recurrent, <i>n</i> (%)			
Primary	15 (79%)	15 (79%)	1.00
Recurrent	4 (21%)	4 (21%)	1.00
Prior EEA	1 (5.3%)	2 (11%)	1.00
Prior XRT	3 (16%)	0 (0%)	0.11
Volume, cm ³ , median (IQR)	5.5 (2.8–13.3)	5.5 (3.0–8.8)	0.64
Approach, <i>n</i> (%)			
Transplanum	17 (89%)	17 (89%)	1.00
Transclival	2 (11%)	2 (11%)	1.00
Extent of resection, <i>n</i> (%)			
GTR	14 (74%)	14 (74%)	1.00
NTR	0 (0%)	3 (16%)	0.11
STR	5 (26%)	2 (11%)	0.40
Surgery time, mins, median (IQR)	231 (193–261)	238 (198–255)	0.99
CSF diversion, <i>n</i> (%)			
Lumbar drain	17 (89%)	17 (89%)	1.00
EVD ^a	0 (0%)	2 (11%)	0.49
VPS ^a	1 (5.3%)	0 (0%)	1.00
None	1 (5.3%)	1 (5.3%)	1.00
Lumbar drain duration, median (IQR)	2 (1–3)	2 (1–3)	0.85
Closure, <i>n</i> (%)			
Gasket	16 (84%)	18 (95%)	0.60
Button	3 (16%)	1 (5.3%)	0.60
NS flap, Adherus/Duraseal, Floseal, NasoPore	19 (100%)	19 (100%)	1.00
Postop leak, <i>n</i> (%)	1 (5.3%)	2 (11%)	1.00
Other adverse events, <i>n</i> (%)			
Postop vision change requiring re-exploration	3 (16%)	0 (0%)	0.23
Aseptic meningitis	1 (5.3%)	0 (0%)	1.00
Delayed SDH	0 (0%)	1 (5.3%)	1.00
Follow-up, months, median (range)	5.9 (1.0–12.6)	19.0 (12.7–54.0)	< 0.01

ADM acellular dermal matrix, IQR interquartile range, SS suprasellar, SDH subdural hematoma

^a Placed prior to surgery for hydrocephalus

gasket-seal, a button approach was used in which two layers of ADM are sutured together in the middle for an inlay-onlay composite [35]. Both the inlay and the onlay must be larger than the defect, the former to hold the button in place and the latter to fully cover the defect.

The gasket-seal or button was then covered with a pedicled, vascularized nasoseptal flap [41], which is held in place with fibrin sealant (DuraSeal, Integra LifeSciences Corporation or Adherus, Stryker Co., Kalamazoo, MI, USA). The margins of the nasoseptal flap extend beyond the margins of the graft so

that it is in direct opposition with the bone of the skull base. Thrombin hemostatic matrix (FlosSeal, Baxter Healthcare Co., Deerfield, IL, USA) is placed over the flap for hemostasis and gently packed with a resorbable nasal dressing (NasoPore, Stryker Co., Kalamazoo, MI, USA).

In most cases, a lumbar spinal drain is placed at the beginning of the operation and used to introduce intrathecal fluorescein [43] and for intermittent drainage for at least 24 h after surgery. Postoperative patients were administered with broad-spectrum antibiotics while the spinal drain was in place and a standard dexamethasone steroid taper.

Patients are seen by the otolaryngologist for nasal hygiene on postoperative day 10 and at 6 weeks, 12 weeks, and 24 weeks.

Statistical analysis

Univariate characteristics and outcomes were compared by Fischer exact test for categorical data and Mann-Whitney *U* test for continuous and discrete numerical data. Confidence intervals for proportions were calculated using the binomial exact calculation. Power analysis was performed assuming a 10% population CSF leak rate with fascia lata and a 10% non-inferiority limit to determine required numbers to demonstrate non-inferiority of ADM with 80% power at the 5% significance level.

Results

Nineteen consecutive patients underwent watertight skull base repair following expanded endoscopic endonasal approaches using ADM in lieu of fascia lata as part of the gasket-seal or button closures (Tables 1 and 2). All patients had high-flow intraoperative CSF leaks. There was 1 postoperative CSF leak at the last follow-up (median 5.9 months, range 1.0–12.6 months).

The ADM cohort had a median age of 50 years (range 7–82), including 3 pediatric patients and 5 patients over the age of 65. There were 11 female and 8 male patients. Mean BMI was 29.3 ± 9.2 kg/m³, including 7 obese patients (BMI ≥ 30). There were 8 suprasellar meningiomas, 8 suprasellar craniopharyngiomas, 1 suprasellar pituicytoma, and 2 clival chordomas. Fifteen patients had first time operations and 4 had reoperations, including 3 with prior radiation therapy and 1 with a prior EEA (a staged procedure on the same admission). The median tumor volume was 5.5 cm³ (IQR 2.8–13.3 cm³). Gross total resection (GTR) was achieved in 14 patients and subtotal resection (STR, <95%) in 5. All patients had high-flow intraoperative CSF leaks. Seventeen patients had a perioperative lumbar drain for median of 2 days (IQR 1–3 days). One patient had a prior ventriculoperitoneal shunt (VPS), and CSF diversion was not used in one patient.

Seventeen patients received a gasket closure, and 2 received a button closure. All patients received a nasoseptal flap held in place with a layer of Adherus or Duraseal glue followed by FlosSeal and NasoPore packing.

There was only 1 CSF leak (5.3%, 95% CI 0.1–26.0%) in the ADM cohort at the last follow-up. Patient 17 was a 27-year-old male with a BMI of 31.0 who underwent resection of a craniopharyngioma without immediate complication and with improvement in his preoperative vision deficit. He was readmitted POD 16 with a CSF leak without infectious symptoms. The gasket-seal was found to be dislodged and was revised. He underwent lumbar drainage for 5 days and a short course of broad-spectrum antibiotics, which was stopped after CSF cultures remained negative.

A matched fascia lata cohort was similar to the ADM cohort on all measured variables with the exception of follow-up, attributable to the historical nature of the comparison group (Tables 1 and 3). There were 2 CSF leaks (10.5%, 95% CI 1.3–33.1%) in the fascia lata cohort, both of which occurred less than 1 week from surgery. Patient A, who underwent resection of a clival chordoma and had a gasket-seal closure, developed a leak postoperative day (POD) 5, which was managed with lumbar drainage and antibiotics without further complication. Patient K, a multiply recurrent craniopharyngioma patient who received a button closure, was readmitted POD 6 with a leak requiring two reoperations and which was ultimately complicated by meningitis and hydrocephalus requiring a prolonged hospitalization. In addition, one patient developed chronic bilateral subdural hematomas (SDH) requiring evacuation 1.5 months after surgery.

The risk of CSF leak was not significantly different in the ADM group compared with the fascia lata group (OR 0.47, 95% CI 0.04–5.70, $p = 1.00$). The present study has a power of 19.1% at the 5% confidence level. If we assume a CSF leak rate of 10% with fascia lata based on our preliminary sample and reported rates in the literature, we would need 224 patients (112 in each group) to demonstrate non-inferiority of ADM with a 10% limit and 80% power at the 5% significance level.

Three patients who received ADM gasket-seal closures had new or worsened postoperative vision deficits that required re-exploration. None had observed vascular injury or vasospasm intraoperatively. Patient 1 experienced a delayed near-complete loss of vision in the left eye after vomiting in the recovery room several hours after surgery. On return, the OR there was no leak and the gasket was not dislodged but it may have shifted slightly. It was revised and replaced, after which her vision immediately returned to baseline. Patient 8 woke immediately after surgery with new blurriness in the left eye. On exploration, the graft was not compressing the nerve but it was nonetheless replaced. There was no significant improvement with hypertension and hypervolemia but some improvements at the 4-month follow-up. Patient 18 developed delayed complete loss of vision (no light perception) in the right eye

Table 2 Acellular dermal matrix cohort

Number	Age	Sex	BMI (kg/cm ³)	Pathology	Primary (1°) vs recurrent	Volume (cm ³)	EOR	Closure	LD	LD duration (days)	Complications	F/U (months)
1	31	F	27.3	Meningioma (SS)	1°	5.5	GTR	Gasket	Yes	3	Re-exploration	14.6
2	65	F	31.5	Meningioma (SS)	Recurrent (prior crani and XRT)	0.2	GTR	Gasket	Yes	1	None	13.2
3	9	F	21.8	Craniopharyngioma (SS)	Recurrent (prior crani and XRT)	11.6	STR	Gasket	Yes	4	Chronic sinusitis	10.6
4	40	F	21.1	Meningioma (SS)	1°	5.3	GTR	Gasket	Yes	2	None	9.2
5	66	F	29.9	Meningioma (SS)	1°	2.3	GTR	Gasket	Yes	1	None	9.0
6	63	M	53.7	Chordoma (clival)	1°	14.3	STR	Button + fat	Yes	7 ^c	None	8.8
7	7	M	23.6	Craniopharyngioma (SS)	Primary (prior transventricular biopsy and VPS)	10.6	GTR	Gasket	No, V-P-S ^b	NA	None	8.6
8	50	F	38.1	Meningioma (SS)	1°	6.6	GTR	Gasket	Yes	1	Re-exploration	7.9
9	79	M	30.0	Craniopharyngioma (SS)	1°	0.4	GTR	Gasket	Yes	1	None	7.0
10	25	M	39.9	Chordoma (clival)	Primary (prior staged EEA) ^a	26.1	GTR	Button + fat	Yes	2	Chemical meningitis	5.8
11	83	F	20.8	Craniopharyngioma (SS)	Primary	2.4	STR	Gasket	No	NA	None	5.2
12	49	F	24.6	Meningioma (SS)	1°	3.2	GTR	Gasket	Yes	1	None	4.0
13	64	F	21.6	Meningioma (SS)	Recurrent (prior crani)	4.6	GTR	Gasket	Yes	1	None	3.3
14	53	F	24.2	Pituitaryoma (SS)	1°	0.8	GTR	Gasket	Yes	1	None	3.1
15	45	M	47.1	Craniopharyngioma (SS)	Recurrent (prior crani and XRT)	15.8	STR	Gasket	Yes	1	None	2.8
16	27	M	31.0	Craniopharyngioma (SS)	1°	15.0	GTR	Gasket	Yes	2	CSF leak (POD 16)	1.4
17	8	F	17.0	Craniopharyngioma (SS)	1°	37.2	GTR	Gasket	Yes	5	None	1.2
18	71	M	28.7	Craniopharyngioma (SS)	1°	4.8	GTR	Gasket	Yes	3	Re-exploration	1.0
19	69	M	25.4	Meningioma (SS)	1°	12.3	STR	Button	Yes	3	None	1.0

CSF cerebrospinal fluid, *crani* craniotomy, *EEA* endoscopic endonasal approach, *EOR* extent of resection, *F/U* follow-up duration, *GTR* gross total resection, *LD* lumbar drain, *NA* not applicable, *SS* suprasellar (including planum sphenoidale, tuberculum sellae, and diaphragm), *STR* subtotal resection, *XRT* radiation therapy

^a Multi-stage procedure for large, complex chordoma involving occipital cervical fusion, initial EEA for partial resection, and then reopening of closure 5 days later for completion

^b Ventriculoperitoneal shunt placed prior to EEA for hydrocephalus

^c Patient failed initial clamp trial with increased nasal leaking postoperative day (POD) 4, which resolved with increased drainage to 10 cc/h. Drain clamped POD 6 and removed POD 7 without further leak

several hours after the surgery. The graft was removed and replaced without evidence of hematoma or compression, but vision dramatically improved with hypertension and hypervolemia over the next several days with reliable finger counting in the affected eye at discharge.

Patient 10, in the ADM group, underwent a multi-stage procedure for a large, complex chordoma and developed chemical meningitis 3 weeks after the procedure. He presented with headache, neck pain, fever, and an inflammatory CSF profile. He was readmitted for 3 days and treated with antibiotics (until cultures were negative at which point they were

discontinued) and a steroid taper, after which symptoms resolved.

Discussion

In this paper, we have demonstrated that reconstruction of high-flow CSF leaks following extended endoscopic endonasal procedures may be effectively completed using an ADM allograft, in lieu of fascia lata as part of the gasket-seal or button closures. This is significant because these closure

Table 3 Fascia lata cohort

Pt.	Age	Sex	BMI (kg/m ³)	Tumor type	Primary (1°) vs recurrent	Volume (cm ³)	EOR	Closure	LD	LD duration (days)	Complications	F/U (months)
A	81	F	22.3	Chordoma (clival)	1°, prior VPS	0.5	NTR	Gasket	Yes		2 CSF leak (POD 5)	54.0
B	68	M	26.9	Chordoma (clival)	1°	4.8	GTR	Gasket	No	NA		48.0
C	50	F	49.6	Meningioma (SS)	1°	6.4	GTR	Gasket	Yes		1 None	33.3
D	27	F	18.3	Meningioma (SS)	1°	5.7	GTR	Gasket	Yes		1 None	33.0
E	75	F	40.1	Meningioma (SS)	Recurrent, prior crani	0.9	STR	Gasket	Yes		2 None	32.8
F	53	F	33.5	Meningioma (SS)	1°	8.1	GTR	Gasket	Yes		1 None	30.6
G	65	F	23.6	Meningioma (SS)	1°	20.9	NTR	Gasket	Yes		2 None	28.2
H	61	F	32.0	Meningioma (SS)	1°	2.1	GTR	Gasket	Yes		1 None	26.1
I	35	F	26.6	Meningioma (SS)	1°	0.5	GTR	Gasket	Yes		4 None	19.0
J	76	M	33.1	Craniopharyngioma (SS)	1°	5.7	GTR	Gasket	Yes		3 None	18.1
K	57	M	31.8	Craniopharyngioma (SS)	Recurrent, prior EEA and XRT	2.8	NTR	Button	Yes		3 CSF leak (POD 6)	17.4
L	41	M	31.0	Craniopharyngioma (SS)	Recurrent, prior EEA	3.6	GTR	Gasket	Yes		2 None	17.1
M	10	M	25.1	Craniopharyngioma (SS)	Recurrent, prior transventricular drainage	9.4	STR	Gasket	Yes		1 None	14.5
N	36	M	38.8	Craniopharyngioma (SS)	1°	14.4	GTR	Gasket	No, E-V-D ^a		4 ^b None	14.4
O	59	F	24.9	Craniopharyngioma (SS)	1°	3.1	GTR	Gasket	Yes		2 None	14.4
P	76	F	29.2	Meningioma (SS)	1°	5.5	GTR	Gasket	Yes		3 SDH	14.4
Q	56	M	26.7	Craniopharyngioma (SS)	1°	16.7	STR	Gasket	No, E-V-D ^a		8 ^b None	13.0
R	31	F	22.8	Craniopharyngioma (SS)	1°	5.6	GTR	Gasket	Yes		2 None	13.0
S	27	M	18.8	Craniopharyngioma (SS)	1°	5.5	GTR	Gasket	Yes		3 None	12.7

CSF cerebrospinal fluid, *crani* craniotomy, *EOR* extent of resection, *F/U* follow-up duration, *GTR* gross total resection, *LD* lumbar drain, *NA* not applicable, *NTR* near-total resection (95–99%), *SDH* subdural hematoma, *SS* suprasellar (including planum sphenoidale, tuberculum sellae, and diaphragm), *STR* subtotal resection (< 95%), *XRT* radiation therapy

^a External ventricular drain (EVD) placed prior to endoscopic endonasal surgery for hydrocephalus

^b Reflects duration of EVD in place primarily for hydrocephalus management rather than CSF leak prevention. Not included in the summary statistics

techniques are among the most reliable reported in the literature, but they have previously relied on harvested fascia lata graft. The modification spares the patient potential donor site pain and complications yet does not seem to increase the risk of CSF leak or other complications.

Postoperative CSF leaks are a serious complication of expanded endoscopic endonasal approaches. CSF fistulae increase the risk of meningitis up to 100-fold [23, 31] and may lead to other dangerous sequelae such as tension pneumocephalus and subdural hematoma. Improvements in technique have fortunately brought reported CSF leaks down from the 20–50% seen in early series [9, 13, 17, 26, 28, 46, 48,

49]. For expanded approaches, the uses of a vascularized, pedicled nasoseptal flap [22, 27, 39, 57] and CSF diversion with perioperative lumbar drainage [58] have both been shown to decrease CSF fistula formation. However, there remains a wide variety of primary defect repair techniques, mostly using multilayer constructs of autologous or non-autologous materials [11, 12, 15, 28, 42, 48, 50].

We have previously reported a single closure protocol with a minimal variation which achieved sustained low rates of CSF leak in a large series [42]. The protocol preferentially uses a gasket-seal, when the bony defect allows, and a button closure when it does not, both then followed by a nasoseptal

flap. That reconstruction strategy evolved from the early experience of our endonasal program. Other than the advent of the nasoseptal flap [39, 41], there was a concerted effort to shift from autologous to allograft materials to minimize both the risk of CSF leak and the overall invasiveness of the procedure. The gasket-seal began as an onlay of fascia lata buttressed by a piece of vomer [32]. We then began incorporating porous polyethylene when the vomer was not adequate to create a “gasket-seal” closure. Porous polyethylene could more readily be fashioned to the precise size of the defect, allowing it to be wedged over fascia lata into the defect, creating both a watertight seal and a rigid buttress [16, 33]. We also migrated away from using an inlay of fat graft to reduce the “dead space” and now prefer collagen-based dural substitute for this purpose. In the present series, we have entirely removed harvested fascia lata from our closure protocol and eliminated the use of any donor sites in the gasket-seal, our preferred closure. Only the less frequently used button closure still sometimes requires fat for a non-rigid buttress and additional CSF barrier.

The elimination of fascia lata is significant as its harvesting may result in surgical complications, pain, and impaired cosmesis [20, 54]. Complication rates as high as 11% have been reported, with the most common being incisional cellulitis (7%) and seroma (3%) or hematoma (1%) formation [54]. In a questionnaire-based study of patients’ perceived quality of life following transsphenoidal surgery, pain from fascia lata donor sites was more frequently bothersome than that from the nasal cavity itself [36]. In another survey of 55 patients who underwent fascia lata harvesting for endoscopic endonasal skull base repair, pain at rest was still present 6 months following surgery in 52% of patients (mild (75%) or moderate (25%)) and 40.9% reported pain on walking (mild (76%) or moderate (23%)). Muscle prolapse was evident in 13% of patients; hypoesthesia was present in 9% [20]. This is in line with other series demonstrating some type of symptom in 50% of patients following fascia lata harvest [54].

The desired qualities of a repair material are strength, revascularization, and integration into host tissues. Autologous fascial grafts have long been known to become well-vascularized and integrated [10]. ADM, such as AlloMax, is a sterile sheet of acellular dermal collagen that is derived from human tissue and retains their constituent architecture. ADM has shown early cell ingrowth and revascularization with comparable strength with prosthetics [3, 38, 40, 51]. Used first in the treatment of burn wounds, ADM has been found to have utility in periodontal surgeries, dural replacements in neurosurgery, and abdominal, breast, and head and neck reconstruction surgeries, among other uses [1, 25, 30, 53].

Several centers have reported using ADM products exclusively or in conjunction with other grafts in skull base reconstruction, though to our knowledge, it has not previously been

reported as a substitute for fascia lata in gasket-seal or button closures, and the present series is the largest of entirely high-flow expanded approaches (Table 4) [2, 6, 17–19, 24, 26, 34, 44, 56]. Most large series reported using it to repair primarily low flow leaks such as those seen following pituitary macroadenoma resection [6, 18] or in encephalocele repair [19, 34]. The Pittsburgh group reported an early experience with ADM to repair large ventral skull base defects [17, 26, 48]. Rather than a gasket-seal or button, their protocol involved a Duragen inlay, followed by another ADM, AlloDerm RTM (Biohorizons, Birmingham, AL, USA), sutured to the dura with nitinol u-clips, and then a second, larger AlloDerm RTM onlay overlapping the margins of the repair. This was then covered with a fat graft and held in place with a Foley catheter balloon. However, reported CSF leak rates were as high as 20–30% with this technique [48]. A later series combining a single layer of AlloDerm RTM and a nasoseptal flap reported a CSF leak rate of 10.7% overall and 14.5% for intra-arachnoidal lesions [28].

Limitations

CSF leak has become a relatively rare event and a very large series will be needed to statistically compare leak rates. Our power analysis, which assumes a 10% population leak rate with fascia lata and allows a generous 10% non-inferiority limit, estimates that at least 112 ADM cases will be needed. One could argue that a possible increased CSF leak of 10%, double the current rate, is unacceptable and reducing this non-inferiority limit would further increase sample size requirements (e.g., a 5% limit would increase the total sample size to 445). Demonstrating equivalence or superiority would further increase the sample size, as would an increase in power above 80%. Given the relative rarity of these extended approaches, small series in the literature, and those techniques continue to evolve over time, it would not be realistic to attain such large sample sizes and preliminary results may drive best practices.

While our experience with ADM remains early and we do not yet have sufficient experience to statistically demonstrate non-inferiority, the single CSF leak in our initial 19 cases is promising. Other than the substitution of ADM for fascia lata, we used the same protocol that has been in place at our institution since 2010 which has been highly successful [16, 42]. The ADM cohort was similar to the matched fascia lata cohort and included pathologies with high rates of CSF leak in the literature including meningioma (pooled 9.8% [55]), chordoma (pooled 11.8% [55]), and craniopharyngioma (range 14.6–23.4% in recent series from other centers [4, 29, 55]). There were no purely sellar cases, which have the lowest rate of postoperative CSF leak (4.8% [55]). Most patients had parasellar and anterior fossa defects, which have pooled leak rates of 9.0 and 13.0% [55], respectively. The series did include 2 patients with posterior fossa/clival defects, which are

Table 4 Reported uses of acellular dermal matrix in endoscopic skull base surgery

Publication	Number	Pathology	Intraop CSF leak, n (%)	Repair method	NS flap	Lumbar drain	Postoperative CSF leak rate	Other repair complications
Citardi et al. [6]	13	Pituitary adenoma	5 (38%)	ADM + septal cartilage/bone + fibrin glue	No	No	1 (7.6%)	1 sphenoid sinusitis
Lorenz et al. [34]	34	Various incl. 9 (26%) CSF leak (iatrogenic and spontaneous), 24 (71%) pituitary adenoma	21 (62%)	ADM inlay + septal cartilage/bone + 2nd ADM inlay + mucosal free graft + fibrin glue	No	Yes	2 (6%)	None
Germani et al. [19]	55	Various, incl. 21 (38%) meningioencephalocele, 10 (18%) esthesioneuroblastoma	NR	30/55 (55%) included ADM; of these ADM alone (40%), ADM + mucosal graft (50%), ADM + bone (7%), ADM + cartilage + mucosal graft (3%)	No	11 (20%)	1 (3%)	None
Ismail et al. [24]	21	CSF leak: 12 (57%) spontaneous, 3 (14.3%) iatrogenic	100%	ADM inlay + fibrin glue + ADM onlay + fat graft + fibrin glue	No	Yes	2 (10%)	None
Snyderman et al. [48]	450	Various	450 (100%)	Duragen inlay + ADM sutured to defect + ADM onlay + fat + Surgicel + Foley balloon	No	Dependent on degree of leak	20–30%	NR
Gardner et al. [17]	16 ^a	Craniopharyngioma	16 (100%)	Duragen inlay + ADM onlay + fat ± NS flap + fibrin glue + Foley balloon	Some ^a	Yes	11 (58%)	None
Sautter et al. [44]	9	CSF leak: 5 (56%) iatrogenic, 4 (44%) spontaneous	8 (100%)	ADM inlay + ADM onlay ± bone/cartilage ($n=3$) ± fat ($n=1$) + mucosal free flap	No	7 (88%)	2 (25%)	NR
Kassam et al. [28]	75	Various	75 (100%)	Duragen inlay ± ADM onlay + NS flap + fibrin glue + packing/Foley balloon	Yes	Dependent on degree of leak	8 (10.7%)	1 epistaxis
Eloy et al. [14]	10	Various cribriform tumors	NR	Fascia lata inlay + ADM inlay/onlay + NS flap	Yes	No	0 (0%)	NR
Gaynor et al. [18]	163	Pituitary adenoma	100 (61%)	ADM inlay + collagen sponge + ADM overlay	No	No	2 (1.2%)	1 meningitis
Alvarez Berastegui et al. [2]	1	Empty sella ^b	No	ADM + injectable bone substitute (if intraop leak)	Yes	Yes	0 (0%)	None
Yoo et al. [56]	2	Esthesioneuroblastoma	2 (100%)	ADM single-layer	No	NR	0 (0%)	1 infection

ADM acellular dermal matrix, CSF cerebrospinal fluid, Intraop intraoperative, NR not reported, NS nasoseptal

^aNumber of closures using acellular dermal matrix (ADM) protocol, including nasoseptal flap, not available

^bTreated prolactinoma with sagging of optic chiasm into a large, empty sella

associated with the highest rates of failure (19% [55]). The patients also had many of the other potential risk factors for CSF leak including larger defects [21, 58], opening of an arachnoid cistern or ventricle [48], obesity [7, 48], and prior radiation or surgery [48].

The 3 cases of postoperative vision decline in the ADM group also did not meet statistical significance but warrants continued monitoring of results. The immediate improvement with revision of the gasket-seal in one patient is likely related to the closure, which we attribute to direct pressure from the solid porous polyethylene and have previously observed in one fascia lata gasket-seal case not included in our matched cohort. In the case that responded to hypertension and hypervolemia, we suspect vasospasm while in the one that did not respond, we suspect an ischemic event or trauma to the nerve from tumor dissection. We nonetheless recommend immediate re-exploration without delay in the event of vision decline following a gasket-seal closure to maximize the chance of recovery in the event that direct pressure is responsible. Additional interventions include substituting a button closure if the gasket cannot be safely revised with confidence that the nerve is free of pressure.

Finally, it should be noted that there is likely a learning curve with any complex skull base closure, and results may not be immediately generalizable. Several centers have reported the surgeon experience is an important factor with improved results later in reported series [4, 27–29].

Conclusion

ADM may be a viable non-autologous alternative to fascia lata for watertight repair following extended endonasal approaches when using either the gasket-seal or button closures, reducing or eliminating the need to harvest autologous graft material. Our preliminary series included patients at high risk of CSF leak based on defect location, tumor pathology, and other patient and surgery characteristics. These patients were spared the known pain, side effects, and complication risks of harvesting fascia lata. Given the low rate of CSF leak with current techniques, an extremely large series would be needed to statistically demonstrate non-inferiority.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (Weill Cornell Medicine Institutional Review Board) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

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