Clinical Value of Hernia Mesh Pathology Evaluation

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BACKGROUND: Hernia mesh removal is growing in demand. Meanwhile, there is no standard for handling the mesh specimen or any consensus on the clinical value of the surgical pathology findings.

STUDY DESIGN: All hernia mesh specimens gathered from 2013 to 2018 were analyzed. Patients were categorized based on indication for mesh removal. The "mesh reaction" group included those with clinical reaction deemed to be related to the mesh material. The "mesh nonreaction" group included patients who had mesh removed for a clinical indication unrelated to the mesh material.

RESULTS: One hundred and one patients had 115 mesh specimens that were microscopically evaluated. Patients with clinical diagnosis of mesh reaction were significantly younger (39 vs 56 years; $p = 0.023$) and more likely to be female (71% vs 39%; $p < 0.001$) than those without mesh reaction. Although the clinical symptoms were significantly different, the pathology findings were quite similar.

CONCLUSIONS: There is no clinical value in submitting mesh specimens for microscopic surgical pathology evaluation, regardless of clinical indication for the mesh removal. Also, no clinical claims can be made based on pathology findings from explanted mesh. In addition, microscopic evaluation does incur additional costs to the consumer. We recommend explanted mesh be submitted for gross examination only for documentation purposes in the medical records. (J Am Coll Surg 2019;228:776–781. © 2019 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

Mesh removal is necessary in a subset of patients who have undergone hernia repair. The indications for mesh removal are varied and include infection, chronic pain (eg due to meshoma, nerve entrapment, or mesh erosion), and incidental removal (eg at the time of recurrent hernia repair or unrelated operation).[1,2] A rare indication for mesh removal is serious allergic, immunogenic, or inflammatory reaction to the mesh product itself. We term these as *mesh reactions*.

Microscopic examination of hernia mesh shows an array of foreign-body reactions in the adjacent tissue.[3,4] What has not yet been shown is the clinical value of these pathology findings. As a result, there is currently no standard as to whether explanted mesh should be sent to surgical pathology for microscopic evaluation. Also, it is unclear if any clinical deductions can be made from the pathology findings or whether these findings would change clinical management of the patient.

Meanwhile, we are seeing a surge in the number of patients who are seeking to have their mesh removed. This is reflected not only in our clinical practice, but also in lay discussions in online forums and social media. On Twitter, for example, the term *#mesh* has been tagged more than 180,000 times and *#meshremoval* has been tagged 1,500 times in the past year alone, resulting in close to 250,000,000 potential views on this subject.[5]

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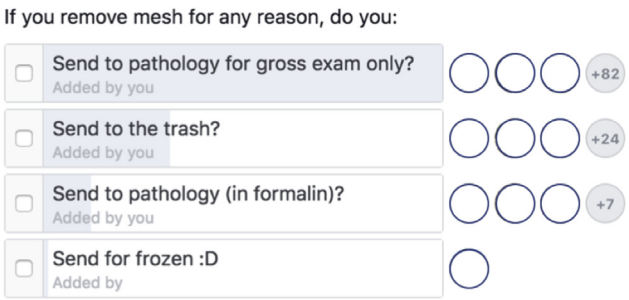

Figure 1. Online survey of international group of hernia surgeons. n = 122.[8]

On the patient discussion board, HerniaTalk.com, there are more than 500 posts specifically discussing mesh removal.[6] Patients seeking medicolegal consultation are required to have their mesh sent to surgical pathology as "potentially unique and important evidence."[7]

To date, there is no standard as to how to handle the mesh specimen. In an online survey of international hernia surgeons, there was no standard practice on the handling of mesh specimens—70% sent mesh for gross examination only, 7% sent their specimen for microscopic evaluation, and 20% discarded the specimen (Fig. 1).[8]

We present our experience with removing hernia mesh to analyze the surgical pathology findings from explanted mesh and correlate these findings with clinical symptoms. Using these data, we can make a judgment about the value of pathologic mesh evaluation.

METHODS

Records were reviewed for all patients who underwent mesh removal by a single surgeon from July 2013 to October 2018. Data collection included patient demographics, area from which mesh was removed, clinical indication for mesh removal, and mesh specimen surgical pathology findings. All of the surgical pathology reports and slides of the specimens were re-reviewed by a board-certified pathologist (BB) to confirm the original reported findings.

The patients were categorized into 2 clinical groups: the "mesh reaction" group included patients who were diagnosed with physical systemic reaction to their implanted hernia mesh, and that reaction was reported as the indication for mesh removal and the "mesh nonreaction" group included all other patients who had hernia mesh removed.

Mesh reaction is defined as a systemic manifestation of symptoms that occur after, and are considered to be related to, implanted mesh. The diagnosis is challenging and only made after an extensive preoperative workup.[2] Patient symptoms are not typical; they present with a syndrome that can include chronic fatigue, joint pain, extremity edema, rash, headache, fevers, nausea, sleep difficulty, concentration difficulty ("brain fog"), bloating, erythema, and/or edema over the area of the implant. All potential causes of these symptoms, including autoimmune disorders, are ruled out preoperatively by blood tests, imaging, and evaluation by specialists, such as rheumatologists and allergists. Many of the patients undergo skin patch allergy testing to the mesh to support a diagnosis of mesh reaction. Surgical removal of the mesh results in resolution, in whole or in part, of the symptoms.

Cost analysis was performed based on relative value unit-based cost to the consumer as determined by the 2018 MediCare Physician Fee Schedule. We used Current Procedural Terminology codes for gross and microscopic pathologic evaluation.[9]

Statistical analysis was done using SPSS (IBM Corp, 2017) with chi-square test or Fisher's exact test for categorical variables and 2-tailed Student's *t*-test for continuous variables. Linear regression analysis was used for univariate analyses. Significance was defined as $p < 0.05$. All patients were consented and enrolled in an IRB-approved, prospectively maintained database.

RESULTS

Patient population

During a span of 5.25 years, 101 patients underwent removal of 115 pieces of mesh, and their mesh specimen pathology was reviewed (Table 1). Of note, 9 patients did

Table 1. Demographic Characteristics of Patients from Mesh Reaction and Mesh Nonreaction Clinical Groups

Characteristic	Mesh reaction	Mesh nonreaction	p Value
Patients, n	17	84	—
Mesh removed, n	27	88	—
Male sex, n (%)	5 (29)	51 (61)	0.023
Age, y, mean (range)	39 (22–58)	56 (21–85)	<0.001
Area of mesh removal, n (%)			0.104
Pelvic/groin	23 (85)	61 (69)	—
Abdomen	4 (15)	27 (31)	—

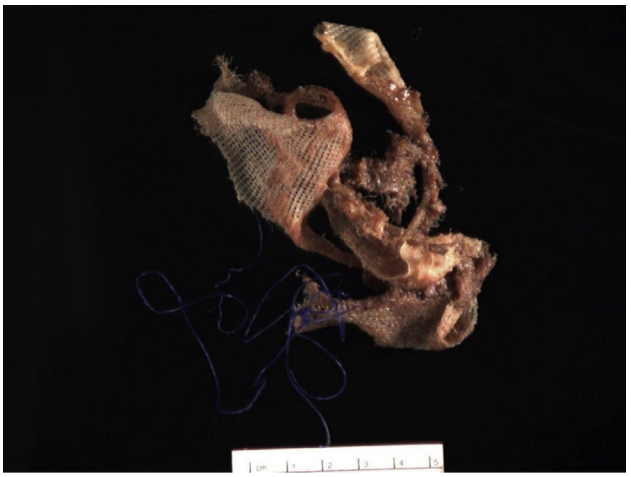

Figure 2. Explanted mesh for gross evaluation only.

not have pathology records available, and 11 patients had their mesh sent to pathology for "gross only" evaluation (Fig. 2). These patients were not included in our analysis.

In the mesh reaction group, 17 (17%) patients had 27 (23%) mesh specimens removed (Table 1). The specimens included polypropylene (17 of 27 [63%]), polypropylene with expanded polytetrafluoroethylene (3 of 27 [11%]), biologic mesh (Strattice; Lifecell) (2 of 27 [7%]), and hybrid mesh (Zenapro; Cook Medical) (1 of 27 [4%]).

In the mesh nonreaction group, 84 (82%) patients had 88 (77%) mesh specimens removed for a variety of other indications not related to the mesh material itself. These other indications included pain (n = 57 [65%]), infection (n = 17 [19%]), hernia recurrence (n = 32 [36%]), neuropathy (n = 16 [18%]), and/or meshoma (n = 13 [15%]). Some patients had more than one indication for mesh removal, for example, meshoma-related pain and hernia recurrence. The specimens in this group included polypropylene (70 of 88 [80%]), polypropylene with expanded polytetrafluoroethylene (9 of 88 [9%]), expanded polytetrafluoroethylene (3 of 88 [3%]), polyester (4 of 88 [5%]), and biologic mesh (Strattice) (1 of 88 [1%]).

The patients in the mesh reaction group were significantly younger ($p < 0.001$) and more likely to be female ($p = 0.023$) compared with the mesh nonreaction group (Table 1). The 2 groups had similar ratios of mesh removed from the pelvis/groin vs the abdomen ($p = 0.104$).

Pathology findings

The surgical pathology findings from the tissue adjacent to the mesh were compared between the 2 clinical groups and found to be similar (Table 2; p = NS for all findings). Commonly noted pathology findings in both the mesh reaction and the mesh nonreaction groups included foreign-body reaction, fibrosis, and chronic inflammation (Fig. 3). Acute inflammation was an uncommon finding.

We analyzed the time that had passed between mesh implantation to mesh removal. The mesh reaction group averaged 2.6 years (range 0.17 to 9.2 years, mode 1.5 years) and the mesh nonreaction group averaged 4.0 years (0.02 to 18.7 years, mode 0.71 years). This was a nonsignificant difference ($p = 0.1099$). We also analyzed whether there was a difference in pathology finding based on this time interval. Using each pathology finding as the dependent variable, time was not found to be a signficant predictor of pathology ($p > 0.05$).

Costs

The pathology Current Procedural Terminology code used for level I gross only evaluation of mesh is 88300, with a Medicare-based cost to the consumer of $16.92. A combination of gross and microscopic evaluation of each tissue adjacent to the mesh can include Current Procedural Terminology codes 88304 or 88305, with a cost to the consumer ranging from $41.76 to $70.20 per slide of specimen processed and analyzed. Most of our patients had only 1 slide examined per specimen. Five patients had 2 slides examined. Each additional microscopic examination increases the cost to the consumer by 250% to 415%.

Using our patient population as an example, if all 115 mesh specimens had been sent for gross examination only, the total Medicare-based cost to the consumer would have been $1,945.80. If microscopic evaluation were also requested, assuming only 1 slide was processed for each specimen, the cost would have increased by an additional $2,856.60 to $6,127.20. Each additional slide processing and evaluation would incur a multiple of that amount.

Table 2. Surgical Pathology Findings of Mesh Removed Mesh Reaction and Mesh Nonreaction Clinical Groups

	Mesh reaction (n = 27)		Mesh nonreaction (n = 88)		
Pathology finding	**n**	**%**	**n**	**%**	**p Value**
Foreign-body reaction	14	52	41	47	0.632
Fibrosis	6	22	19	22	0.945
Acute inflammation	1	4	3	3	0.942
Chronic inflammation	7	26	26	30	0.801

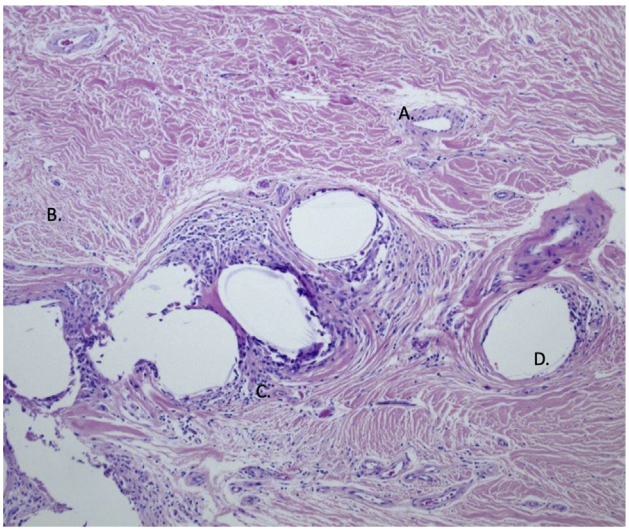

Figure 3. Microscopic pathology slide of explanted mesh and adjacent muscle tissue. (A) Foreign-body giant cell reaction, (B) fibrosis, (C) chronic inflammation, and (D) refractile exogenous material, likely suture or mesh.

DISCUSSION

Mesh is removed after hernia repair for a variety of indications, and the demand for this procedure is increasing.[2] However, there is no standard for how to handle the specimen after it is removed, or understanding of the clinical implications of the pathology findings. Although some researchers have analyzed explanted mesh microscopically, most have not correlated their pathology findings with clinical symptoms.[3,10,11] One study on 33 explanted mesh specimens reports a significantly higher density of nerve fibers in mesh removed for pain.[12] We present the largest study to date analyzing the clinical value of pathology evaluation of explanted mesh.

In our study, we compared the microscopic pathology findings between 2 groups of patients who underwent hernia mesh removal—those who demonstrated a clinical reaction to the mesh material itself ("mesh reaction") and those who did not ("mesh nonreaction"). Presumably, patients with a clinically relevant reaction related to the mesh implant would show different pathology findings at the tissue level than those without clinical symptoms related to the mesh material.

The mesh reaction patients were significantly younger (39 vs 56 years; $p < 0.001$) and more likely to be female (71% vs 39%; $p = 0.023$) than the mesh nonreaction patients. This finding is similar to larger population studies that show younger and female patients are more likely to experience complications after mesh implantation.[13] Location of mesh placement was similar in both clinical groups. We have previously shown that there was no difference in risk of mesh reaction based on type of mesh implant, despite studies showing varying scanning electron microscopy results.[2,14]

Although the 2 groups were significantly different clinically, they were similar in the microscopic pathology findings from their explanted mesh. That is, about half showed evidence of foreign-body reaction. Other common findings included fibrosis and chronic inflammation of the tissue adjacent to the mesh.

Although all specimens had at least 1 of these microscopic findings, most specimens did not have all of the findings. In fact, in the situation of 1 patient having 2 separate mesh specimens removed, we noted that the pathology findings differed between them. This is why we reported our pathology results as per specimen and not per patient.

One reason for varying pathology findings per specimen can be sampling error. Typically, only 1 slide was examined per specimen, and there is little tissue associated with the mesh specimen. Although pathologists consider time to play a role in pathology findings, our study showed no difference in pathology based on time since implantation of the mesh. Host immunity is another possible contributor to differences in pathology finding. We could not assess this from our data.

Acute inflammation from the mesh was a rare finding in both groups. This finding was noted in patients with and without mesh infection. We do not recommend sending infected mesh for surgical pathology. A swab of the specimen can be sent for bacterial culture.

One research protocol analyzed nerve density in hernia mesh specimens.[12] They stratified their results based on 2 clinical groups: those with pain ($n = 19$) and those without ($n = 14$).[12] They did not find a significant difference in nerve density in the tissue adjacent to the mesh. Analyzing 3 blocks per specimen, they did find a significantly higher median nerve density at the level of the mesh itself, and with much wider variance (0.15; range 0.01 to 0.75 per 200× high-power field vs 0.05; range 0 to 0.09 nerves per 200× high-power field). It is not standard to report nerve density in mesh pathology specimens. Reporting nerve twig sizes or numbers are required for skin biopsies for some rare diseases. This process requires cutting the entire specimen, otherwise the findings are not meaningful. At this time, we do not have enough evidence to support routine reporting of microscopic innervation patterns of entire mesh specimens.

The type of tissue reaction seen from hernia mesh has been shown with other implants as well, such as vascular grafts, breast implants, and joint replacements.[15] Nevertheless, pathology findings of foreign-body reaction, fibrosis, and inflammation have been used in lawsuits to

support clinical complications associated with hernia mesh.[16] Our findings do not support such a claim. As we are still learning about the clinical effects of mesh on the human body, we recommend a large population research protocol that specifically analyzes pathology findings related to varying patient populations, clinical symptoms, and mesh types.

Requesting microscopic evaluation of a mesh specimen is not without risks. Based on Medicare 2018 Fee Schedule, there is at minimum an additional $24.84 to $53.28 cost to the consumer per slide that is processed and evaluated. The true costs of microscopic evaluation handed down to the consumer are unknown, as we did not collect health insurance and hospital billing information for our patients. Most pathologists' fee schedules are multiple times the Medicare fee schedule, and some of these charges can be transferred to the patient. Also, the profit or loss to the pathologist for processing and evaluating these specimens is unknown, as the true cost of providing the service of tissue examination is not made known to us.

There is no standard as to how explanted mesh specimen should be handled. In one study on vaginal mesh, 48% of the specimens were sent for microscopic evaluation.[17] Based on our study, we recommend that explanted hernia mesh be sent to the pathology department for gross evaluation only. Gross evaluation helps document that mesh was indeed removed. It will identify the structure and its dimensions. The mesh specimen can be transported either dry or soaked in saline; no formalin is indicated. No additional microscopic evaluation should be considered.

In summary, we confirm that findings of foreign-body reaction, fibrosis, and chronic inflammation are ubiquitous to explanted mesh and do not correlate with patients' clinical symptoms. No clinical deductions can be made from the pathology findings and pathology findings would not change clinical management of the patient. As a result of our study, we have changed our practice: We now send hernia mesh specimens for gross pathology evaluation only. If there is concern for infection, a swab or sample of the specimen is sent for culture. The patient has the option to request retrieval of their specimen from the pathology department, such as in the case of a lawsuit.

CONCLUSIONS

We show no clinical value to microscopic evaluation of hernia mesh specimen, regardless of the indication for mesh removal. Findings of foreign-body reaction, fibrosis, and chronic inflammation are common, expected, and do not support any clinical diagnosis related to the mesh. Mesh removed from an earlier hernia repair should be sent to surgical pathology for gross examination only—not in formalin—for documentation purposes. Any additional evaluation incurs additional cost to the consumer.

Author Contributions

Study conception and design: Mazer, Towfigh
Acquisition of data: Fadaee, Sharma, Capati, Balzer, Towfigh
Analysis and interpretation of data: Fadaee, Mazer, Sharma, Balzer, Towfigh
Drafting of manuscript: Fadaee, Mazer, Sharma, Balzer, Towfigh
Critical revision: Fadaee, Mazer, Sharma, Capati, Balzer, Towfigh

REFERENCES

1. Amid PK. Radiologic images of meshoma: a new phenomenon causing chronic pain after prosthetic repair of abdominal wall hernias. Arch Surg 2004;139:1297–1298.
2. Sharma R, Fadaee N, Zarrinkhoo E, et al. Why we remove mesh. Hernia 2018;22:953–959.
3. Klinge U, Klosterhalfen B, Müller M, et al. Foreign body reaction to meshes used for the repair of abdominal wall hernias. Eur J Surg 1999;165:655–673.
4. Costello CR, Bachman SL, Ramshaw BJ, et al. Materials characterization of explanted polypropylene hernia meshes. J Biomed Mater Res B Appl Biomater 2007;83:44–49.
5. Twitter Analytics. Available at: www.Tweetbinder.com. Accessed November 29, 2018.
6. Hernia Patient Discussion Forum. Available at: www.HerniaTalk.com. Accessed November 29, 2018.
7. Multiple plaintiffs v. Ethicon, Inc. Case #2:12-MD-02327 (D. SD West Virg., filed 2015). Available at: https://www.wvsd.uscourts.gov/mdl/ethicon/pdfs/PTO_190.pdf. Accessed January 6, 2019.
8. International Hernia Collaboration. Available at: www.facebook.com/groups/herniacollab. Accessed November 29, 2018.
9. Medicare Physician Fee Schedule, 2018. Available at: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PhysicianFeeSched/PFS-Federal-Regulation-Notices-Items/CMS-1676-F.html. Accessed November 25, 2018.
10. Iakovlev V, Iakovleva G, Bendavid R. Explanted surgical meshes: what pathologists are missing? Mod Pathol 2015;28:19A.
11. Smith SE, Cozad MJ, Grant DA, et al. Materials characterization of explanted polypropylene hernia mesh: patient factor correlation. J Biomater Appl 2016;30:1026–1035.
12. Bendavid R, Lou W, Grischkan D, et al. A mechanism of mesh-related post-herniorrhaphy neuralgia. Hernia 2016;20:357–365.
13. Fränneby U, Sandblom G, Nordin P, et al. Risk factors for long-term pain after hernia surgery. Ann Surg 2006;244:212–219.
14. Cozad MJ, Grant DA, Bachman SL, et al. Materials characterization of explanted polypropylene, polyethylene terephthalate, and expanded polytetrafluoroethylene composites: Spectral

and thermal analysis. J Biomed Mater Res B 2010;94:455–462.

15. Tang L, Eaton JW. Natural responses to unnatural materials: a molecular mechanism for foreign body reactions. Molecular Med 1999;5:351–358.
16. Brown, et al. Atrium Medical Corporation et al. Case #1: 17-cv-00004 (D. New Hamp., filed 2017). Available at: https://45ijagbx6du4albwj3e23cj1-wpengine.netdna-ssl.com/wp-content/uploads/https-ecf-nhd-uscourts-gov-doc1-11711835179.pdf. Accessed January 6, 2019.
17. Smith TM, Smith SC, DeLancey JO, et al. Pathologic evaluation of explanted vaginal mesh: interdisciplinary experience from a referral center. Female Pelvic Med Reconstr Surg 2013;19:238–241.