Mathematical Model of Anal Canal for Anal Fistula Surgery

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Received: 18 Sep 2023
Accepted: 24 Oct 2023
Published: 30 Oct 2023
J Short Name: ACMCR

Keywords:
Anal fistula; Mathematical model; Skeletal muscle;
Smooth muscle; Sphincter pressure

1. Abstract

1.1. Purpose: Surgery is necessary for the treatment of an anal fistula. However, excision of some sphincter muscle would compromise sphincter integrity or function, which is the cause of a reduced success rate in the long term. In order to develop an appropriate surgical plan, a mathematical model that describes the relationship between the internal pressure of the anal canal and the structure of anal sphincters was established in this study.

1.2. Methods: The anatomical structure of the anal canal and the corresponding sphincter pressure can be measured by endoanal ultrasound (EAUS) imaging and manometry, respectively.

1.3. Results: Based on the information of the internal and external sphincters, two mathematical models, the thick-wall cylinder model and the two-layer model, have been created.

1.4. Conclusions: The proposed thick-wall cylinder and two-layer models could describe the relationship between the internal anal canal pressure and the structure of anal sphincters, from which the influence of complete or partial excision of the sphincter muscle may be estimated.

2. Introduction

Anal fistula, also called fistula-in-ano, and abscesses of the perianal region are different manifestations of the same clinical disease. Perianal abscesses usually develop from the proctodeal glands, which originate from the inter-sphincteric plane and perforate the internal sphincter with their duct. The abscesses may break through into the anal canal and resolve completely, but they can also spread by a submucosal, inter-sphincteric or trans-sphincteric route and develop into fistulas. Superficial infections may lead to submucosal or subcutaneous abscesses. If the abscess perforates the external sphincter, an ischiorectal abscess develops. If inter-sphincteric abscess spreads cranially beyond the levator muscles, a pelvirectal abscess results. Semicircular and, mostly, posterior progression of the infection leads to a horseshoe abscess or fistula formation (Figure 1). A fistula develops as the result of spontaneous perforation of the abscess or a surgical incision in up to 50% of patients with abscesses. Other situations that can result in a fistula include Crohn’s disease, radiation, trauma, and malignancy. The abscess is most often the result of an acute infection in the internal glands of the anus. Occasionally, bacteria, fecal material, or foreign matter can clog the anal gland and create a condition for an abscess cavity to form. The symptoms of perianal fistula depend on the severity of the inflammation. Bland fistulas may excrete pus, sometimes serous fluid and rarely feces, leading to pruritus, itching, and skin maceration. Fatigue and general malaise, as well as accompanying fever or chills, are also common. Severe symptoms occur only occasionally when spontaneous closure of the fistula leads to recurrent abscess formation [6, 14, 23]. Anal fistulas can be categorized into inter-sphincteric, trans-sphincteric, supra-sphincteric, and extra-sphincteric based on the relation-
ship of the fistula to sphincter muscles, either simple or complex. A simple anal fistula includes low trans-sphincteric and inter-sphincteric fistulas that cross 30% of the external sphincter. Fistulas are complex if the primary tract includes high trans-sphincteric fistulas with or without a high blind tract, suprasphincteric and extra-sphincteric fistulas, horseshoe fistulas, multiple tracks, an anteriorly lying track in a female patient, and those associated with inflammatory bowel disease, radiation, malignancy, pre-existing incontinence, or chronic diarrhea.

Although spontaneous recovery occurs, recurrence is more common. So the infected anal glands and ducts must be removed to allow healing of the tract. Surgery may be performed at the same time as the drainage of an abscess, although sometimes the fistula does not appear until weeks or years after the initial drainage. Staged or multiple operations may be required. The surgery option (i.e., fistulotomy, seton, advancement flap procedures, fibrin glue, bioprosthetic plug) depends on the position of the anal fistula. If the fistula is a straightforward, a fistulotomy may be performed. 85-95% of cases are treated by fistulotomy for straightforward fistula. This procedure involves connecting the internal opening within the anal canal to the external opening, creating a groove that will heal from the inside out, and often requires dividing a small portion of the sphincter muscle, which has the unlikely potential to affect the control of bowel movements, and cutting open the whole length of the fistula in order to flush out the contents, which heal into a flattened scar one to two months later. A more complicated fistula, such as a horseshoe fistula (where the tract extends around both sides of the body and has external openings on both sides of the anus), is usually treated laying open just the segment where one fuse joins and the remainder of the tracts is removed. A seton is a piece of thread (silk string or rubber band) left in the fistula tract for patients at high risk of developing incontinence when the fistula crosses the sphincter muscles. During advancement flap procedures, the fistula tract is not removed from the tract or from the skin around the anus, and the flap is re-attached where the opening of the fistula was, which reduces the amount of sphincter muscle to be cut. The operation is effective in about 70% of cases. The fibrin glue is injected into the fistula to seal the tract, and then the opening is stitched and closed, which is currently the only non-surgical treatment option. It is a simple, safe, and painless procedure, but its long-term results are poor with the success rate dropping from 77% to 14% after 16 months. Bioprosthetic plug in the shape of a cone is made from human tissue and used to block the internal opening of the fistula. Two trials show success rates of over 80%, but long-term success rates are uncertain. Most of the operations can be performed on an outpatient basis, but may occasionally require hospitalization. After surgery, most people are prescribed medicine for pain relief. Antibiotics are usually not needed but may be required for some people, including those with diabetes or decreased immunity. Complications after surgery can include heavy bleeding, increased pain, swelling or discharge, a high temperature of 38°C (100.4F) or more, nausea, constipation, difficulty passing urine, and infection.

The fistula should be classified prior to surgery by endoanal ultrasound (Figure 2) [4] or MRI [8, 13] or manometry [1, 16], since the crucial point for the appropriate therapeutic management and functional results is the exact preoperative localization of the tract of the fistula. Outcomes following surgical treatment of patients with anal fistulas are related to the eradication of tracts and the internal opening. A total of 102 patients with primary cryptogenic anal fistulas were prospectively examined with a 360-degree rotating 10-MHz EAUS probe equipped with a three-dimensional (3D) imaging system and an injection of hydrogen peroxide through the external opening. The overall concordance between EAUS and surgical findings was 94.1% for primary tracts, 91.2% for internal openings, 96.1% for secondary tracts, 100% for abscesses, and 96.1% for horseshoe tracts. The accurate EAUS assessment of the relationship between fistulas and sphincters has been the main factor in choosing a sphincter-saving surgical procedure, avoiding fecal incontinence [20].

However, in some situations, the fistula involves a significant amount of the anal sphincter muscle, and complete excision or laying open of the tract would compromise sphincter integrity or function. How much muscle can be sacrificed to ensure a cure yet preserve anal function remains a challenge even to the most experienced surgeons. 375 patients (intersphincteric fistula: 180, transphosphincteric: 108, suprasphincteric: 6, extraspahincteric: 6, unclassified: 75) were followed up 29 months after surgery of anal fistula (fistulotomy and marsupialization: 300, seton placement: 63, endorectal advancement flap: 3, and other: 9) [6]. 8% had a fistula recurrence, and 45% complained of postoperative incontinence by univariate and multivariate regression analysis. 59 patients with high anal fistulas of cryptoglandular origin treated with cutting seton (n = 12) or the two-stage seton fistulotomy (TSSF, n = 47) were retrospectively reviewed with similar mean follow-up (27 months for cutting seton and 33 months for TSSF). There were no differences in the rate of fistula recurrence (1 of 12 vs. 4 of 47), difficulty holding gas (6 of 12 vs. 25 of 47), underwear staining (6 of 12 vs. 18 of 47), stool incontinence (3 of 12 vs. 12 of 27), overall incontinence (8 of 12 vs. 31 of 47) and mean incontinence score (4.9 vs. 4.2) as well as the healing time and degree of satisfaction. Both techniques are equally effective in eradicating the fistula, and both are associated with a similar rate of incontinence [5]. Twenty patients whose complex anal fistula (trans-sphincteric: 18, suprasphincteric: 2) was treated with the loose-seton technique (LST) a minimum of 10 years previously were assessed. The success rate of the LST for complex anal fistula falls over time, and the long-term results were lower than those in the short term (4 vs. 13 of 20). Sixteen patients had persisting or recurrent sepsis, necessitating further surgery. In the long term, more external
3. Structure and Function of Muscle

Muscle is a soft tissue in most animals and is primarily responsible for maintaining and changing posture, locomotion, and the movement of internal organs, such as the contraction of the heart. Most muscles in the human body are excitable, contractile tissue that can be classified into striated muscle and smooth muscle.

The elemental contractile unit of striated muscle is the sarcomere, which is composed of overlapping thick and thin myofibrils made of protein myosin and actin, respectively, and bounded by two neighboring Z-lines as shown in Figure 3a [21]. The actin filaments are attached at one end but free along their length to slide with respect to the myosin filaments and to build up chemical connections at different locations with the molecular heads of myosin, which is called a cross-bridge. For each fiber, the maximum force-generating capacity occurs over a certain range of lengths, as shown in Figure 4, which is explained by the sliding-filament model and the cross-bridge cycle [9, 15]. The number of active cross bridges is the maximum at the optimum length of the muscle. When the muscle is stretched beyond it, the number of active cross-bridges decreases because of the decrease in the overlap between the actin and myosin fibers. As the muscle becomes shorter than the optimum length, the thin filaments at opposite ends of the sarcomere first begin to overlap and interfere with each other’s movements, which results in a slow decrease in tension as the sarcomeres get shorter. Then, as the sarcomeres get shorter, the thick filaments come into contact with the Z lines, and the decrease in tension with decreasing length becomes even steeper [25]. The total force generated by a muscle is the sum of the active and passive forces. The active force is generated by many independently cycling actin-myosin cross-bridges when the muscle is stimulated to contract. The passive force is measured before muscle contraction because muscle becomes stiffer when it is distended. It takes increasing amounts of passive force to progressively elongate the muscle cell.

The contractile filaments in striated muscle are highly ordered, which generates the alternating light and dark banding pattern. This banding pattern and the relationship between muscle length and active tension in skeletal muscle are due to overlapping filaments that slide over one another during active shortening. The length-tension relationship is shown in Figure 5. Notice also that the normal operating range is restricted to a narrow band (e.g., skeletal muscles never change length more than about 10%). The contractile mechanism of smooth muscle is similar to that of striated muscle [10]. However, there are some important differences: 1) tension is developed extremely slowly but can be maintained for a long period of time with a very low energy cost; 2) the force is generated over a much broader range of lengths compared to skeletal muscle; 3) it is innervated by the autonomic and enteric nervous systems, which serve to modify the rate and strength of contraction.
4. Thick-Wall Cylinder Model

The anal canal consists of two muscular cylinders. The inner cylinder, called the internal anal sphincter (IAS), is about 3 cm long and a thickened continuation of the circular smooth muscle of the rectum. The outer one, called the external anal sphincter (EAS), is a downward extension of the skeletal muscle of the puborectalis with a length of about 4 cm. Therefore, if the geometry and internal pressure are known, the anal canal can be treated as a thick-wall cylinder with circumferential stress ($\sigma_\theta$). However, since the biomechanical properties of soft tissue are too complex, it is challenging to find an exact solution for this model. With some assumptions, the model can be simplified to make it more manageable for a general prediction. The geometry and pressure are usually measured in a static condition with minor deformation. So

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**Figure 3**: (a) Structure, (b) SEM image, and (c) pathological photo of a skeletal muscle.

**Figure 4**: Length-tension relationship of a muscle fiber [25].

**Figure 5**: Length-tension relationship for (a) skeletal muscle and (b) smooth muscle [21], where $l_0$ is the length at which maximum active force is generated.
it can be assumed that the anal canal is a linearly elastic and isotropic thick wall cylinder, and the circumferential stress ($\sigma_\theta$) within a homogeneous thick wall in general is given below [11]:

$$\sigma_\theta = p\left(\frac{R_i^2}{R_o^2-R_i^2}\right)\left(1 + \frac{R_o^2(i,j)}{r^2}\right)$$

(1)

where $p$ is the internal pressure and $R_i$ and $R_o$ are the inner and outer radius, respectively. However, soft tissue is non-linear, viscoelastic, and anisotropic. In order to make the model more reasonable and practical, the anal canal will be divided into a finite number of elements, as shown in Fig. 6. Each element $(i,j)$ has a specific internal pressure, $p(i,j)$, which can be measured by placing sufficient numbers of pressure sensors along the internal surface of the anal canal. The pressure along the axial direction (i.e., in the different cylindrical layers) can be further presented by dividing the thick wall into $K$ elements. Thus, there are a total of $I*K*K$ elements in this model.

Eq. (1) can be rewritten as below:

$$\sigma(i,j,k) = p(i,j)\left(\frac{R_i^2(i,j)}{R_o^2(i,j)-R_i^2(i,j)}\right)\left(1 + \frac{R_o^2(i,j)}{r(i,j,k)}\right)$$

(2)

Using Eq. (2), the stress of each muscle component in the anal canal wall can be calculated. The relationship between the calculated stress and internal pressure, $p$, is different from the conventional engineering application, where the pressure in the hollow cylinder causes the stress in the cylinder wall. Because the stress generated by the muscle is the underlying mechanism of the internal pressure of the anal canal, the biomechanical properties of the muscle elements can be characterized by the stress, and the pressure change can be estimated if the sphincter is excised partially.

The three-element Hill-type muscle model represents the mechanical response of muscle, as shown in Figure 7 [7]. The model is composed of a contractile component (CC) and two non-linear spring elements: the series elastic component (SEC) and the parallel elastic component (PEC). The active force of the contractile component comes from the force generated by the actin and myosin cross-bridges at the sarcomere level. It is fully extensible when inactive but capable of shortening when activated. The surrounding connective tissues (fascia, epimysium, perimysium, and endomysium) produce the passive force represented by the parallel component when it is stretched, even when the contractile element is not activated, and affect the muscle’s mechanical behavior. The series element represents the tendon and the intrinsic elasticity of the myofilaments. It also has a soft tissue response and provides an energy-storing mechanism. Although both the external and internal sphincters consist of a contractile component and an elastic component, there is a significant difference between them. For the external sphincter, which comprises striated muscle, the active force is controlled by the voluntary nervous system. The passive and active states are well-defined by the absence or presence of neural stimulation. However, the internal sphincter, consisting mostly of smooth muscle, is more complex because the smooth muscle contraction is controlled by the involuntary nervous system through chemical modification (phosphorylation and dephosphorylation) of regulatory proteins attached to the myosin head. Therefore, no unambiguously defined active and passive states have yet been defined for smooth muscle [17]. Fecal incontinence is associated with reduced anal closure pressure and mechanical stress for maintaining tissue closure of the anal canal, resulting in the inability to control the passage of gas or stools through the anus. During the resting situation of a human, the pressure to close the anal canal to prevent fecal incontinence is generated by the passive force of the external sphincter and both the active and passive forces of the internal sphincter. The squeezing pressure is generated by the active force of the external sphincter only. Since it is not possible to acquire EAUS images under dynamic contraction, the anal canal is modeled in its resting state only. Passive fecal incontinence is a more serious and embarrassing social problem for the patient, who is not aware of the leakage and directly relates to the resting pressure.

The stress in the sphincters is produced by a single muscle fiber, which equals the summation of the contractile active stress due to the cross-bridges and passive stress due to the elastic elements in the Hill-type muscle model. The relationship between passive stress $p_{passive}$ and muscle fiber length $l$ is in an exponential way [7, 11, 7, 18]

$$\sigma_{passive} = \sigma_{passive}(l) = \beta e^{\alpha l}$$

(3)

The stress produced by contractile elements in the sphincters depends on the length of the muscle fiber, the specific shortening velocity, and the activation of contractile elements. Active stress $\sigma_{active}$ can be written as [17]:

$$\sigma_{active} = \max(\sigma_{active}) f_{act} f_{r}$$

(4)

where $\max(\sigma_{active})$ is the stress in a fully activated muscle fiber due to the force production of cross-bridge under isometric conditions at the optimal length for the contractile element, $f_{act}$ is the activate state and varies between 0 (none cross-bridge activation) to 1 (full cross-bridge activation), $f_{r}$ denotes the nonlinear relationship between the length of the contractile element $l$ and $l_0$ is the length in which the maximum stress can be generated (Figures 4 & 5), $f_{r}$ is a function that relates the active stress and the nominal longitudinal strain rate. Thus, the stress $\sigma(i,j,k)$ generated in each muscle can be written as:

$$\sigma(i,j,k) = \sigma_{active} + \sigma_{passive} = \max(\sigma_{active}) f_{act} f_{r} + \sigma_{passive}(l)$$

(5)

If only the resting pressure needs to be considered in the treatment planning of anal canal fistula surgery, the active stress within the external sphincter will be omitted since the external sphincter can be controlled voluntarily. For element $(i,j,k)$ located in the external sphincter region, the stress $\sigma^e(i,j,k)$ can be written as

$$\sigma^e(i,j,k) = \sigma_{passive}(l^e) = \beta^e e^{\alpha^e l^e}$$

(6)

For element $(i,j,k)$ located in the internal sphincter the stress $\sigma^i(i,j,k)$ is written as
\[ \sigma^i(i, j, k) = \max \left( \sigma^i_{\text{active}}(i), \sigma^i_{\text{active}}(i) + \sigma^i_{\text{passive}}(i) \right) \]  \tag{7}

In Eqs. (6) and (7), the superscripts \( e \) and \( i \) denote the external and internal sphincters, respectively, \( i \) denotes the length of the sphincters. Obviously, the expression of the stress of the internal sphincter is much more complex, and it is not possible to solve this equation with only one boundary condition, \( p(i, j) \). Referring to Eq. (4), there are three factors affecting the active force of muscle fiber: the length of the muscle fiber, the specific shortening velocity, and the activation of the contractile elements. When considering the maximum resting pressure only, the specific shortening velocity and the state of activation can be assumed at the maximum condition, which means both \( \dot{f} \) and \( \ddot{f} \) are equal to 1. The only factor left is the length of the muscle fiber. However, the exact relationship between stress and the length of smooth muscle has not been discovered yet. A parabolic function is used to describe the stress-length relationship, referring to Figure 5:

\[ \sigma_{\text{active}} = a(i^3) + b i + c \]  \tag{8}

Therefore, Eq. (7) can be rewritten as

\[ \sigma^i(i, j, k) = a(i^3)^2 + b i^2 + c + \beta^i e^{i^j} \]  \tag{9}

Subsequently, the total stress \( \sigma(i, j, k) \) for a muscle element is

\[ \sigma(i, j, k) = \sigma^i(i, j, k) + \sigma^f(i, j, k) = a(i^3)^2 + b i^2 + c + \beta^j e^{i^j} + \beta^k e^{i^k} \]  \tag{10}

Combining Eqs. (2) and (10)

\[ p(i, j) \left( \frac{k^i(i, j)}{\alpha^i(i, j) + \beta^i e^{i^j}} \right) \left( 1 + \frac{k^f(i, j)}{\alpha^f(i, j) + \beta^f e^{i^j}} \right) = a(i^3)^2 + b i^2 + c + \beta^j e^{i^j} + \beta^k e^{i^k} \]  \tag{11}

Eq. (11) represents the relationship between the internal pressure \( p(i, j) \) and the sphincters, which are characterized by constant parameters.\( a, b, c, \alpha^i, \beta^i, \alpha^f, \beta^f \).

5. Two-Layer Model

The two-layer model is created based on the combination of muscle elements. As shown in Figure 8 (each circle represents one muscle element), there are two combination structures of the muscle elements: in series and in parallel. When there is any change in the length of each element, active forces will be generated and passive forces will vary. A combination of muscle elements in parallel will increase the potential force. In a series combination, all elements will bear the same force, increasing the total length. The weakest element will determine the maximum load on the chain. Thus, a series combinations of muscle elements has no advantage with respect to force development, and only in a parallel combination can the forces of muscle elements add up. If there are \( n \) muscle elements and each element is identical, \( F_p = n \cdot F_e \). From an anatomical view, a parallel combination of the sphincter muscle elements will affect the radial thickness of the sphincter. Therefore, the thickness of the sphincter is a very crucial parameter that affects the forces generated by the sphincters as well as the internal pressure of the anal canal.

As shown in Figure 6d, \( h_1(i, j) \) and \( h_2(i, j) \) are the thicknesses of the internal sphincter and external sphincter, respectively, and \( \sigma_1(i, j) \) and \( \sigma_2(i, j) \) are the circumferential stresses generated by the internal sphincter and external sphincter, respectively. Under the equilibrium condition

\[ p(i, j) = \frac{\sigma_1(i, j) h_1(i, j)}{\sin \theta} + \frac{\sigma_2(i, j) h_2(i, j)}{\sin \theta} = 0 \]  \tag{12}

where \( \Delta z \) is the length of element \( (i, j) \) in the \( i \)-direction of the anal axis of the anal canal. By applying an approximation of \( \sin \theta \approx \frac{\Delta z}{z} \) for a very small \( \theta \), Eq. (12) can be rewritten as

\[ p(i, j) R_1(i, j) = \sigma_1(i, j) h_1(i, j) + \sigma_2(i, j) h_2(i, j) \]  \tag{13}

where \( p(i, j) \) can be measured by the anal manometry, \( R_1(i, j), h_1(i, j), \) and \( h_2(i, j) \) can be measured from EAUS images. Eq. (13) shows that the internal pressure, \( p(i, j) \), is not solely dependent on the thickness, \( h_1(i, j), h_2(i, j) \), but also on the stresses \( \sigma_1(i, j) \) and \( \sigma_2(i, j) \) that relate to tissue properties by \( \sigma_1(i, j) = f_1[h_1(i, j), h_2(i, j)] \) and \( \sigma_2(i, j) = f_2[h_2(i, j)] \). Unfortunately, such a relationship between stress and thickness is hard to model exactly. Therefore, there is no simple prediction of the change of both stress (i.e., \( \sigma_1(i, j) \) and \( \sigma_2(i, j) \)) and internal pressure after anal fistula surgery for the decreased \( h_1(i, j) \) and \( h_2(i, j) \). However, the equation Eq. (13) can be expressed by a general function \( f(\cdot) \) as

\[ p(i, j) = f[h_1(i, j), h_2(i, j)] \]  \tag{14}

Although an explicit solution may not be available, an artificial neural network can be applied to find out the relationship between the sphincter thickness and the internal pressure of the anal canal [2, 12, 19]. As a result, an approximate solution to the two-layer model can be sought, which will be used to guide the anal fistula surgery.
Figure 6: Schematic diagram of a finite element model, (a) 3D structure of the thick-wall cylinder model, (b) dividing into a cross-section, (c) dividing into a sector element in each cross-section, and (d) dividing in the radial direction. So the total number of elements is $I*J*K$.

Figure 7: Principal connection schemes of the most common form, CC+SEC, and alternative form, CC, of Hill-type muscle models. CC: contractile component, SEC: series elastic component, PEC: parallel elastic component. It is noted that with passive stretch, where the force across CC is zero, only PEC is stretched in the CC+SEC model, yet both in the CC model. However, because SEC is usually much stiffer than PEC for most muscles, these two models are almost identical [24].

Figure 8: Model of muscle element combination (a) in series and (b) in parallel.

6. Conclusion
Anal fistulas do not heal spontaneously without surgery, and the infected anal glands and ducts must be removed. EAUS or anal manometry could illustrate the localization of the opening of the tract and the anal pressure profile accurately and reliably, respectively. However, the amount of muscle to be dissected to ensure a cure as well as to preserve anal function remains a challenge even for the most experienced surgeons. In order to develop a surgical plan to facilitate the operation, a mathematical model of the anal fistula should be established. Length-tension relationships for skeletal and smooth muscles, two major components of the external and internal anal sphincter, respectively, were reviewed first. Then thick-wall cylinder and two-layer models were proposed to describe the relationship between the internal anal canal pressure and the structure of anal sphincters, from which the influence of complete or partial excision of the sphincter muscle can be estimated. In the next step, the performance and confirmation of these two models will be evaluated.
References


