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Development of a computational tool to simulate the use of synthetic meshes for pelvic organ prolapse repair

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Resumo

O prolapso dos órgãos pélvicos é uma situação clínica caraterizada pelo descaimento da vagina e dos órgãos adjacentes, útero, bexiga, uretra, intestino, e recto, das suas posições naturais, causando a protusão (ou mesmo exteriorização) dos órgãos pélvicos contra a parede vaginal. Esta acontece devido ao estiramento ou enfraquecimento da rede de tecidos que suportam a região pélvica. Este problema tem grande impacto na vida social e profissional das mulheres, sentem um considerável desconforto, sensação de pressão e dor na zona pélvica, por vezes incontinência urinária ou fecal, entre outros. Os tratamentos existentes para esta situação dividem-se em conservativos e invasivos. Os invasivos são direcionados para mulheres com prolapso sintomático, e têm como objetivo corrigir a posição anatómica do pavimento pélvico, para aliviar os sintomas e corrigir alterações funcionais dos órgãos pélvicos. O tipo de procedimento adotado vai depender dos objetivos futuros da mulher, da sua idade, do caso clínico, se pretende voltar a engravidar ou não, sendo que existem abordagens laparoscópica, abdominal e vaginal, e podem ou não envolver o uso de malhas sintéticas. O uso destes implantes ainda é incerto, existem conflitos sobre a sua eficácia, se melhoram os resultados e sobre a segurança da sua utilização. Até recentemente os cirurgiões utilizavam as malhas em cirurgias reconstrutivas, mas a 16 de Abril de 2019 a U.S. Food and Drug Administration proibiu o seu uso em reparações transvaginais, por a sua confiança e eficácia ainda não terem sido comprovados num ensaio clínico em contexto populacional.

Neste sentido, estudar e analisar melhor o comportamento das malhas sintéticas é essencial para perceber melhor o modo de atuação destas e se realmente melhoram os resultados obtidos na cirurgia. Assim, o estudo de modelos computacionais é cada vez mais uma ferramenta útil na medicina, por permitir obter resultados clínicos diretamente do modelo, sem necessidade de executar testes experimentais no próprio paciente. Estudar o comportamento da malha no modelo virtual é importante para aumentar o conhecimento deste tipo de reparações. Para além disso, este modelo pode representar a variabilidade anatómica de paciente para paciente, o que permite criar um modelo personalizado para cada mulher e, posteriormente, desenhar malhas sintéticas adaptadas a cada caso por forma a detalhar a informação pré-cirurgica.

Como tal, esta dissertação tem como objetivo estudar uma malha sintética em específico denominada *Restorelle* e, principalmente, introduzir um estudo inovador sobre estas malhas, atualmente sem literatura publicada a respeito deste tópico, mais concretamente, a incorporação da porosidade no modelo biomecânico da malha sintética. No geral, o processo de estudo foi feito com uma abordagem de modelagem multi-escala, isto é, separando a análise em duas, partindo da micro para a macroanálise, já que é necessário considerar os poros internos e o seu impacto. As simulações numéricas começam com a microestrutura da unidade representativa, a complexa estrutura tricotada de monofilamentos de polipropileno que se repete ao longo desta malha. Em seguida, o modelo completo de malha foi desenvolvido e testado com recurso a simulações de teste de tração uniaxial.

Os resultados obtidos forneceram informação sobre como a unidade representativa se comporta em testes de tração uniaxial, bem como o módulo de Young efetivo extraído do modelo, nas

direções x e y. O modelo poroso desenvolvido para a *Restorelle* mostrou ter uma rigidez superior à desejada, o que pode estar relacionado ao facto de o deslocamento aplicado não ter sido elevado o suficiente ou a necessidade de aprimorar a caracterização do modelo, portanto, análises e investigações adicionais devem ser feitas.

Abstract

The pelvic organ prolapse is a clinical situation characterized by the descent of the vagina and the adjacent organs, uterus, urinary bladder, intestine, and rectum, of their natural positions, causing the protrusion (or even the exteriorization) of the pelvic organs against the vaginal wall. This happens due to the stretching and weakening of the tissue network that supports the pelvic region. This problem has a great impact on women's social and professional life, they feel considerable discomfort, pressure and pain in the pelvic area, sometimes urinary or fecal incontinence, among others. The existing treatments are divided into conservative and invasive. The invasive treatments are meant for women with symptomatic prolapse, and aim to correct the anatomical position of the pelvic floor, to relieve the symptoms and correct functional changes in the pelvic organs. The type of procedure adopted will depend on the future objectives of the woman, her age, clinical case, whether she intends to become pregnant or not, ans such. There are laparoscopic, abdominal and vaginal approaches, and these may or may not involve the use of synthetic meshes. The use of these implants is still uncertain, as there are conflicts about their effectiveness, whether they improve the results, and the safety of their use. Until recently, surgeons relied on the use of meshes in reconstructive surgery, but on April 16, 2019 the U.S. Food and Drug Administration prohibited their use in transvaginal repairs because their reliability and efficacy has not been proven in a clinical trial in a population context.

Thus, studying and better analyzing the behaviour of the synthetic meshes is essential to better understand their function and whether they really improve the results obtained after surgery. Thus, the study of computational models is increasingly a useful tool in medicine, as it allows clinical results to be obtained directly from the model, without the need to perform experimental tests on the patient himself. Studying on a virtual model the behavior of the mesh is important to increase the knowledge of this repair. In addition, this model can represent the variability from patient to patient, which allows to create a customized model for each woman and then to design synthetic meshes adapted to each case in order to detail the pre-surgical information.

Therefore, this dissertation aims to study a specific synthetic mesh named *Restorelle* and, particularly, introduce an innovative study on these meshes, so far with no research published regarding the topic, that is, the incorporation of porosity on a mesh model. Overall, the process of study was a multiscale modeling approach, this is, separating the analysis into two, starting from the micro to macro analysis, as it is necessary to consider the inner pores and their impact. The numerical simulations start with the microstructure of the representative unit, the knitted complex structure of polypropylene monofilaments that repeats through the mesh. Afterwards, the entire mesh model is developed and tested with uniaxial tensile testing simulations.

The results provide the information on how the representative unit behaves in uniaxial tensile testing, as well as the extracted effective Young's modulus, in both the x- and y-direction. The developed porous model of *Restorelle* showed to have a higher stiffness than desired. It can be related to the fact that the displacement applied was not high enough or the characterization of the model should be improved, thus further analysis and investigation is needed.

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Rafaela

"We are drowning in information,
while starving for wisdom."

Edward Osborne Wilson

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Abbreviations

ATFP	Arcus Tendineus Fasciae Pelvis
ASC	Abdominal Sacrocolpopexy
AUGS	American Urogynecologic Society
CAD	Computer-Aided Design
EMG	Electromyography
FDA	U.S. Food and Drug Administration
FEA	Finite Element Analysis
FEM	Finite Element Method
IAP	Intra-abdominal Pressure
IC	Iliococcygeus
ICS	International Continence Society
LSC	Laparoscopic Sacrocolpopexy
MRI	Magnetic Resonance Imaging
PC	Pubococcygeus
PFD	Pelvic Floor Dysfunctions
PFM	Pelvic Floor Muscles
POP	Pelvic Organ Prolapse
POP-Q	Pelvic Organ Prolapse Quantification
PP	Polypropylene
P-QoL	Prolapse Quality of Life Questionnaire
PR	Puborectalis
PU	Pubourethral
PV	Pubovesical
SC	Sacrocolpopexy
SEM	Scanning Electron Microscopy
SS	Sacrospinous
US	Uterosacral

Chapter 1

Introduction

1.1 Context

The pelvic organ prolapse (POP) is a common dysfunction that affects up to 50% of women over 50 years old that have given birth one or more times, with a lifetime prevalence risk of 30-50% [1]. This condition is the major reason for women to go under gynecologic surgery [2]. POP is a type of pelvic floor dysfunction (PFD), along with urinary incontinence, and fecal incontinence. The prevalence of PFD increases with age so, with the rise of life expectancy, the number of women suffering from these disorders will rise substantially in the future, particularly the number of POP cases will increase by 46%, to 4.9 million, from 2010 to 2050 [3]. In fact, a study done by the United States Census Bureau states that the American population aged 85 and older will triple from 2008 to 2050. Considering that most of POP epidemiology information comes from surgical databases, the known prevalence and incidence underestimates the magnitude of this condition, as the number of cases who never seek medical treatment is unrecognized. Women with this condition suffer a significant negative impact on their quality of life, this includes physical, social, and emotional suffering. Also, the economic impact on the health care system is significant. Therefore, it's important to have more in-depth studies regarding these disorders, ensure the clinicians have the adequate knowledge as more women will seek treatment, but also for the detection of women at high risk [3].

POP, also called urogenital prolapse, is characterized by the descent of at least one pelvic organ (bladder, uterus, vagina, or bowel), due to the weakness or damaging of the pelvic muscles and tissues that no longer can support the organs [4]. Some of the functional consequences of POP are urinary incontinence, voiding dysfunction, sexual dysfunction, posthysterectomy vaginal prolapse, and fecal incontinence. Even though some women treat their symptoms with conventional methods, such as medication, behavioral changes, or with reinforcement of intimate hygiene, the ones that feel more incapacitated seek surgical procedures. The fact that 1 in 3 women need further intervention after a surgical operation increases its associated risks to the health of women, besides being disabling and compelling for them. Plus, the procedures are expensive, which greatly increments the economic burden on society [5].

1.2 Motivation

Computational modelling has been a great tool for the design of anatomic structures, as it also allows the analysis and simulation of certain loading conditions and its effect on the biological tissues, thus improving the understanding of studied conditions. The pelvic floor is a complex anatomical region, with elaborate attachments between organs, bone, ligaments, fascia, and muscles, thus, stating the difficulty in obtaining a real representation of the pelvic cavity geometry. The development of a computational model of this region enables the experimentation of various conditions without having to test on living tissues, but also the evaluation of pathologic and biomechanical defects of the pelvic tissues. The model can also be general with a standard pelvic geometry, or it can be personalized to a certain patient, providing a patient-specific study and, perhaps, a personalized treatment [6].

One recurrent invasive treatment is the use of surgical meshes on the vaginal prolapse repair, to hold a certain organ in place. Recently, there has been an increased number of reports to the U.S. Food and Drug Administration (FDA) protesting about the implants complications postoperative. Particularly, since 2007, 2874 complains were presented to the FDA regarding the use of synthetic meshes for POP (1503) and stress urinary (1371) repairs. Furthermore, the rates of recurrence for surgery are very high, so it is especially important these days to study the mechanical impact of these meshes on the organs and tissues of the pelvic floor, to hopefully personalize them and decrease the complications associated. A better understanding of the surgical mesh devices is crucial to prevent women from suffering these potentially avoidable adverse events, that include pain, infection, bleeding, mesh exposure, organ drilling, and many more. More in-depth studies about these synthetic meshes should be performed so that these procedures can be safer for women. In particular, this study aims to introduce an innovative study on these meshes, with no research published regarding the topic. The purpose of the dissertation is to create and represent a model more truthful to the surgical meshes, by introducing the porosity to the geometrical model, instead of a continuous structure as seen in the literature. POP is a condition affecting millions of women and increasing, having a strong impact on their daily life, so advances in the understanding of this dysfunction and the treatments will improve many lives [1].

1.3 Objectives

This dissertation aims to understand the complex structure of a surgical mesh and its impact on the overall behaviour of the device. To do so, the study undergoes different analysis on the space continua, from a study of the microstructure to the full macro mesh, this approach is also known as a multiscale modeling method. Therefore, the numerical simulations are separated into two sections, the first considering a biomechanical model of the microstructure, as well as the entire surgical mesh on a macro scale. In particular, the synthetic mesh named *Restorelle* is the subject of study, used to hold and support pelvic organs in their natural position, with the purpose of repairing the POP.

1.4 Document Structure

The remaining of this work is structured as follows: Chapter 2 exposes a review of the female pelvic anatomy, especially focused on the pelvic bone and pelvic cavity; Chapter 3 describes some important aspects regarding the pelvic organ prolapse, mainly the diagnosis and treatment existing; Chapter 4 exposes the fundamentals of computational modelling, the finite element method and the some of the developed models; Chapter 5 presents the computational models developed for the study of this dissertation and the methodology for their design; Chapter 6 presents the gathered results and consequent discussion; and lastly, Chapter 7 summarizes the major conclusions and presents alternative methods to improve the results obtained, as well as ideas for future development to further study the surgical meshes and their impact on medical procedures.

Chapter 2

Background

The pelvic organ prolapse happens in a very complex region, the female pelvic cavity, so one of the focuses of the study is to know this part of the body. The basic concepts to understand the anatomy of the female pelvic cavity are wide and need to be exposed. First, a crucial topic consists of an introduction to the female pelvic anatomy, with an overview of the pelvic bone structures, namely a more detailed description of the sacrum, coccyx, ilium, pubis, and ischium. Finally, describing of the pelvic cavity, with a focus on the pelvic wall and floor, mentioning the muscles, endopelvic fascia and ligaments of this region.

2.1 Female Pelvic Anatomy

The prevention of POP relies on the support given by the pelvic floor, thus stating the importance of knowing the pathophysiologic mechanisms behind this condition, as to effectively manage it. To identify them, it's important to understand the anatomy and function of the pelvic floor and its structures [7].

The pelvis is the region of the trunk below the abdomen. Even though the abdominal and pelvic cavities are continuous, the two areas are considered separately. The female pelvic anatomy is a complex arrangement between muscles, ligaments, blood vessels, and nerves, that provide dynamic support to the bladder, urethra, uterus, and rectum [8].

The pelvis' bone major function is to transfer the body's weight from the vertebral column to the femurs. Further, it contains, protects, and gives support to the pelvic viscera and attaches the trunk to the legs [9].

The pelvis is divided into two main regions: the abdominal cavity containing the superior region - false (greater) pelvis -, and the pelvic cavity containing the inferior region - true (lesser) pelvis - which is closed by the pelvic floor. The basin pelvic cavity is continuous with the abdominal cavity above, while the hoop (the pelvic inlet) is entirely surrounded by bone. The pelvic cavity above is separated from the perineum below by the pelvic floor, which is a fibromuscular structure. The bony pelvis is constituted by four bones: the two pelvic hip bones (right and left), forming the lateral and anterior walls, the sacrum and the coccyx, both part of the vertebral column

forming the back wall. The term "female pelvic floor" has different meanings according to different health professionals. Following the meaning presented in [10], the female pelvic floor includes all structures within the bony pelvis, that is, from the simphysis pubis to coccyx, and from lateral to lateral pelvic sidewall. Therefore, besides the reproductive tract, lower gastrointestinal tract, and lower urinary tract, it also includes the neuromuscular components. The superior region is related to the upper part of the pelvic bones and lower lumbar vertebrae; the true pelvis is mainly composed of bone, muscle, and ligaments, thus being related to the inferior parts of the pelvic bones, sacrum, and coccyx, with an inlet and outlet [11].

The female pelvis is unique, it can be viewed as three bony rings and four fibro-osseous rings, that has several sites for the attachment of ligaments, muscles, and fascial layers. The female pelvis has several differences compared to men's (Figure 2.1). First, the female pelvic inlet is typically larger and more circular compared with the heart-shaped male pelvic inlet. The wider inlet facilitates the parturition, however the wider outlet induces the weakness of the subsequent pelvic floor. Secondly, the angle formed by the pubic arch is larger in women (80º-85º) than in men (50º-60º). Finally, the ischial spines are normally more projected into the pelvic cavity in men than in women [7] [11].

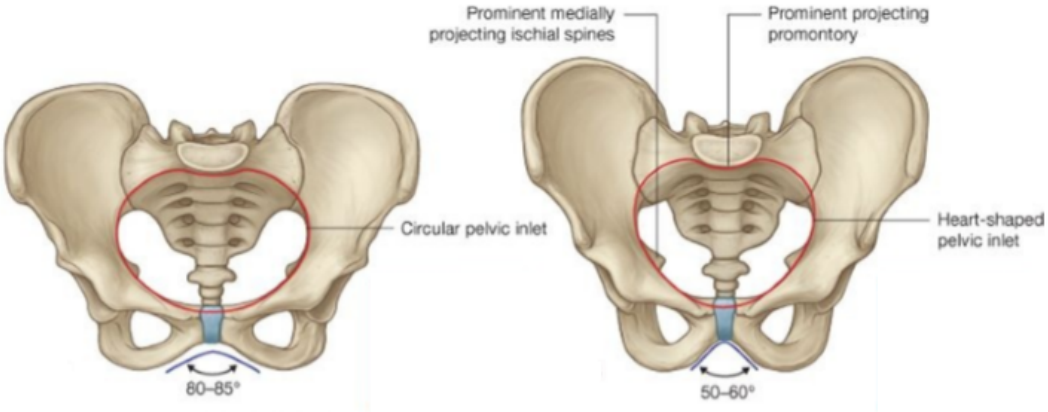


Figure 2.1: Structure of the bone pelvis in women (left) and in men (right) [11].

Injuries on the female pelvic floor, mainly due to vaginal delivery, can cause the loss of support to the pelvic viscera, which may lead to many problems such as uterine and vaginal prolapse [9].

2.2 Pelvic Bone

The bones of the pelvis establish a rigid foundation for the anchor of all pelvic structures. The bones comprising the female pelvis are four, two innominate (or hip) bones, the sacrum (the back of the pelvis), and the coccyx (the base of the spine and pelvis) (Figure 2.2). Each innominate bone is constituted by three elements: the ilium, pubis (or pubic bone), and ischium. At birth, these bones are linked with cartilage in the acetabulum area, later, during youth, they fuse together into

a single bone (Figure 2.3). The anchoring points of the true bony pelvis are the pubic rami, ischial spines, and sacrum. The bones forming the true pelvis are the ilium, ischium, pubis, sacrum, and coccyx [11][8].

The study of this anatomy is important to be made in a standing position, which provides the dispersion of forces that minimize the pressure on the pelvic viscera and muscles and directs the forces to the bones that can better support the long-term accumulative pressures of the daily life. In this standing position, the pelvis is oriented in a nearly vertical plane, transmitting the body weight to the femurs, while the mid-line articulation of the pubic rami is almost horizontal. Since most of the weight of the abdominal and pelvic viscera is supported by the inferior bone articulation, an increment in the intraabdominal pressure is partially incumbent by the bones of the pelvis. An understanding of the normal mechanisms of the support on the pelvis is a crucial step to evaluate female PFD [10].

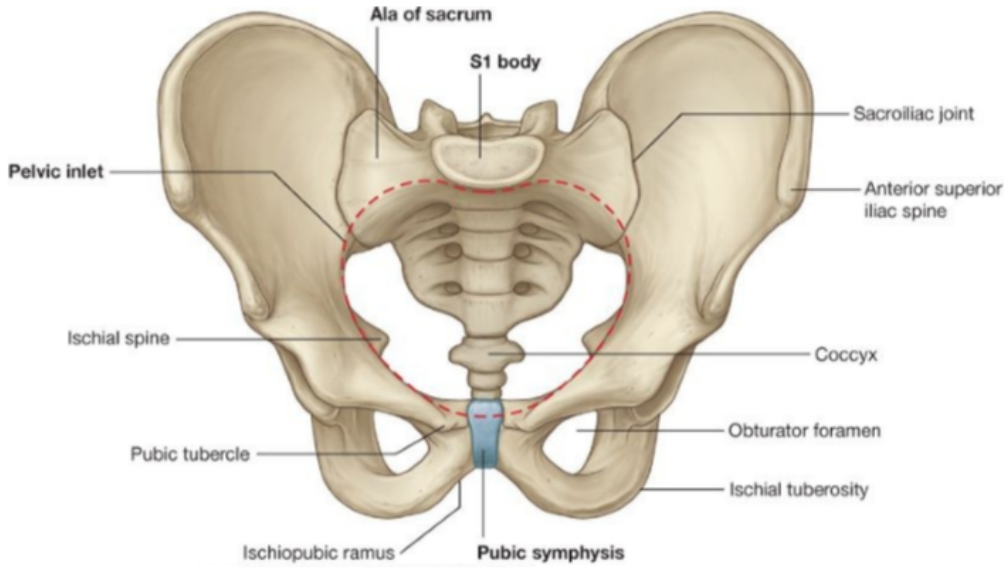


Figure 2.2: Anterior view of the pelvic bone with main components identified [11]

Sacrum

The sacrum is a single bone with a triangular shape and has a forward concavity, formed by five rudimentary vertebrae fused together. The base (upper border) articulates with the fifth lumbar vertebrae, while the inferior border articulates with the coccyx. It has one large facet on each lateral surface to articulate with the iliac bones, forming the sacroiliac joints (which transfers forces from the legs to the vertebral column). Regarding the joints, the lumbosacral joints are created between the fifth lumbar vertebrae and the base of the sacrum. The anterior border of the body of the first sacral vertebrae creates a protrusion to form the sacral promontory, which is an important point for the measurement of the size of the pelvis [9][11].

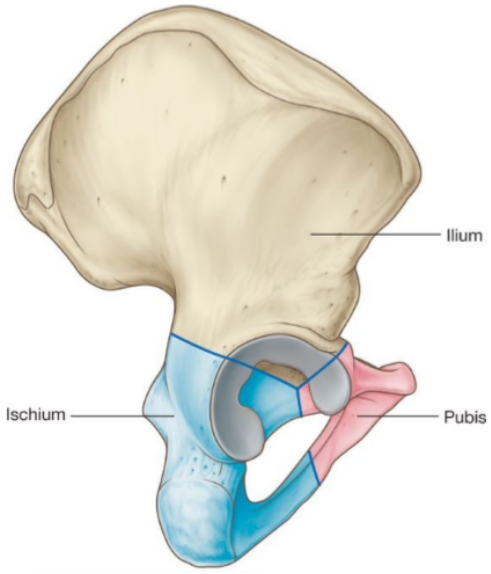


Figure 2.3: Components of the pelvic bone: ilium, pubis, and ischium [11]

Coccyx

The coccyx is a small triangular bone formed by three to four fused coccygeal vertebrae. At the base, it articulates with the lower end of the sacrum. The coccyx does not have vertebral arches nor a vertebral canal [8][9].

Ilium

Together with the ischium and pubis, the ilium formes the hip bones. The ilium is a wide bone, the upper flattened part of the pelvic bone, with an upper border called the iliac crest (which can be felt along its length through the skin). This prominence provides attachment points for the abdominal muscles and fascia (Figure 2.4).

To note that its medial surface is divided in two by the arcuate line, which forms the posterior part of the iliopectineal line, while the pectineal line forms the anterior part of the iliopectineal line. The iliopectineal line delimits the false from the true pelvis. Posteriorly the bone, there's an L-shaped facet that articulates with the sacrum and a rugged region that serves as an attachment for strong ligaments that support the sacroiliac joint. On the inferior line of the anterior superior iliac spine of the crest, that is, on the anterior margin of the ilium, there is a protuberance called the anterior inferior iliac spine, responsible for the attachment of the rectus femoris muscle and the iliofemoral ligament associated with the hip joint [9][11].

Pubis

The *symphysis pubis* (or pubic bone) is the anterior and inferior part of the pelvic bone, with a body and two pubic ramus (superior and inferior) (Figure 2.4). The flattened body articulates with the body of the pubic bone of the opposite side at the cartilaginous *symphysis pubic*. Also, the body has a rounded pubic crest on its superior surface, ending laterally as the pubic tubercle. The

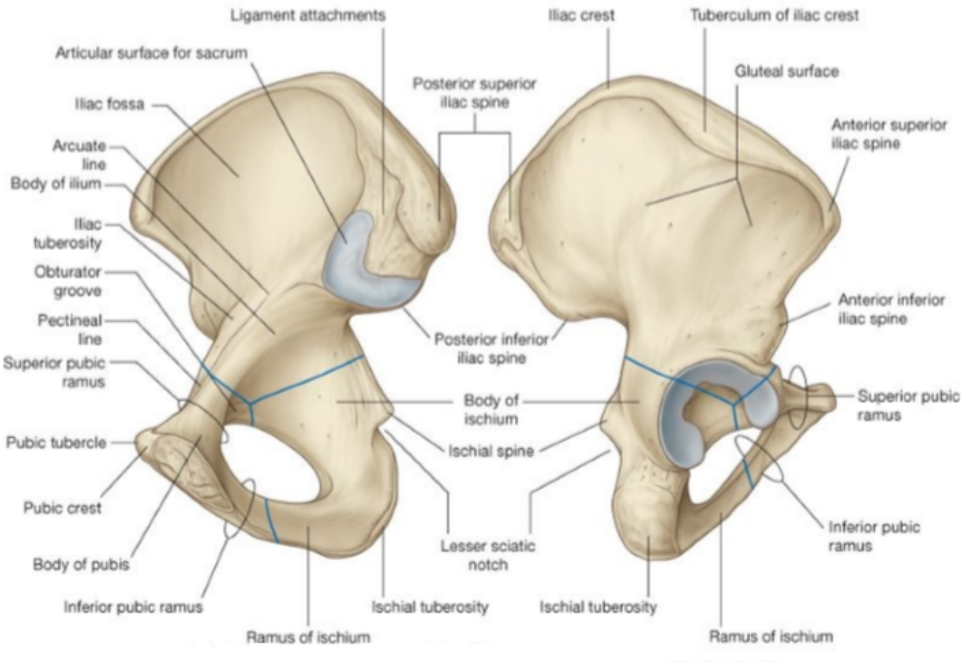


Figure 2.4: Medial surface (left) and lateral surface (right) of the pelvic bone [11]

superior pubic ramus joins with the ilium and ischium at its base, positioned towards the acetabulum, and it has a large opening named obturator foramen on its inferior surface, a triangular-shaped area which is filled in by the obturator membrane [9][11].

Ischium

The ischium is the inferior and posterior part of the innominate bone, with one body and one ramus (Figure 2.3). The ischium forms the posteroinferior part of the acetabulum and allows the insertion of posterior femoral muscles. The broad body projects superiorly to connect with the ilium and the superior pubic ramus. Also, the ramus anteriorly projects to connect with the inferior pubic ramus, completing the obturator foramen. As features, there is an ischial tuberosity (Figure 2.4), a large prominent characteristic on the posteroinferior part of the ischium, and an ischial spine, that marks the posterior margin of the bone. The sacrospinous ligament is fixed on the border of the ischial spine [10][9][11].

2.3 Pelvic Cavity

The pelvic cavity (or cavity of the true pelvis) is bowl-shaped and it can be defined as the area between the pelvic outlet and the pelvic inlet, containing all pelvic organs inside. It can also be defined as the space bounded peripherally by the bony, ligaments, muscular pelvic walls and floor [12]. The pelvic outlet is diamond-shaped like, it can be defined as the superior boundary which is closed by the sacrum on the superior and posterior part, while the pelvic inlet is the circular

opening formed by bone, that is, by the sacrum posteriorly, by the *symphysis pubic* anteriorly, and laterally by bony rim of the pelvic bone. Usually, the pelvic cavity is separated by the pelvic diaphragm, above is located the main pelvic cavity and below is the perineum [9][11].

The pelvic cavity contains the end regions of the ureters, the urinary bladder, rectum, genital organs, nerves, and the blood and lymphatics vessels [12]. In fact, the pelvic cavity contains most of the reproductive tract in women and part of it in men. In women, the vagina passes through the pelvic floor, connecting with the uterus in the pelvic cavity. Then, the uterus is located between the rectum and the bladder. Each fallopian tube extends laterally to the pelvic floor to connect with each ovary. In men, the pelvic cavity is located in the region of connection between the urinary and reproductive tracts (which contains the prostate and the two seminal vesicles) [11].

The pelvic wall on the pelvic inlet and the abdominal wall are continuous, as the pelvic cavity is continuous with the abdominal cavity. However, the pelvic cavity is not on the same vertical plane as that of the abdominal cavity due to the disposition created by the sacrum and pelvic bones attache, which are angled posteriorly on the vertebral column. Thus, the pelvic cavity is posteriorly projected, and the inlet is superior and anteriorly opened [9][11].

2.3.1 Pelvic Wall and Floor

The pelvic cavity is surrounded by the antero-inferior wall, a posterior wall, two lateral walls, and a floor (Figure 2.5). The pelvic wall is surrounded by external bones, ligaments and formed by muscles.

The antero-inferior wall is mainly created by the bodies and rami of the pubic bones, and by the *symphysis pubic*. Its function is sustaining the urinary bladder's weight.

The lateral walls are constituted by the two hip bones (right and left) wherein that each of the bones has an obturator foramen that is closed by an obturator membrane. Most of the lateral walls are formed by the obturator internus muscles (Table 2.1), having the majority of its surface padded by the corresponding attachments. The obturator fascia covers the medial surfaces of these muscles, with a tendinous arch providing the attachment point for the pelvic diaphragm.

The posterior wall (or posterolateral wall and roof) is formed by a bony wall and a roof in the midline, which consists of the sacrum and coccyx, and by musculoligamentous posterolateral walls, composed by the ligaments related to the sacroiliac joints and piriformis muscles. These ligaments comprise the anterior sacroiliac, sacrospinous, and sacrotuberous ligaments.

The pelvic floor consists of a bowl-shaped pelvic diaphragm, formed by the coccygeus and *levator ani* muscle, and the fascias that cover these muscles superior and inferiorly. The pelvic diaphragm is inside the true pelvis, dividing the pelvic cavity from the perineum, thus forming the floor of the pelvis and the roof of the perineum (Figure 2.5) [12][11].

Focusing on the floor of the pelvis, it is built by the pelvic diaphragm and sustains the pelvic viscera above. As previously mentioned, it extends across the pelvis and separates it into the main pelvic cavity (with the pelvic viscera) above and the perineum below [9].

The pelvic floor is subdivided into three sections, the anterior, middle, and posterior. The anterior one is formed by the bladder and the urethra, the middle compartment has the vagina,

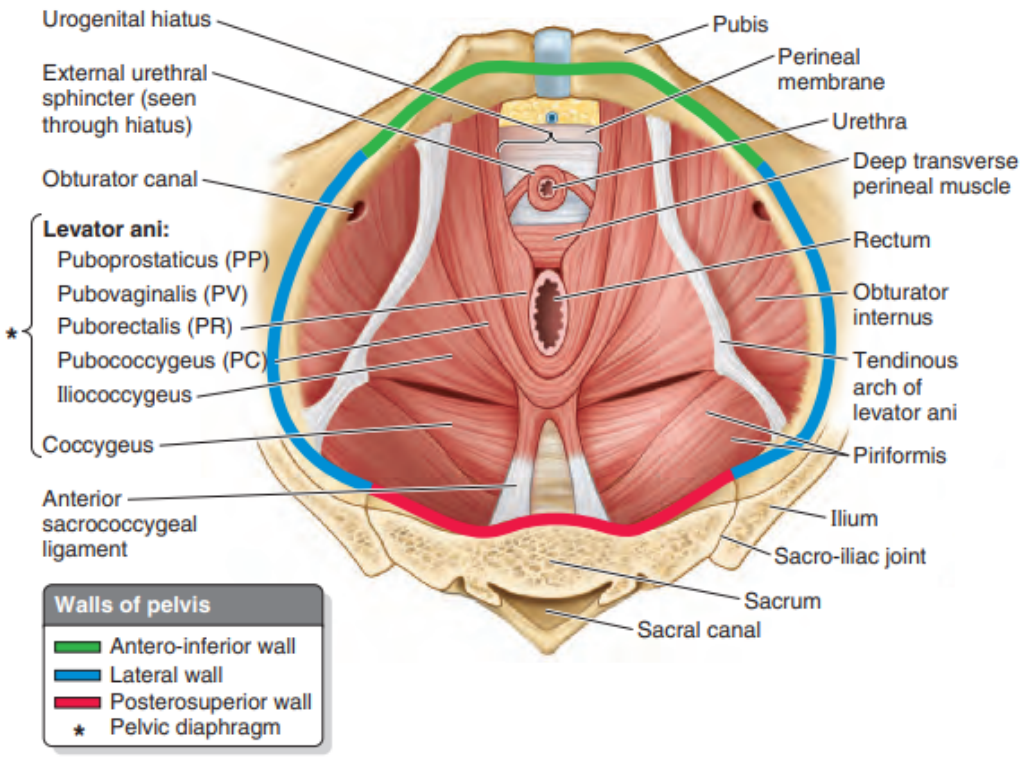


Figure 2.5: Superior view of the floor and walls of the pelvis (adapted from [12])

Table 2.1: Muscles of the pelvic walls and floor (adapted from [12])

Boundary	Muscle	Proximal Attachment	Distal Attachment	Innervation	Main Action
Lateral wall	**Obturator internus**	Pelvic surfaces of ilium and ischium; obturator membrane	Greater trochanter of femur	Nerve to obturator internus (L5, S1, S2)	Rotates thigh laterally; assists in holding head of femur in acetabulum
Posterosuperior wall	**Piriformis**	Pelvic surface of S2–S4 segments; superior margin of greater sciatic notch and sacrotuberous ligament	Greater trochanter of femur	Anterior rami of S1 and S2	Rotates thigh laterally; abducts thigh; assists in holding head of femur in acetabulum
Floor	**Coccygeus** (ischiococcygeus)	Ischial spine	Inferior end of sacrum and coccyx	Branches of S4 and S5 spinal nerves	Forms small part of pelvic diaphragm that supports pelvic viscera; flexes coccyx
	Levator ani (puborectalis, pubococcygeus, and iliococcygeus)	Body of pubis; tendinous arch of obturator fascia; ischial spine	Perineal body; coccyx; anococcygeal ligament; walls of prostate or vagina, rectum, and anal canal	Nerve to levator ani (branches of S4), inferior anal (rectal) nerve, and coccygeal plexus	Forms most of pelvic diaphragm that helps support pelvic viscera and resists increases in intra-abdominal pressure

cervix, and uterus, and the posterior section contains the rectum. The support that it provides is the result of the complex attachment of pelvic floor muscles (PFM), endopelvic fascia, and pelvic ligaments to the pelvic bones surrounded [13].

Pelvic Floor muscles

The PFM are the only transverse load-supporting muscle group in the body. and these are divided into three planes, the superficial, intermediate and deep. The superficial layer is composed of the bulbospongiosus, ischiocavernosus and superficial transverse perinei muscles, and the external anal sphincter. The intermediate layer has the deep transverse perinei, intrinsic urethral sphincter and, in females, the compressor urethrae and the urethrovaginal sphincter. Lastly, the deep layer consists of the *levator ani* muscle and the ischiococcygeus (or coccygeus), parts of the pelvic diaphragm (Figure 2.5). The *levator uni* muscle comprises the puborectalis (PR), pubococcygeus (PC) and iliococcygeus (IC) [14]. The pelvic diaphragm extends from the anterior to the lateral, to the posterior walls of the true pelvis. and closing most of the ring of the pelvic girdle [12].

Regarding the *levator ani*, it is a broad muscular sheet, crucial to the pelvic floor functionality. It fixes into the ischial spines posteriorly, to the pubic bones anteriorly, and to the tendinous arch of the *levator ani* (that is, the obturator fascia) between each of the two bony sites [12].

Focusing on the superficial plane of the pelvic floor, the bulbospongiosus muscles in women (Figure 2.6) has each muscle is attached posteriorly to the perineal body (its origin) and anterolaterally overpasses the inferior surface of the related greater vestibular gland and the bulb of the vestibule, to fix to the perineal membrane and to the surface of the bulb [11]. The bulbospongiosus muscles pack the connected parts of the clitoris, acts as the sphincter of the vagina and assists in the erection of the clitoris [12].

The ischiocavernosus muscles have their origin in the medial ischial tuberosity, covers the clitorial crura at their attachment points to the pubis, and causes the erection of the clitoris [12][8]. The bulbocavernosus and ischiocavernosus muscles are adjacent to the urethra but do not connect to it, from the 79th to the 100th percentile of the urethra [10].

The superficial transverse perinei muscles are bilateral muscles that lie on the posterior part of the superficial perineal pouch. Each of them emerges from the medial ischial tuberosities to insert into the perineal body. The superficial transverse perineal muscles' role is to fix the perineal body at the center of the perineum [10][9].

The external anal sphincter is formed by two layers of fibers, the deeper one fully surrounds the anal canal and fuses superiorly with the pubococcygeus-puborectal muscles (part of the *levator ani* muscle) [10][11]. It's the major muscle in the anal triangle, which contains the anus [11]. The female external anal sphincter is also named the urogenital sphincter, as a part of it forms a true anular sphincter around the urethra with various regions expending from it [12].

In the intermediate layer, there are the deep transverse perineal muscles, that lie posteriorly to the sphincter urethrae muscle. Each muscle originates in the ischial ramus and passes trough medially to be inserted into the perineal body. Its function is to fix the perineal body [9].

The urethral sphincter is attached to the pubic arch, has insertions surrounding the urethra and forms the voluntary sphincter of the urethra [9]. Describing the location of these structures as a percentile of total urethral length, the zero percentile is defined as the internal urethral meatus, while the 100th percentile is located at the external urethral meatus [10].

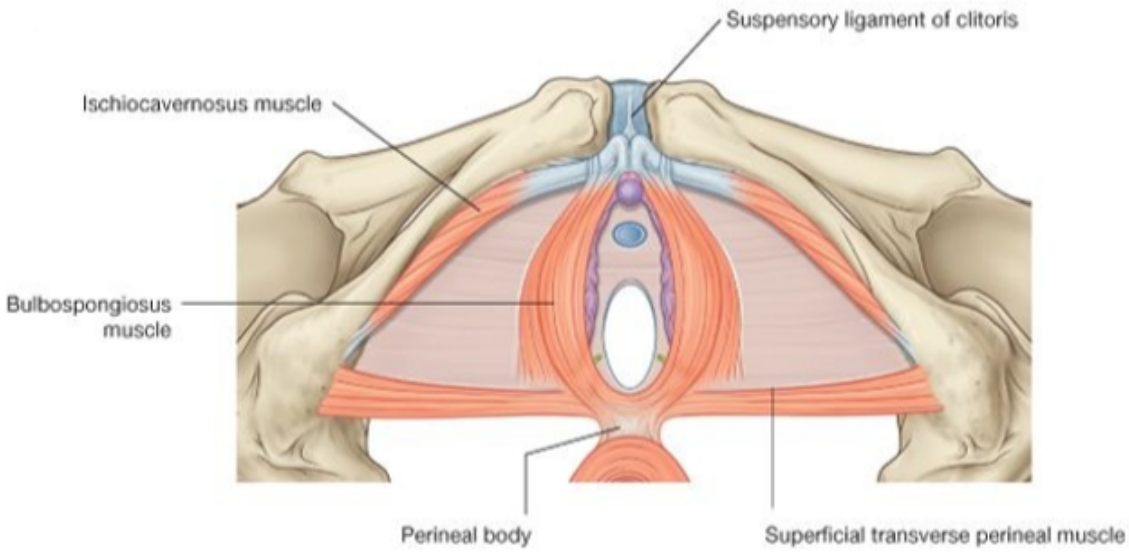


Figure 2.6: Muscles in the superficial perineal pouch in women [11]

The compressor urethrae in women his fixed at he ischiopubic ramus on each side, blends with the other on the opposite side anterior to the urethra, and acts as an accessory sphincter of the urethra [11]. The compressor urethrae and external urethral sphincter compress the urethra [12].

The urethrovaginal sphincter is flat and merges on the abdominal side of the urethra with the urethral compressor, and extends along the sides of the urethra and vagina to enclose them in a circle [10].

In the deep layer, the *levator ani* is a broad muscle considered the most important one in the pelvic floor. It is fixed anteriorly in the bodies of the pubic bones, to the ischial spines posteriorly, and to the *tendinous* arch of the *levator ani* between the two bony sites on each side [12]. The *levator ani* comprises three distinct parts, namely the PR muscle that is the medial part of the *levator ani*, it is narrower and thicker. The PR is formed by muscle fibers continuous between the posterior parts of the bodies of the right and left pubic bones. It has a U-shaped muscular structure (puborectal sling) passing posteriorly to the anorectal junction, to promote the closure of the urogenital hiatus. The PC is the intermediate muscle, wider but thinner section of the *levator ani*. It arises laterally to the *puborectalis* from the posterior part of the pubis body and anteriorly to the tendinous arch, forming an almost horizontal plane posteriorly. Its lateral fibers are connected to the coccyx and the medial fibers merge with those from the contralateral muscle creating a tendinous plate that is part of the anococcygeal body (or ligament) between the anus and the coccyx, commonly referred as the levator plate [12]. Regarding the IC muscle, it is the posterolateral part of the *levator ani*, originated from the posterior tendinous arch and ischial spine. It joins in the midline the obturator internus muscle on the other side to form a ligament that extends from the anal aperture to the coccyx. The IC is thin and frequently underdeveloped, with more of an aponeurotic appearance than muscular) [11][12].

Finally, there are two triangular coccygeus muscles, one on each side, that participate in supporting the posterior section of the pelvic floor, although with age it becomes thin and fibrous. They are attached by their apices to the ischial spine, and by their bases to the lateral inferior margins of the sacrum and coccyx [11][10].

Pelvic Floor fascias

The fascias form the wrapping and insulating materials of the deep structures of the body. Underlying the subcutaneous fascia (or fascia) commonly is the deep fascia, which is an organized and dense connective tissue layer, its deeper extensions pack structures like muscles. In some regions, the deep fascia gives attachment points to the underlying muscles, as an origin of these formations [12].

The endopelvic fascia consists of connective tissue continuous above with the fascia of the abdominal walls, and continuous below with the fascia of the perineum. The pelvic floor fascias can be divided into parietal and visceral layers (Figure 2.7). The parietal pelvic fascia has a variable thickness and lines the inner aspects of the walls and floor of the pelvis (*levator ani*, coccygeus, obturator internus, piriformis, and part of the urethral sphincter muscles). In the deficient anterior locations of the pelvic diaphragm, the parietal fascia becomes continuous through the opening covering the inferior surface of the pelvic diaphragm in the perineum. Usually, the fascia is named after the muscle it covers. Concerning the visceral pelvic fascia, it covers and supports all the pelvic viscera, including the membranous fascia directly enclosing the organs, to forme the adventitial layer of each. The membranous parietal and visceral layers become continuous where the organs penetrate the pelvic floor. In this situation, the parietal fascia thickens to build the tendinous arch of pelvic fascia, a continuous bilateral band from the *symphysis pubis* to the sacrum along the pelvic floor adjacent to the viscera [12][9].

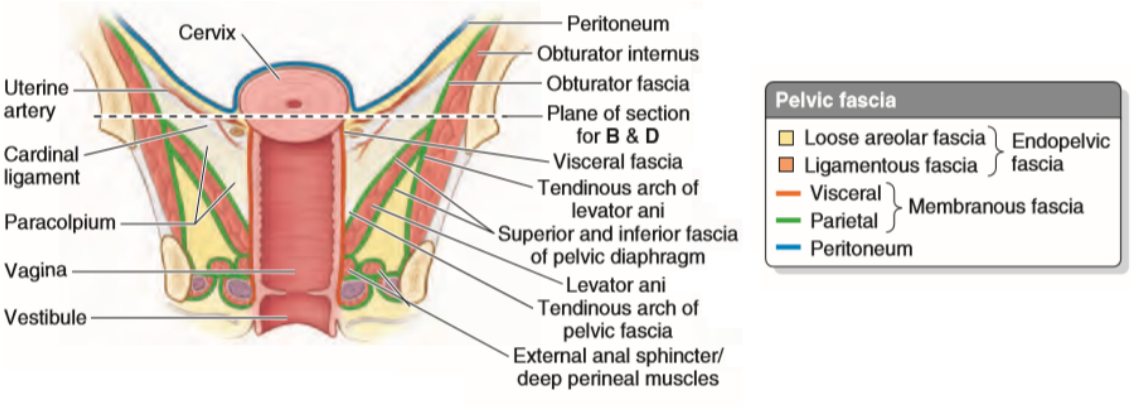


Figure 2.7: Anterior view of the coronal section of the pelvic fascia: endopelvic fascia and fascial ligaments (adapted from [12])

Pelvic Floor ligaments

The ligaments of the pelvic fascia are the product of the union of the fascia that crosses over from the cervix to the pelvic walls. The condensations of fascia generate the ligaments that extend from the cervix to the anterior (pubocervical ligament), posterior (uterosacral ligament), and lateral (transverse cervical or cardinal ligament) pelvic walls (Figure 2.8). The perineal body and membrane, and the *levator ani* muscles together with these ligaments create a supporting structure to stabilize the uterus inside the pelvic cavity [13][14][11].

The most relevant of these ligaments is the cardinal ligament, that extends laterally from each side of the cervix and vagina to the corresponding pelvic wall, providing major passive support for the uterus. The perineal muscles supply the uterus with the dynamic support, as they contract during the states of augmented intra-abdominal pressure (IAP), such as coughing or sneezing. This passive and dynamic assistance combined provide resistance for the tendency of the uterus to fall or to be pushed through the vagina (uterine prolapse) [12].

The pubocervical is formed by two strips of connective tissue located at each side of the neck of the bladder, that firmly connect the posterior surface of the pubis to the cervix. This way holding a portion of this structure [9].

The uterosacral (US) ligaments pass from the posterolateral cervix and vaginal fornices to be inserted on the second to fourth sacral vertebrae. The fragility of this ligament can lead to uterine prolapse since the descent of the uterus plus the cervix and vagina usually suggests this type of dysfunction. The cardinal ligament fuses posteriorly with the uterosacral ligament (sacrouterine), stabilizing the cervix, uterus, and upper vagina posteriorly towards the sacrum [8][13].

Additionally, the sacrospinous (SS) ligament passes posteriorly from the ischial spines to the anterolateral sacrum and coccyx, which gives wide support to the posterior aspect of the pelvis [8]. The SS ligament fixation, with the goal of correctly shifting the support of the vagina to a posterior inclination, constitutes a safe and effective way of correcting vaginal vault prolapse [15].

The pubovesical (PV) ligaments are an extension of the detrusor muscle of the bladder at the vesical neck, to be inserted in the anterior part of the *arcus tendineus fascia pelvis*. It suspends the anterior wall of the bladder and gives rigidity to it [16].

The pubourethral (PU) ligaments consist of structures of connective tissue overpassing from the urethra to the pubic bone, considered responsible for giving support to the urethra and keeping closed the vesical neck [7].

Lastly, the arcus tendineus fasciae pelvis (ATFP) is a thickening of the pelvic fascia 10-cm-long fibrous, it is located laterally to the peritoneum and medially to the obturator internus muscle. Its insertions are on the ischial spine and it crosses anteriorly and downward to the pubovesical ligament. The ATFP suspends the vagina bilaterally [17][7].

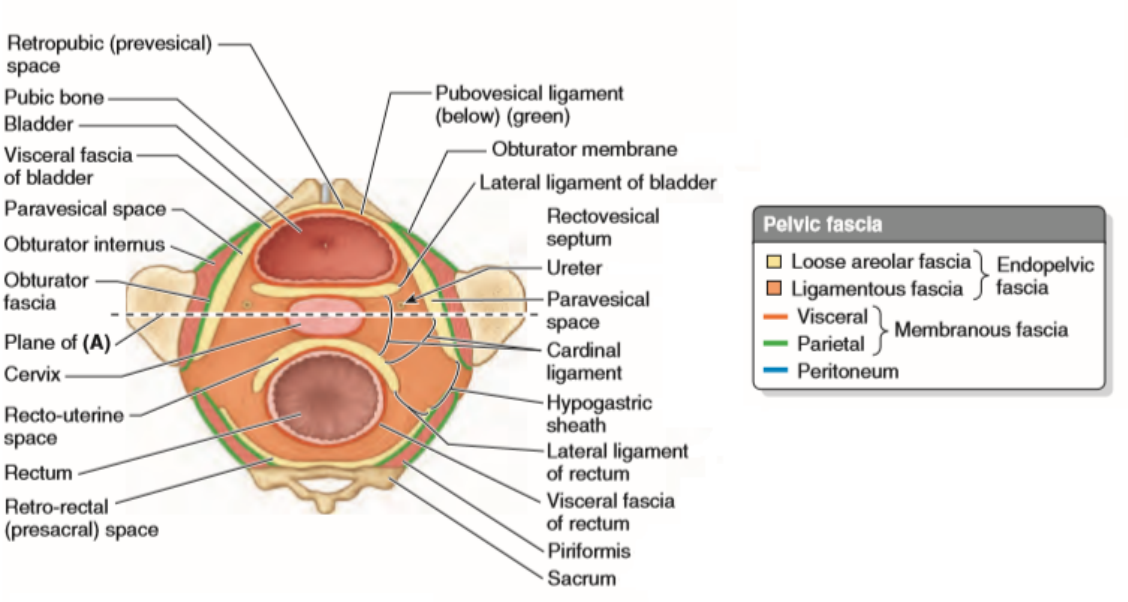


Figure 2.8: Superior view of the transverse section of the pelvic fascia: endopelvic fascia and fascial ligaments (adapted from [12])

Chapter 3

Pelvic Organ Prolapse

The condition at study is the pelvic organ prolapse, so the main subjects regarding the POP need to be presented, with the purpose of gathering the essential knowledge about this pelvic floor dysfunction. Thus, it is important to distinguish the different POP classification systems, since there are various types with different consequences and treatments to them. The pathophysiological conditions to understand the various damage levels associated and the support levels. Information regarding the etiology of the pelvic prolapse and its main risk factors, as also as the epidemiology studies to represent the quantitative distribution of POP are exposed. Furthermore, the general guidelines for the diagnose, and, finally, the several options for the management and treatment of the prolapse, subdivided into the conservative and invasive treatment, need to be introduced, as the main focus of the study is a surgical mesh used in the uterine prolapse correction.

3.1 POP classification

With the support given by the pelvic floor muscles, pelvic ligaments, and fascia described in Chapter 2 it strengthens and keeps positioned the pelvic organs, thus making the functionality of the organs dependent on the integrity of the architecture of the supportive pelvic structure [18]. Therefore, the weakness of the female pelvis promotes the development of PFD, namely POP, the descent of one or more of the anterior or posterior vaginal walls, top of the vagina or the uterus. Sometimes urinary incontinence accompanies the prolapse, increasing to the embarrassment and general discomfort [19].

Traditional terms used to describe each prolapse consist of “cystocele” (anterior prolapse), “rectocele” (posterior prolapse), “urethrocele”, or “enterocele” (Table 3.1), these refer to the protrusion of the vagina below the pelvic floor involving, respectively, the bladder, rectum, urethra, or small bowel. This classified the degree of anatomical deformity and which organ caused the vaginal bulge. However, there is the problem of intra- and interobserver variability, and also the fact that there is implied certainty regarding the structures behind the prolapse, which can be a false

Table 3.1: Traditional anatomical site prolapse classification (adapted from [20]).

Urethrocele	Prolapse of the lower anterior vaginal wall involving the urethra only.
Cystocele	Prolapse of the upper anterior vaginal wall involving the bladder. Generally, prolapse of the urethra is also associated and hence the term cystourethrocele is often used.
Uterovaginal Prolapse	This term is used to describe prolapse of the uterus, cervix and upper vagina.
Enterocele	Prolapse of the upper posterior wall of the vagina usually containing loops of small bowel.
Rectocele	Prolapse of the lower posterior wall of the vagina involving the rectum bulging forwards into the vagina.

assumption especially in women with previous prolapse surgeries. So, the classifications "apical prolapse", "anterior vaginal wall prolapse", and "posterior vaginal wall prolapse" are usually preferable (Table 3.2) [20][21].

Table 3.2: Anatomical classification according to vaginal walls (adapted from [20])

Anterior Vaginal Wall	Cystocele		Urethrocete	
	1. Central (Posterior) 2. Lateral (Anterior) 3. Combined		Uncommon	
Apical Vaginal Wall	Enterocele*	Uterine	Uterovaginal	Vaginal vault
	1. Anterior 2. Posterior		with cystocele, enterocele, rectocele *	Eversion (post-hysterectomy) with cystocele, enterocele, rectocele
Posterior Vaginal Wall	Rectocele			
	1. Low 2. Midvaginal 3. High			

Afterward, the Baden-Walker Halfway Scoring System is used particularly in clinical environments (Figure 3.1). By allocating a score from 0 to 4 to each of six concrete midline points (urethral, vesical, uterine, cul de sae, rectal, and perineal), the information is compact in a short period of time. These references combined with a prolapse map provides a descriptive analysis of

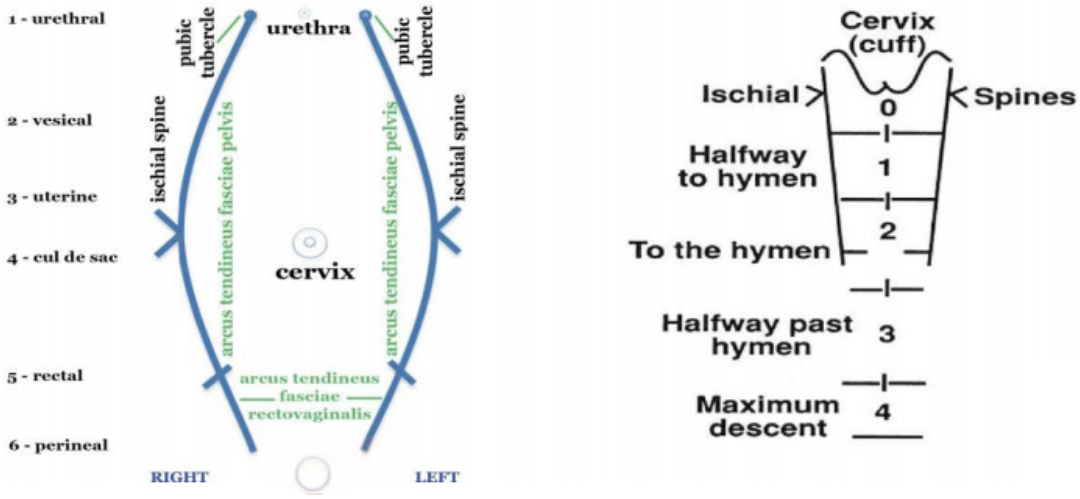


Figure 3.1: Main elements of pelvic support (left) and representation of Baden-Walker halfway system with four grades of prolapse (right) (adapted from [20])

each case. Nevertheless, it is a type of notation that doesn't specify the location of fascial defects, it is subjective and low reproductivity, thus it is not globally validated by the medical community [20].

Finally, in 1996, a new classification emerges from the Pelvic Organ Prolapse Quantification system (POP-Q), recognized by the Society of Gynecologic Surgeons, the American Urogynecologic Society (AUGS), and the International Continence Society (ICS). This system of description, quantification, and staging of pelvic floor dysfunctions uses measurements of specific midline sites of the vaginal wall. It is based on a fixed point, the hymen, and six more reference points (two in the anterior wall, two in the midline posterior wall, and two apical) and the total length of the vagina, genital hiatus and perineal body are evaluated as well. Thus, this system is more reproducible and more precise [20][22].

3.2 POP Pathophysiological Conditions

The uterosacral and cardinal ligaments form a complex of connective tissue comprising the level I support of the vagina (Figure 3.2), with its origin at the cervix and upper vagina and is inserted at the sacrum and pelvic sidewall. Its function is to suspend the upper vagina and uterus, to maintain vaginal length and keep the axis of the vagina in its normal orientation, that is, almost horizontal. Thus, the damage of the level I support is a predisposition to the prolapse of the uterus and/or vaginal apex [23][24].

The level II support is adjacent to the previous complex at the ischial spine. The ATFP suspends laterally the anterior part of the vagina. It begins in the ischial spine and ends on the inferior aspect of the *symphysis pubis*. The middle of the anterior vaginal wall is supported by the anterior

level II, so the loss of these lateral supports contributes to paravaginal defects and prolapse of the anterior vaginal wall [23].

The level III support consists of the posterior lateral suspension. The posterior vaginal wall is attached to the pelvic sidewall laterally. The distal half of the posterior vaginal wall converges with the ATFP between the *symphysis pubis* and the ischial spine. ATFP supports laterally both proximal anterior and posterior vaginal walls. The support of this level to the urethra and to a portion of the vagina is given by the perineal body, perineal membrane, and the muscles of the deep perineal space. In this section, the vagina and the urethra fuse anteriorly, and the vagina and the perineal body fuse posteriorly. Anterior rupture of level II support induces urethral hypermobility and stress urinary incontinence (SUI), and posteriorly it can result in distal rectoceles and/or perineal descent [23].

Furthermore, the interaction between the anterior vaginal wall and the ATFP and *levator ani* muscles provides stability to the suburethral layer, maintains the urethra and bladder neck position, and it is responsible for the posterior movement of the bladder neck. Thus, defects on these attachments can cause proximal urethral support defects or anterior vaginal wall prolapse (cystocele), and SUI [24][23].

3.3 POP Etiology and Risk Factors

The etiology of POP is the result of a combination of different risk factors, these include advanced age, pregnancy, multiparity, smoking, obesity, menopause, connective tissue disorders, chronic obstructive pulmonary disease, and other factors that cause a chronic increase in IAP. The National Institute of Health concluded that age and vaginal delivery are established risk factors [13].

Aging

Age is one of the established intrinsic factors associated with a higher rate of pelvic dysfunction. Hypothetically, it is justified with the fall in estrogen during the post menopause and with the normal physiologic advancement of the components of the pelvic floor. The study conducted by [25] stated that, with a change of 10 years of age, the odds ratio of pelvic prolapse increased from 1.04 to 1.46. However, there are other studies concluding the opposite, that age is not a risk factor to this dysfunction [26].

Genetics

Another intrinsic factor is genetics, with results indicating a positive genetic involvement with heritability associated with prolapse [27].

Ethnicity

A study compared a group of African American and Caucasian women within the same age which revealed that the first group had a higher incidence of detrusor instability and SUI [28].

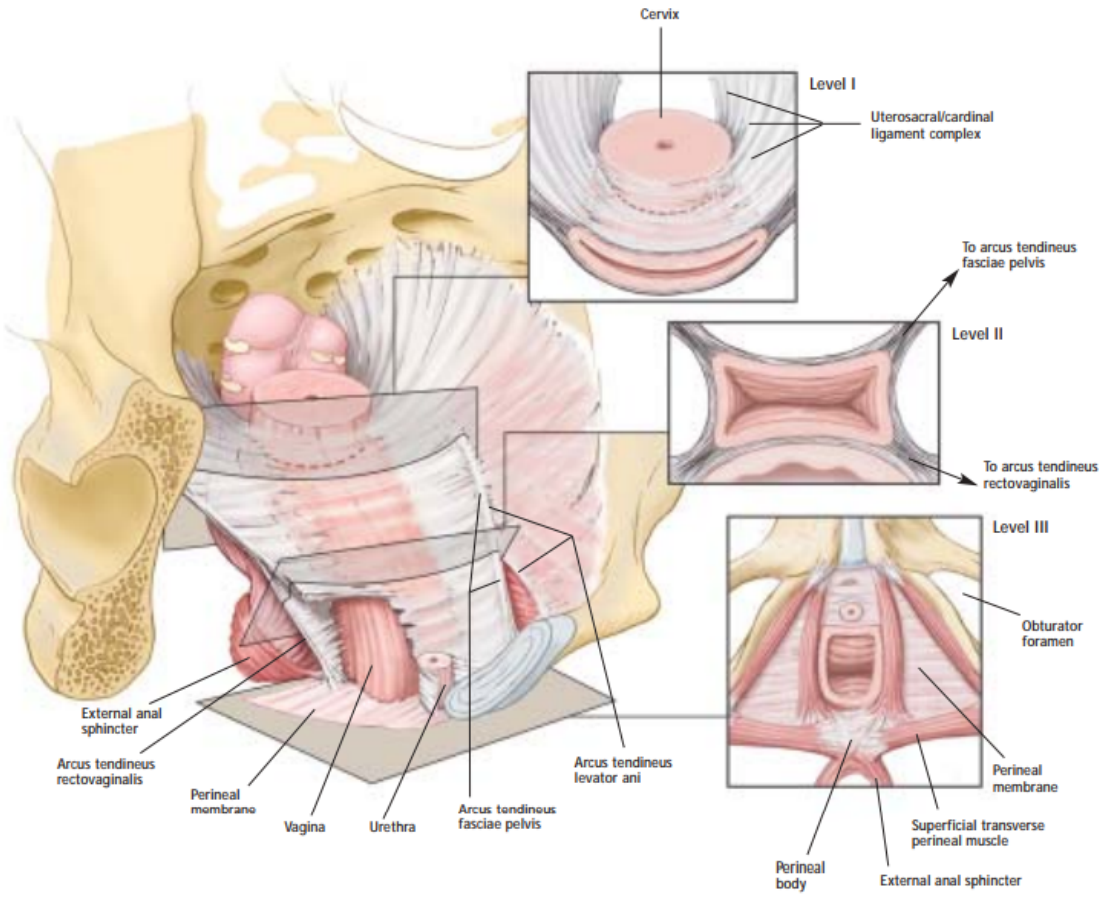


Figure 3.2: Integrated levels of support of the vagina and uterus from the perspective of a standing woman [23]

Another study compared Asians to Caucasians and found that the last group has thicker pelvic floor ligaments and fascia preventing the occurrence of prolapse [29].

Collagen matrix

As the last intrinsic factor, the loss of normal anatomy can be caused by an abnormal collagen matrix foundation. Having a connective tissue disorder, such as Marfans or Ehlers-Danlos, potentiates the incidence of pelvic prolapse and urinary incontinence. Addressing the importance of functional collagen levels in the prevention of these dysfunctions, there is a greatly reduced amount of collagen type III in women with both POP and SUI. This decrease is caused not by a minor production of collagen, but to a high rate of degradation of nascent collagen [30].

More specifically, a study proved that the low expression of collagen type I in sacrouterine ligament was six times more likely to be the risk factor for the occurrence of stage III-IV uterine prolapse [31].

Parity

Regarding extrinsic factors, vaginal deliveries have an important impact. There is a high correlation between parity and prolapse, specially cystocele that was the most frequent. The biggest effect was the initial childbirth, each additional birth lightly raised the odds ratio [30].

On the speculated protection of Caesarian delivery in prolapse, a study said this group actually had a slightly higher rate of new pelvic prolapse of 3%. On the other side, a different study showed that the rates of POP in nulliparous, Caesarean and vaginal delivery women were 4%, 4%, and 8%, respectively, and further that the rates in unlabored and labored Caesarean delivery were 1% and 7%, respectively [30].

Hysterectomy

Hysterectomy does damage to the pelvic floor, it disrupts the local nerve supply, the endopelvic fascia, and the uterosacral-cardinal ligament supports, which potentiates possible future prolapse [30].

Co-morbidities

Chronic transmitted intra-abdominal downward pressure, for example caused by chronic secondary to a chronic pulmonary disease, can damage the pelvic floor components. Obesity also shows to have an impact on pelvic floor function, as patients with a BMI between 25 and 30 kg/m^2 to have 39% of cystocele, 38% of rectocele, and 31% of uterine prolapse [30].

Hormone replacement therapy

As another extrinsic factor, the presence of estrogen may cause collagen degradation, which weakens the anatomical support. Analyzing the proliferation of fibroblasts derived from cardinal ligaments of women with and without POP after estradiol administration, the group with POP showed a much lower rate of proliferation. Therefore, there could be an influence of hormone replacement therapy on POP [30].

Occupation

A study reported that occupation requiring heavy lifting to be connected to a greater number of POP surgeries [32]. In a different study, housewives were at a higher risk of POP than women in managerial positions, as they had greater physical labor [33].

3.4 POP Epidemiology

Currently, there isn't vast information regarding the epidemiologic mechanism and natural history of the POP, as the number of skilled clinicians capable of recognizing this condition is limited and not every woman seeks professional help. Beyond that, the definition of POP, as well as the techniques, are variable, as not every clinician uses the POP-Q system, so standardizing definitions and measures would facilitate data gathering for the epidemiologic study of the prolapse [25][34].

Nevertheless, POP affects millions of women worldwide, with half of all women over 50 years old having this condition. It is a the top of indications for gynecologic surgery, with hysterectomy as the most common procedure. Plus, the risk of needing a reoperation is near 30%. Only in the USA, annually more than 226 000 women have surgery for POP, with direct costs to POP estimated to be $1 billion. The indirect costs of less working time should be also considered in this estimations. As the elderly population rises, the financial burden of POP and the need for pelvic floor specialists increases, that being another reason for improving the studies regarding the understanding of this condition [25][34].

There is a study by [35] of women who enrolled in the Women's Health Initiative that indicates a prevalence of any prolapse as 41.1% in woman with a uterus, with 14.2% having uterine prolapse, 34.3% having cystocele, and 18.6% having rectocele. About 20% has prolapse at more than 2 sites. Regarding women without a uterus, the prevalence of any prolapse lowers to 38%, with 32.9% having cystocele and 18.3% having rectocele. The same prevalence data for cases with and without hysterectomy are compared (Figure 3.3), as well as with nulliparous women, since these two conditions are known to be risk factors to the development of POP.

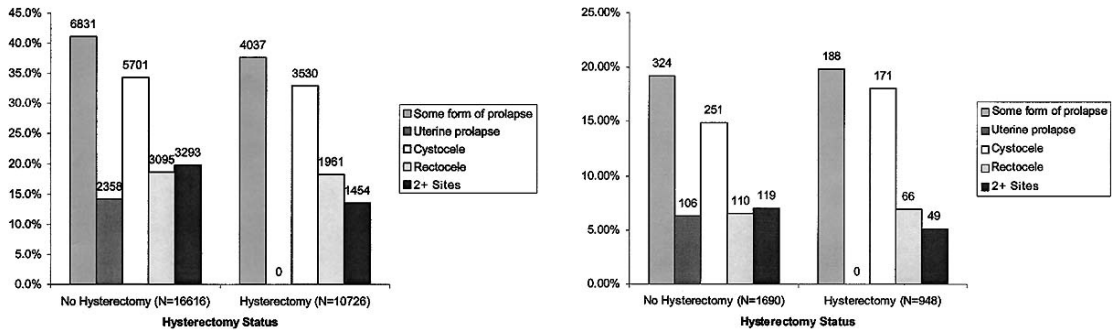


Figure 3.3: POP prevalence with and without hysterectomy (right) and the same parameters in nulliparous women (left) [35]

A study by [36] measured and described the pelvic organ support according to the POP-Q system, and found that the overall distribution of the POP-Q stages was 6.4% for stage 0, 43.3% for stage 1, 47.7% for stage 2, and 2.6% for stage 3.

3.5 POP Diagnosis

To identify the POP, commonly an examination and investigation are done. Nowadays, most evaluation for clinical care is given following a physical examination, however, additional tools are useful for complex cases, such as imaging and urodynamic tests. Normally, the evaluation consists of gathering the symptoms and performing the physical examination by application of the POP-Q system [13][22].

Medical history

The diagnosis starts with a woman having symptoms related to the displacement downward of a pelvic organ, even though most patients with POP are asymptomatic [6]. A standardized questionnaire should be used to record the patient's medical history of pelvic floor symptoms and quality of life [37]. These symptoms of pelvic floor weakness (Table 3.3) include any departure from the normal in structure, function or sensation, such as 'leaking', 'hanging lump', and 'discomfort'. Given the subjective nature of associated symptoms, these symptoms vary day from day, or with the level of activity, fullness of the bladder and rectum, and with the position or even coughing. Due to embarrassment regarding these symptoms prevent them from seeking medical help, which leads the problem to become quite severe before consulting a professional [38][19].

Table 3.3: Symptoms women with POP would more* and most commonly** describe [38].

Potential prolapse-related symptoms	
Vaginal prolapse	Bulge sensation /visualization**, pelvic pressure**, low (sacral) backache*
Urinary tract	Frequency**, recurrent UTI**, incomplete emptying/urinary retention*, slow stream*
Ano-rectal	Incomplete defecation**, digitation/splinting*, rectal urgency*, post-defecatory soiling
Sexual	Dyspareunia*, vaginal laxity*
Other possible associated symptoms	
Urinary incontinence**	Stress, urge, postural, nocturnal, coital
Bladder storage*	Urgency, nocturia,

Physical examination

A comprehensive physical examination includes measuring the severity of the prolapse by evaluation of specific anatomic sites, located in the urethra, perineum, anal sphincter, and vagina (anterior and posterior vaginal walls, vaginal apex and paravaginal wall). This gynecology exam aims to evaluate the integrity of the pelvic floor muscles, of the pelvic tissues and if there are any anomalous mass [39].

Beyond the inspection of external genitals and exam with the speculum, it is crucial to evaluate the existence of POP and quantify it through the POP-Q system (Figure 3.4). This method of quantitative prolapse description considers the hymen as the fixed point of reference, and other six defined points (Aa, Ba, C, D, Ap and Bp), also the genital hiatus (gh), perineal body (pb), and the total vaginal length (tvl). The measurements (cm) are related to the hymen, above or proximal (negative number), or below or distal (positive number), with the plane of the hymen as zero. The measures can be organized in a three by three grid as shown in Figure 3.4 on the left. With this data, it is possible to quantify the prolapse in stage 0, 1, 2, or 3:

- **Stage 0:** — No prolapse is demonstrated;
- **Stage 1:** — The leading part of the prolapse is more than 1 cm above the hymen;

- **Stage 2:** — The leading edge is 1 cm or less above or below the hymen;
- **Stage 3:** — The leading edge is more than 1 cm beyond the hymen, but less than or equal to the total vaginal length;
- **Stage 4:** — Complete vaginal eversion.

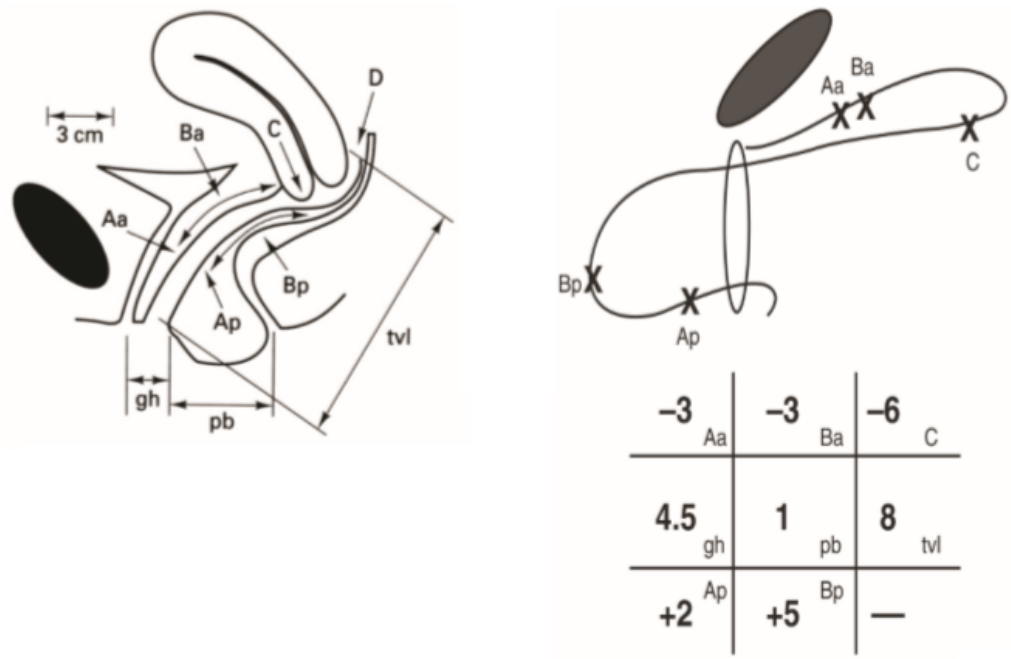


Figure 3.4: Points for PQP-Q system examination (left) and an example of measurements using this system (right) (adapted from [20])

This system is difficult to learn, the patient position affects reproducibility, so the measurements need to be taken in a fixed position, dorsal lithotomy position. There has also been developed a POP-Q simplified system based on similar staging but with only four points measured instead of nine (Aa, Ba, C, D) [39][38][20].

Imaging

Traditional imaging methods include, for example, urodynamics, fluoroscopic cystocolpodefecography, ultrasonography of the bladder neck and anal sphincter, magnetic resonance imaging (MRI), and voiding cystourethrography. Imaging techniques can reveal anomalies not detected during the physical examination [13]. However, only imaging or surgical dissection can provide an accurate diagnosis [21].

From the methods mentioned, urodynamics consists of a functional test of the lower urinary tract, which contains several studies, such as uroflowmetry, cystometry, pressure flow study, post-void residual urine volume, and the assessment of urethral function [40].

The ultrasound diagnosis the presence of PFM dysfunction of an undetected attachment of the puborectalis to the ipsilateral sidewall on any of the three central slices (full avulsion) or on at least one slice (partial avulsion), or a levator-urethra gap of more than 2.5 cm. On the other hand, the position of the PFM in the pelvis can be accessed in relation to defined reference sites in the sagittal plane. Lastly, the hiatal dimension can be defined [40].

Even though MRI can't be done regularly, it is a helpful tool as it gives detailed anatomic information, which can be very valuable to delineate the pre-operatory. It provides the visualization of all three compartments of the pelvic floor and direct view of the PFM and organs [13]. MRI can be used to detect PFM dysfunction with a full disruption of a muscle origin or a disruption of a single fascicle. Abnormalities occur if the morphology of the pubococcygeal part of the *levator ani* muscle is distant from the nulliparous women. The positioning of the PFM can be determined as well [40].

3.6 POP Treatment

The treatment for the POP aims to recover the normal anatomy and functionality, and it has to take into consideration the symptoms, quality of life, physical signs and the associated conditions. The management for symptomatic women consists of observation, hormonal therapy, PFM training, conservative mechanical support, and various surgical procedures [38][6].

The first group of treatment is conservative (non-surgical), which has the purpose of improving symptoms, minimize prolapse progression, and ultimately delay surgical treatment. On the other hand, surgical management also aims to improve symptoms but by correcting anatomically. This kind of intervention can be delayed until the symptoms become intrusive or in situations of real discomfort or failure of the conservative treatments [38][22].

The choice of treatment should be driven by patient preferences. Therefore, for them to make an informed decision, the physician should provide structured information, his medical condition, and data on the functional success rates and complications of each option, and its implications on sexual life, bladder and bowel functions, and any further required procedures [37].

3.6.1 Conservative Treatment

Conservative options include clinical observation, pessary therapy, pelvic floor rehabilitation, lifestyle alteration.

Lifestyle modification

Regarding this last option, it is the intervention in the management of lifestyle-related health problems, it focuses on changing bad habits, such as obesity and smoking, or reducing the risk factors of chronic constipation, coughing or heavy weightlifting, in order to avoid the worsening of the prolapse by decreasing IAP. Fluid consumption or restriction as a way of bladder training, dietary modifications or elimination, or regular participation in physical activity can be a therapy applied on their own or combined with others [40][38][37].

Pessary therapy

A pessary is a mechanical device to be inserted into the vagina to support the structure of one or more descending vaginal compartments, such as the anterior vaginal wall (and bladder), posterior vaginal wall (and rectum), vaginal apex, or the uterus (Figure 3.5). This device allows to reduce the prolapse, contain the pelvic organs and diminish the pressure on the bladder and intestine. The pessary therapy is a viable nonsurgical option for patients with symptomatic POP [6]. About two-thirds of women with POP decide to start with a pessary, and 77% continues with it after the first year [38][6].

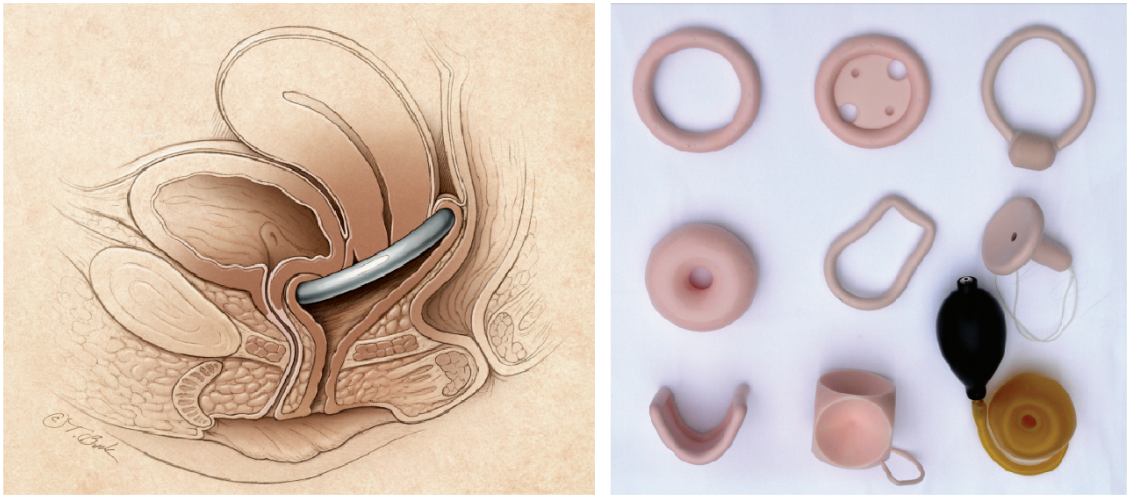


Figure 3.5: Ring pessary *in situ* (left) and some common pessaries (right). First row *(left to right)*: ring, ring with support, and incontinence ring; second row: donut, SmithHodge, and Gellhorn; third row: Gehrung, cube, and Inflatoball [6].

Pessaries are mainly made from medical-grade silicone. They can be divided into two types, supportive, which comprehends the ring, ring with support, Gehrung, Hodge, and the space occupying pessaries, such as donut, Gellhorn, cube, inflatable pessaries. The continence pessaries contain a knob to gather the urethra to help in SUI problems [38]; [6].

The use of pessary is simple, safe and effective, and it can be an option for all stages of POP. However, patients need regular appointments to avoid complications as infections, erosion or fistula [22]. The most common complications involved are irritation, bleeding, vaginal discharge, pain, ulceration, and odor. Also, bacterial vaginal happens in about 30% of the women with pessary [6].

Pelvic physiotherapy

Physical therapy reduces botheration and symptoms, and improves pelvic floor functionality by training the PFM. This approach includes several specialized therapies, physical activity, cognitive behavioral therapy, biofeedback, electrical muscle stimulation, and bladder, bowel habit, muscle, and coordination training [38].

The **biofeedback training** is an adjunctive therapy consisting of the use of an external sensor to indicate body processes, mostly to change the measurement quality. The aim is to identify and to isolate the PFM with the visualization of the muscle force and duration. With the electromyography (EMG) assessment of PFM, the surface EMG of the muscle recorded is interpreted, to describe qualitatively the muscle activation pattern [40].

The **electrical therapy** uses electric potential or currents to obtain therapeutic muscle responses. It applies electric direct pulses to striated PFM (end-plate) in order to easy contractions. This stimulation can cause indirectly the inhibition of the detrusor muscle contraction [40].

3.6.2 Invasive Treatment

This intervention should be only carried out in symptomatic patients or patients who feel discomfort and nuisance by the POP [40]. Additionally, cases of pessary failure, prolapse combined with urethral sphincter incompetence or faecal incontinence, or patients who desire a definitive treatment are also indicates for this management [41]. The decision for surgery should come from a previous discussion with the clinician to understand the patient's goals and expectations, namely regarding body image and sexual function [6].

The risk of patients by the age of 80 years having to undergo surgery for prolapse or incontinence is, at least, 11%. These surgeries aim to relieve symptoms, restore the normal anatomy of the vagina, retain sexual function, urinary, and anal continence. Normally, dysfunctions caused by vaginal delivery involve all of the pelvic floor and the supports for pelvic organs, even if only organ prolapses. In cases of more than one compartment affected, a combination of different approaches may be necessary. Interventions can be classified according to their defective compartment and approach (Table 3.4) [41].

Anterior compartment

In the anterior compartment can occur prolapse of the urethra (urethrocele), of the bladder (cystocele) or both (cystourethrocele) into the vagina.

Anterior colporrhaphy aims to correct cystourethroceles, by placing a mesh in the anterior vaginal wall to add support if a previous repair has failed. There are some intraoperative problems, such as cystotomy, haemorrhage, and haematoma, even if these are uncommon. The major postoperative complications include difficulties in voiding and prolapse recurrence.

Colposuspension is performed in cases of urethral sphincter incontinence combined with second or third-degree cystourethrocele. The sutures set through the ipsilateral iliopectineal ligament approximate the paravaginal fascia on either side of the bladder neck and the bladder's base to the pelvic side wall.

The use of synthetic implants reduces the risk of recurrence by one-third. Plus, the success rate for anterior repair increased from 52% to 86% with mesh augmentation. In general, recurrent surgeries were more frequent after synthetic mesh placement, for recurrent prolapse or mesh complications. Anterior repair lowers afterwards the risk of recurrence and the risk of *de novo* dyspareunia

Table 3.4: Classification of prolapse operations by compartment and by approach [41]

Compartment	Vaginal route	Suprapubic route
Anterior	Anterior repair with or without mesh; paravaginal	Colposuspension; paravaginal
Middle	Vaginal hysterectomy; vault repair (fascia); sacrospinous fixation; bilateral iliococcygeal hitch	Sacrohysteropexy; sacrocolpopexy
Posterior	Levator plication; fascial repair with or without mesh; transanal repair	Mesh interposition;sacrocolpopexy with mesh interposition

(previously undetected/untreated painful intercourse), which occurs usually after transobturator synthetic mesh implantation [41].

Posterior compartment

In the anterior compartment can occur the prolapse of the rectum into the vagina, that is, the rectocele.

Cases of rectocele can be repaired with the levator plication or fascial repair method. If it's not the first surgery for prolapse, a mesh can be placed in the posterior vaginal wall to add support. The major disadvantage of **levator plication** is dyspareunia, caused by muscle fibers' atrophy, leading to cicatrization [41]. Regarding the **fascial repair method**, it uses midline suturing of the fascia to repair the posterior vaginal wall, which has a cumulative success rate higher at 86% than the 70% correspondent to the defect-specific repair. The recurrence risk is greatly lower with the midline fascial repair, thereby it is the most suitable for primary rectocele recovery. However, levator plication is the standard approach, even though the approximation of the *levator ani* is not necessary for the posterior repair as it has a lower success rate than with the midline fascial suture [37].

Posterior vaginal wall repair was shown to reduce by half the risk of recurrence, compared with the use of biological implants, thereby the use of biological implants should be avoided as they show offering no benefits. Although there are no randomized studies, non-controlled prospective and retrospective studies show a lower rate of recurrence when using non-absorbable synthetic

meshes. Therefore, the lack of comparative studies does not encourage the use of this synthetic meshes on primarily posterior wall repair [37].

Middle compartment

In the apical compartment, it can occur the uterine or vaginal vault prolapse and enterocele. Vaginal vault prolapse occurs when the vagina's upper part descends into the vaginal canal or outside of the vagina, which can happen combined with uterine prolapse or after a hysterectomy.

The **vaginal hysterectomy** is the preferred treatment for uterine prolapse, which removes the uterus through the vagina, and, if the case also has a rectocele or a cystocele, this procedure can be associated with an anterior and/or posterior repair. On the other hand, indications for **sacrohysteropexy** (or hysteropexy) include the desire of the patient in maintaining their uterus, of carrying children, cases of failure of conservative treatment in healthy and young nulliparous patients, cases of congenital anomaly, and women who have declined a hysterectomy. Sacrohysteropexy consists of the use of a Y-shaped surgical mesh to perform the attachment of the uterus to the anterior longitudinal ligament over the sacrum [41][42].

To operate the vault prolapse and enterocele, vaginal surgery is an option that has the great advantage of not requiring an abdominal incision, which reduces the hospital stay and the pain of the women. Now, the procedures available as vaginal surgery are sacrospinous fixation, iliococcygeal hitch, and pubocervical rectovaginal fascia repair. **Sacrospinous fixation** implies the unilateral or bilateral fixation of the vault to the sacrospinous ligament. However, there can be complications after an injury of the pudendal nerve and vessels. On the **bilateral iliococcygeal hitch** approach, the vault is suspended bilaterally to the fascia of the iliococcygeus muscle and anteriorly to the ischial spine [41].

The **sacrocolpopexy** (SC) is the standard procedure for the treatment of vaginal vault prolapse, which consists of the attachment of the vault to the longitudinal ligament over the sacrum with a mesh (Figure 3.6). This approach comprehends the two alternatives of abdominal SC (ASC) and the laparoscopic SC (LSC), which depends on the route used to operate. Comparing the sacrospinous fixation with the ASC, the last one has a higher success rate, although it requires longer operative and recovery time, thereby increased associated costs. LSC takes longer than ASC, but it decreases significantly the risk of postoperative ileus/small bowel obstruction, the intraoperative blood loss, and hospitalization stay. The vaginal apex can be suspended using the woman's own tissues and sutures (native tissue repair), or mesh can be placed abdominally, to suspend the top of the vagina to the sacrum (SC), or transvaginally (transvaginal mesh) [41][43][6].

About complications due to mesh placement, studies show rates of vaginal erosion posterior to ASC from 0 to 10% after seven years, while the rates after vaginal mesh implantation reported were from 0 to 30%. Thereby, the use of vaginal mesh has been evaluated by the U.S. Food and Drug Administration regarding its potential complications [6]. Since 2005, the FDA has received thousands of reports of complications with the use of surgical mesh devices for POP repair, the most common complains were bleeding, pain (general and during coitus), infection, urinary

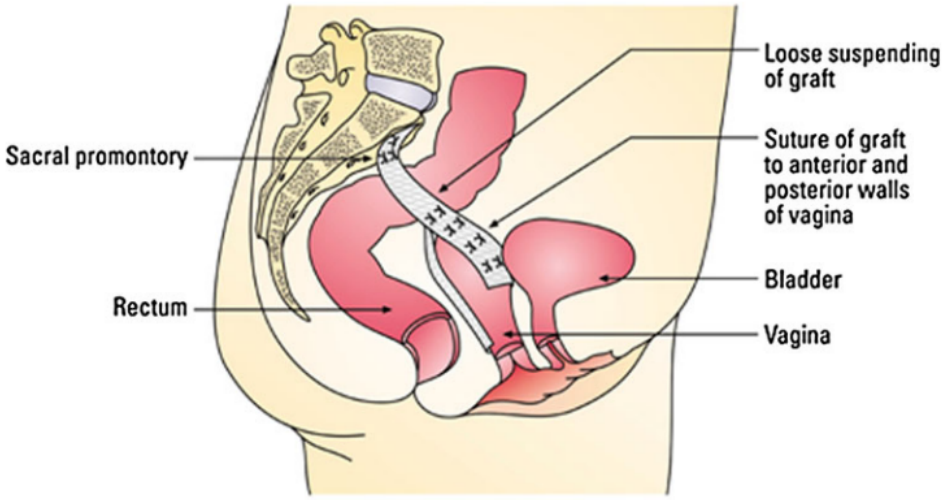


Figure 3.6: Abdominal sacrocolpopexy [44].

problems, mesh erosion through the vagina (or exposure, extrusion or protrusion), and organ perforation. Until recently, surgeons relied on the use of meshes in reconstructive surgeries, but on April 16, 2019, the FDA has forbidden its use for transvaginal repair of anterior compartment POP, since its safety and effectiveness was not demonstrated in the context of patient population in a clinical trial [1].

The risk factors for erosion include obesity, the use of polytetrafluoroethylene meshes, hysterectomy, and smoking (which affects both abdominal and vaginal mesh implantations). Surgeries to repair prolapse can improve dyspareunia but it can also be its cause, in fact, dyspareunia and chronic pain were reported in 3 to 13% of cases, especially following vaginal mesh placement. When the discomfort is due to tension of the mesh or its fixation sites, the solution consists of incision of the mesh or of its fixation arms, mesh mobilization, and abscission of total or part of the mesh [37].

Thereby, the FDA evaluated the reported adverse events, so recently increased data requirements for the use of these meshes for POP, and their classification changed from class II to class III, making them high-risk devices. This transition influenced, even outside the U.S., the use of synthetic meshes on transvaginal procedures. Thus, a study of 2018 at the Careggi Hospital, Italy, aimed to evaluate the veracity of these complaints, since they claimed to have performed mesh surgeries for POP since the 1990s and have persisted since their results have been consistently satisfactory. The surgeries to postmenopausal POP-Q stage II patients were done between May 2008 and December 2013, with a mean follow-up of 5.6 years. The overall results obtained were a success rate of 92.5% at one year and at the follow-up in May 2016 this rate was 84.4%, with this data remaining stable over time. Early complications occurred at 3% of the patients, late at 7.8% of which mesh extrusion happened in 6.3%. Also, it was shown an improvement in the prolapse quality of life questionnaire (P-QoL) from preoperative to postoperative data, remaining

stable with time. Cases of *de novo* dyspareunia were 17.6% at 12 months and 10.3% in May 2016. Therefore, this study claimed the safety of the use of meshes in prolapse repair as there were a low rate and grade of complications and an expressive improvement in the quality of life [45]. Until recently, surgeons relied on the use of meshes in reconstructive surgeries, but on April 16, 2019, the FDA has forbidden its use for transvaginal repair of anterior compartment POP, since its safety and effectiveness was not demonstrated in the context of the patient population in a clinical trial. Due to the big controversy regarding the synthetic mesh implants, more research and studies will need to analyze its impact on the surgical procedures.

Chapter 4

Computational Modelling of the Female Pelvic Cavity

The approach for the study of the synthetic mesh is by using computational models. So, this chapter focuses on the topic of biomechanical modelling and the finite element method (FEM). Accordingly, a general introduction to this method is relevant and some fundamentals behind the construction of the anatomical representation as well as examples of models developed recently and the one to be used in this study.

4.1 Finite Element Method

The development of computer modelling tools is growing as an important instrument in Medicine, as they enable directly to demonstrate clinical outcomes simulated on the model. Considering experimental studies *in vivo* are difficult to execute, imaging and biomechanical modelling allows the demonstration of the role of PFM defects on the pelvic support system [46]. Also, computational models of the pelvic cavity can help the surgeon on the evaluation and planning of the procedure, as well as with the physiological conditions of meshes, having a numerical model capable of appreciating the interaction between the prosthesis and the biological tissues involved [47]. Surgical planning is especially important for surgeons with less experience on a certain technique, improving the safety of the procedure and providing a patient-tailored surgery [48].

However, this kind of knowledge requires a great description of the pelvic architectural structure and accurate models that truly represent the biomechanical behaviour of the pelvic cavity, regarding its organs and supportive tissues [18]. For the development of computational models, data from images of MRI are collected to better visualize the structures of the pelvic cavity. Hence, the anatomy, and perhaps the material properties, vary from patient to patient, thus stating the importance of calibrating the model to each geometry with the MRI images [49].

The FEM consists of a numerical tool useful to find an accurate solution to a broad spectrum of complex problems. With this technique, mathematicians were able to solve ordinary and partial

differential equations, obtaining their numerical solution, enabling the use in difficult boundary value [50]. The FEM allows validation of an anatomical and physiological pelvic support system comparing the analysis of a normal to a pathological patient. It helps to investigate the process of developing a prolapse, to develop specific tools for the diagnosis or treatment, and it enables a patient-tailored treatment [51].

The basis of this method is the decomposition of a solid into simple finite elements interconnected at specified joints named nodes or nodal points. This way, an approximated solution is found for the analysis of the structure. The combination of the elements and nodes is called the mesh. By assuming that the variation of a variable inside a finite element can be described by a simple function (interpolation models), these functions can be defined in terms of the variable values at the nodes. Solving the equations, the nodal values of the variable are discovered, which can be the elements strain and stress of solid or structural mechanic.

The type of elements (for example, triangular, tetrahedral, cubic) usually is determined by the type of structure itself, as to use a congruent geometry. This is easy to idealize for a regular body but for others it's not that intuitive, so those require a deeper selection. Then, the idealization is made, for example, with the accuracy wanted, the complexity of the equations, and the number of degrees of freedom.

The size of the elements is a parameter that needs attention, as it affects the approximation to the exact solution. With a bigger element, the final solution is less accurate but the computational time decreases. The size of the elements may be different in the same structure.

The number of elements is parallel to the accuracy desired, the number of degrees of freedom involved, and the size of the elements. Despite the fact that a higher number of elements usually causes more precise solutions, there is a border number from which no greater results can be obtained [52][50].

A tridimensional element can be characterized by the nodal information it contains, providing parameters such as the nodal force vector f^e, and the nodal displacement vector δ^e for the element e. The nodal forces are those that balance the concentrated or distributed loads pressing on the element. After applying a load, the values of the displacement are calculated to obtain the consequent shape of the element. Note that the number of components in the vectors reflect the degrees of freedom in the element [53].

The relationship between the nodal forces and the nodal displacements is related to the occurred element deformations, an association that can be described by the following equation:

$$f^e = k^e \delta^e \tag{4.1}$$

With the square stiffness matrix k^e for the element e. In complex problems, the stiffness coefficients can be estimated based on the given displacement functions [54].

4.2 Biomechanical Models

Computer 3D reconstruction of the pelvic region provides an instrument to understand the mechanical behavior of the pelvic floor and study the different dysfunctions associated with this cavity. The pelvic region is a very complicated anatomical region with a complex architecture. One of the difficult most difficult tasks is to build a true representation of the organs and the interaction between them, which may lead to a refined model with a high computational cost. Thus justifying why most models figure only part of the pelvic cavity [47]. A short bibliographic review of biomechanical models of the pelvic cavity and surgical meshes will be presented.

Several finite element models of the PFM have been built over time to study the PFD. The model built by [55] aims to understand the contribution of the PFM to the development of SUI. They used clinical data from 26 patients with pelvic muscular defects for the modelling. The starting point was to design a two-dimensional sagittal and symmetric model of the supportive structure based on the female pelvic anatomy (not considering the fascia and the uterus for simplification) (Figure 4.1). It included the elements PC-PR muscle band, the IC muscle, perineal membrane, cardinal ligament, and uterosacral ligament; the organs bladder, rectum, and vagina; and as bones it includes the sacrum and the pubic bones. The information of the POP-Q and muscle strength measurements were added to the model to quantify the defects of active and passive supports. As these tissues are hyperelastic, the mechanical behaviour of the pelvic floor muscles, ligaments and vagina was modelled using an exponential force-elongation relation. The effect of the PFM defects on the bladder neck and vaginal apex supports for each patient was obtained using the patient-specific stiffness properties of the vagina and ligaments. The simulation of the model showed the contribution of the weakened PFM to the vaginal apex and bladder neck prolapse, a factor commonly related to SUI [55].

The model developed by [51] aims to simulate the biomechanical behaviour of the pelvic cavity using the FEM (Figure 4.2). They used MRI data to rebuild the geometry so that individual models of the bladder, rectum, uterus, vagina, rectum, pubic bones and sacrum are created with computer-aided design (CAD). The attachment of the uterus is assured by the round and utero-crowned ligaments anteriorly, by the paracervix and uterosacral ligaments to suspend it, and by the perineal body to give support. Anatomically during surgery, only five sets of ligaments (10 in total) can be easily located, the pubic vesical, vesico uteral, utero, round, and parametrium ligaments. Meanwhile, eight sets of ligaments (16 in total) can be determined by adding the lateral and posterior rectal ligaments, and the vesical lateral ligaments. So, the final models presented has five and eight sets of ligaments. This model considers the real hyperelastic behaviour of the pelvic tissues, the pelvic organs, and muscles as deformable bodies, the uterus, outer pelvic bone, and sacrum as non-deformable [51].

About the model to be used, it includes the pelvic organs, the bony pelvis, and other major supportive structures, which was developed based on MRI of nulliparous healthy women. With Abaqus software, the mesh created was formed by tetrahedral elements. The bones were considered rigid and fixed, and the organs to have a hyperelastic response. Meanwhile, isotropic

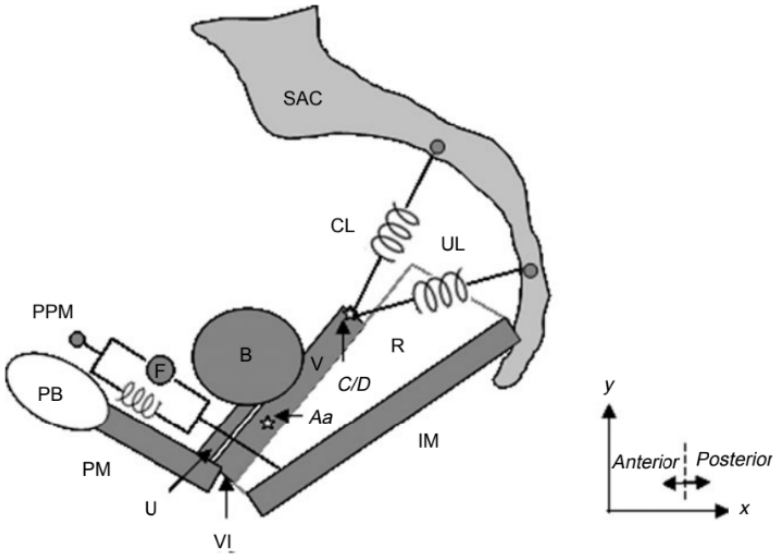


Figure 4.1: Pelvic support system biomechanical model in standing position [55]. Point Aa approximates the position (cm) of the bladder neck measured from the VI; C or D approximates the position (cm) of the vaginal apex measured from the VI for women without and with uterus, respectively; PPM, PC-Pr muscle band; CL, Cardinal ligament; Ul, uterosacral ligament; PB, pubic bone; SAC, sacrum; PM, perineal membrane; IM, IC muscle; V, vagina; VI, vaginal introitus; R, rectum; B, bladder; U, urethra; GH, genital hiatus.

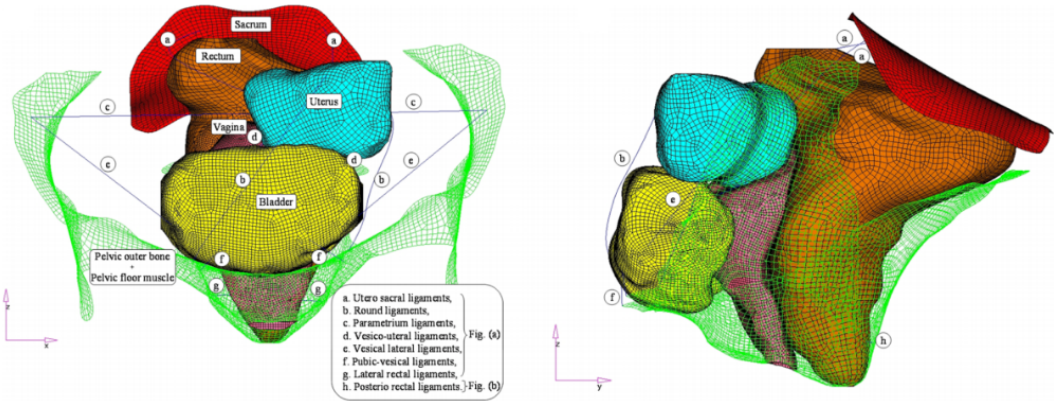


Figure 4.2: FEM of the pelvic system front view (left) and side view (right) [51].

simple models were used for the muscles and ligaments. The supporting structures represented in this model, that is, the levator ani, the PU, cardinal, uterosacral, and the lateral ligaments of the rectum, the ATFP, and the pubocervical fascia, were connected to the bone and organs by using multi-point constrains. On the other hand, the attachment between organs was modelled as frictionless. The synthetic mesh was modeled with specific dimensions (150 mm x 10 mm) of

a polypropylene monofilament band and a hyperelastic mechanical behaviour. The implant was placed over the superior surface of the middle of the urethra, below the bladder neck to end on the superior rim of the pubic bone, where it would be put in surgery [46][56]. Characterization of the *pubovisceralis* muscle was performed with this model by numerical simulation. To do so, three groups were used to build individual isotropic hyperelastic models, women with SUI, POP, and without any of these pathologies (control group). The results obtained show that women with POP have the highest stiffness values, the biggest force produced by the *pubovisceralis* muscle and the highest values for its material parameters. These outcomes are accordingly with other studies that prove the elasticity module of prolapsed tissues is higher compared with normal tissue [57][58].

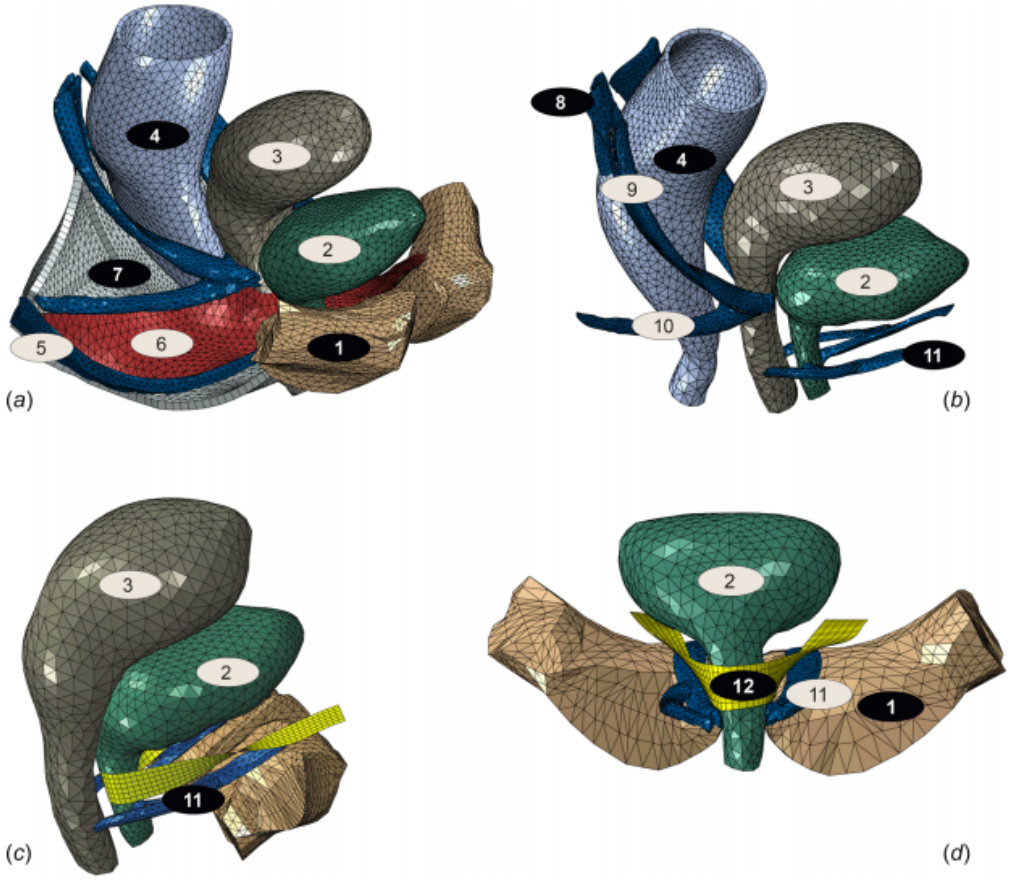


Figure 4.3: Pelvic finite element model in (a) and (b). Finite element model of the implant placed as it would in surgery in (c) and (d). (1) pubic bone, (2) bladder, (3) uterus, (4) rectum, (5) arcus tendineous fasciae pelvis, (6) pelvic fascia, (7) levator ani, (8) lateral ligaments of the rectum, (9) uterosacral ligaments, (10) cardinal ligaments, (11) pubourethral ligaments (vaginal and urethral portions), and (12) midurethral sling [56].

Chapter 5

Computational Modelling of the Surgical Mesh

The main task to the analysis of the synthetic mesh is to create and design the models for the structures to be simulated. This chapter focuses on the topic of biomechanical modelling of the surgical mesh at study, and the consequently used methodology to create them, with the several computational models are shown and explained.

A common material used in uterine prolapse surgeries are synthetic meshes made of polypropylene (PP). They are binding porous structures that can hold pelvic organs in place when there is loss of supportive capacity of the tissues around them. The one to be studied is *Restorelle® M Flat Mesh* (Figure 5.1), made of a ultra-lightweight and non-adbsorbable sheet with knitted monofilaments of popypropylene. It is used for the treatment procedure of uterine prolapse called sacrocolpopexy, by lifting the vagina and holding it in place [59].

Restorelle is a porous material with the original dimensions of 15 x 10 cm, while a single square pore has the dimensions of 1.80 x 1.80 mm [60] [61]. Since the introduction of the porosity on the model is the main differentiating factor, the analysis of the impact of the inner pores on the entire mesh occurs in a large range of spatial dimensions, consequently, this study requires a complex process across different scales. Hence, it is not possible to study the whole mesh as a single space continuum. As a result, the study should be done in a multiscale modeling approach, considering different space continua, each representing a case study at a specific space scale. This is, separating the analysis into two, starting from the micro to macro analysis, as it is necessary to consider the inner pores and their impact.

5.1 Representative Unit Model

Based on the images obtained from Scanning Electron Microscopy (SEM) of *Restorelle* (Figure 5.1), a very complex microstructure inside was revealed, with multiple filaments interconnected forming the material. In particular, a representative unit was found to be common and

repeated throughout the formation of the mesh. This elaborate knotted interaction of filaments must influence the overall behaviour of the surgical mesh, such as giving distinct characteristics and mechanical properties. For that reason, it is interesting to study more about this microstructure, named here as representative unit.

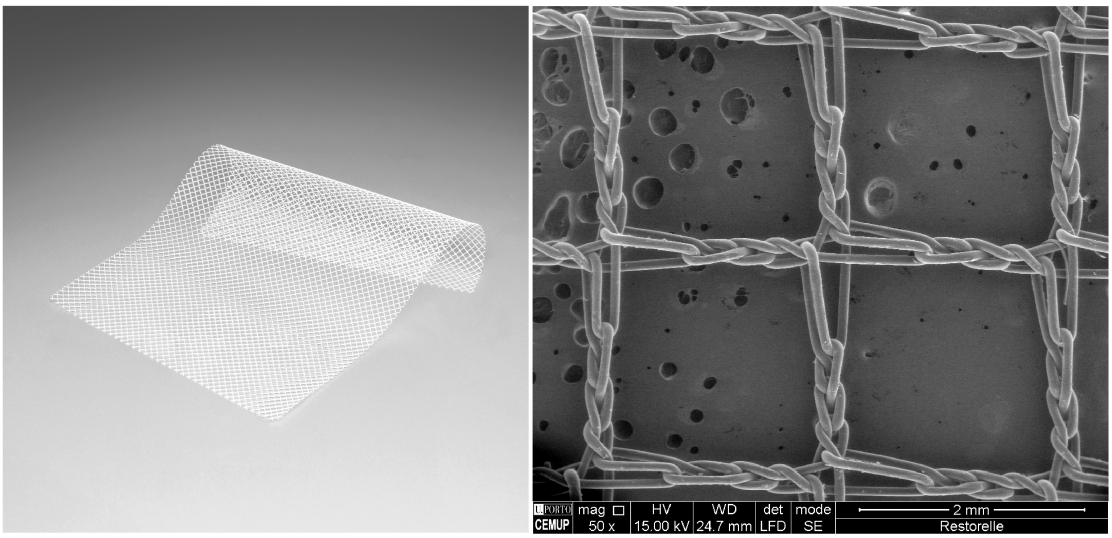


Figure 5.1: *Restorelle M Flat Mesh* surgical mesh used in surgery to fix the uterine prolapse. *Restorelle* sheet (left) and its SEM image showing the microstructure (right).

Regarding this unit, the commercial software *Rhinoceros 6 Evaluation* was used to design and create its model to be simulated. In the Figure 5.2 is presented the resultant geometrical model of the representative unit.

The process to create this model was very complex. Based on the images obtained from the SEM shown in Figure 5.1 at the right, as well as the literature [60] [61], the necessary dimensions were examined. The monofilaments have a diameter of 0.080 mm, while the pores are square 1.80 mm uniform. Also, the thickness of the sheet is 0.3 mm. With the *Rhinoceros* software, the primary distribution of the monofilaments was outlined by drawing the two-dimensional curves. Then, the third-dimension was added, by changing the height of different parts of the curve, according to the truthful z-axis alignment shown in the SEM images. Consequently, each intersection between filaments was checked and aligned correctly, in order to portray the real complexity of the microstructure. Afterwards, the line filaments were filled with the operation *pipe*, to provide volume by giving the diameter input value of 0.080 mm. This step is to duplicate the monofilaments of polypropylene characteristics of *Restorelle*. The intersections were confirmed again so that there were no undesired overlaps of monofilaments, as the design of the unit was aiming to be close to the actual structure. The final structure has approximately the dimensions of 2.0 x 0.5 x 0.3 mm, and it's presented in the Figure 5.2.

Since the thickness of the synthetic mesh is about 0.3 mm, it can be considered negligible

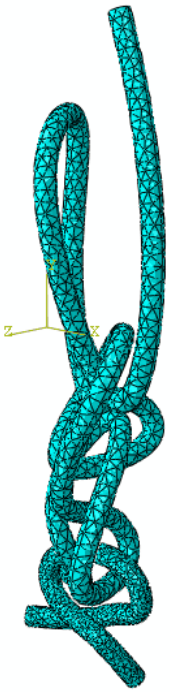


Figure 5.2: Developed geometrical model of the representative unit with the .

when compared to the length and width of 15 x 10 cm, hence *Restorelle* is considered a sheet. Therefore, the mechanical behaviour of the computational model of *Restorelle* can be fairly characterized considering properties in two dimensions. Accordingly, to study the impact of the complex microstructure on the entire synthetic mesh properties, uniaxial tensile tests were made on the representative unit in the y-direction and x-direction, neglecting the z-direction. These tests are performed as a way of characterizing and understanding the mechanical behaviour of a repetitive element in the mesh. Accordingly, the geometry of the unit model was imported to the *Abaqus CAE* software to carry out the biomechanical simulations.

5.2 Surgical Mesh Model

As the next step, the model of the entire synthetic mesh is also created with the software *Rhinoceros*. This time, since the microstructure was studied, the complex representative unit can be substituted by a simple parallelepiped, having similar dimensions as the ones seen in the representative unit. This procedure aims to reduce the complexity of the model developed and, as a consequence, reduce the computational time of upcoming simulations. Therefore, *Restorelle* can be represented by an even intersection of crossed parallelepipeds, that will have as input properties the outputs of simulating the representative unit. In the *Rhinoceros* software, the first square of parallelepipeds was designed, with dimensions of 2.0 x 0.5 mm, with the inside empty representing the square

macropore characteristic of the *Restorelle* mesh, seen in the closeup in the Figure 5.3. This square is repeated until the overall dimensions of the mesh model are 150 x 40 mm.

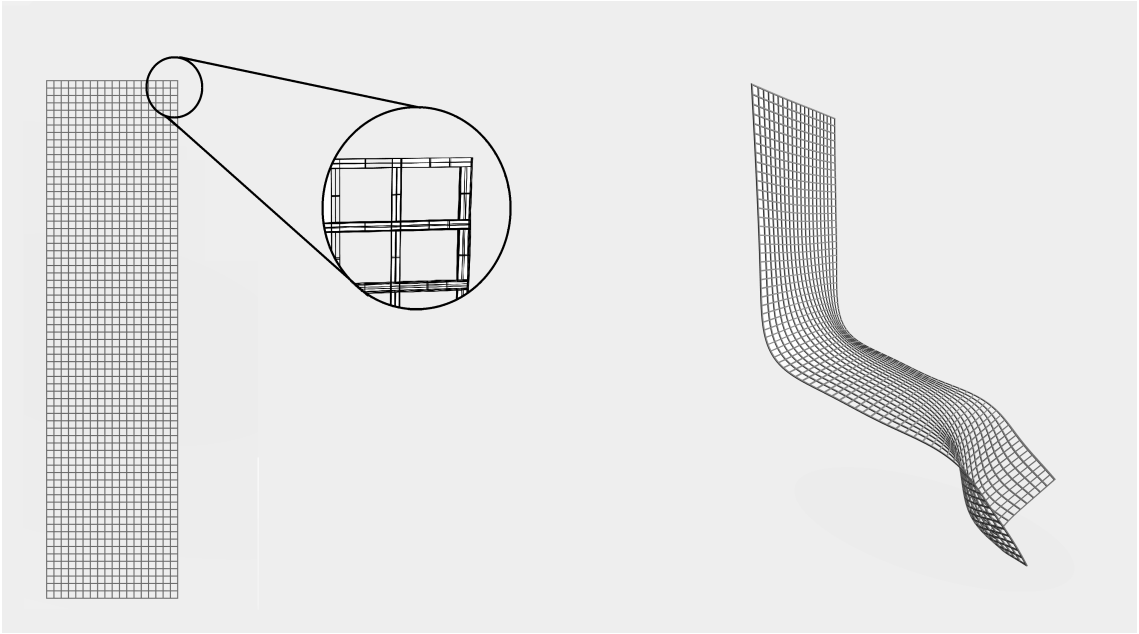


Figure 5.3: Developed geometrical model of the surgical mesh *Restorelle*, used to correct the pelvic organ prolapse. *Restorelle* flat (left) and adjusted to the uterus (right).

The created mesh is represented in Figure 5.3. The right image is the flat model, which was obtained straight from the process described before. It is ideal for performing tensile tests. The left one, the deformed version, was created to directly implant in the full female cavity model so that it would fit the uterus and connect it to the sacrum. The procedure to adjust correctly the geometry of the flat mesh was extensive. The three-dimension pre-outline of the wanted deformed geometry was drawn with a curve, at first loosely close to the desired. Then, the fitting to the uterus was done by extracting the uterus mesh points of the female cavity model and creating a surface from those mesh points. This surface needed to have the same dimensions as the flat mesh model, that is, with a width of 40 mm. Then, this surface was to substitute the bottom part of the pre-outline geometry, made previously. Moreover, the outline curve dimensions were adjusted so that it would satisfy the flat model dimensions of 15 x 40 mm, only then a surface was created from the outline curve with the function *EdgeSrf*. If the outer dimensions aren't correct, the pores and filaments deface, the original flat geometry is no longer present and the object is disfigured and invalid. Now, having the flat model (with the parallelepipeds and pores) and the surface with the desired deformation, the command *FlowAlongSrf* allows the flat mesh to be fitted to the surface, creating a deformed porous mesh model. At last, this deformed version is already adjusted and fitted, ready to be attached to the uterus.

The geometry of the mesh model presented is a simplification of the complex knotted mesh, although it should still truly represent *Restorelle* mechanical behaviour if the input properties

correspond to the results obtained from the representative unit tensile tests. To understand this issue, the geometry of the model was imported to the *Abaqus CAE* software to perform uniaxial tensile tests in the y-direction, and afterwards compare it with the experimental results obtained previously from the working group.

5.3 Mechanical Properties of the Models

The selection of the most suitable mechanical properties for the materials to be used in the computational models is crucial since they define the way materials react to applied forces or displacements, for example. The definition of these mechanical properties should represent the real characteristics of the structures the most truthfully possible so that the simulations can provide a reliable result. While simulating with a complex model, there are a wide set of interactions between the different organs and structures, such as fixed boundary conditions between structures attached. Thus, the definition of mechanical properties and interactions between materials impact on the way the model deforms due to the external applied loads.

Representative Unit

Restorelle is a device used in surgery to repair pelvic organ prolapses, made of polypropylene monofilaments knotted between them. Therefore, the mechanical properties used for the representative unit simulation were extracted from the polypropylene properties found in the literature [62]. The constant values used are shown in Table 5.1.

Table 5.1: Mechanical properties of Polypropylene, used in the representative unit model [62].

Density (g/cm^3)	Young's modulus (MPa)	Poisson's modulus	Friction coefficient
0.906	1300	0.42	0.44

Surgical Mesh Model

After simulating the tensile tests on the representative unit in both directions with the *Abaqus CAE* software, the stress and strain values are extracted from all nodes to provide the stress-strain curve. From this graphics, the effective Young's modulus of the basic unit of the surgical mesh is obtained, for the two orthogonal directions. Thereby, the input properties of the whole surgical mesh model are now the effective values of the Young's moduli.

Chapter 6

Results and Discussion

POP is characterized by the descent of one or more organs. It is usually due to insufficient pelvic support when the muscles and ligaments lose their strength. For the uterine prolapse, the uterosacral ligaments are the ones that provide the most support to the uterus. Usually, for more severe cases, the treatment of the prolapse consists of a surgery that aims to rebuild the anatomy and recover the function of the pelvic organs. One synthetic mesh used to fix the anatomical position is *Restorelle*. It substitutes the support made by the uterosacral ligaments. In the computational model it is positioned posteriorly in the uterus, connecting it to the sacrum.

The present study of *Restorelle* was done across different spatial scales, starting from the microscale to the macroscale as the entire mesh model. These analyses focused on the simulation of uniaxial tensile tests on the several models manually designed.

6.1 Primary Study

As a pre-step, it was created a very simple model, to verify that the stress observed after an applied force or displacement is the same, as a primary task before going to the mesh models. As it's known from the Equation 4.1, the stiffness matrix relates the forces acting on the element nodes to their displacements. So, FEM automatically generates the stiffness matrix and, determining the nodal displacements, the resultant applied forces are obtained.

Accordingly, a simple model with two U-shape segments was created in *Rhinoceros* (Figure 6.1 left) and then imported to *Abaqus* in order to simulate uniaxial tension tests on the model in the y-direction. These were done by fixating the upper segments with encastre boundary condition, and then pull down the bottom by applying concentrated force and displacement conditions, as portrayed in Figure 6.1 at the right, and compare the two results. Although first, the two filaments were not touching, so the bottom had to be pushed with displacement conditions until the filaments were in contact. Then, that geometry was duplicated, one for applying displacement and the other for concentrated force. The deformed models obtained were compared to verify that the stress is similar in both cases, thus validating that displacement can be used to apply movement and its simulation results are still valid.

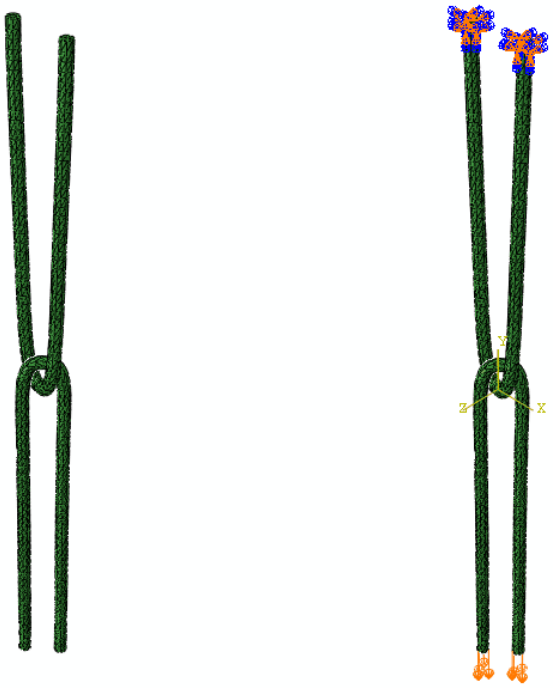


Figure 6.1: Simple model designed for verifying the concentrated force and displacement conditions (left), and the boundary conditions used on the uniaxial tension tests (right).

The obtained deformed models are shown in Figure 6.2 with the application of concentrated force (left) and displacement (right) in the y-direction. The verified magnitude of the output displacement of both models is very close.

To further analyse, each stress-strain curve was plotted, and its graphics are shown in Figure 6.3. The tensile test with displacement provided the value of Young's modulus of 1278.95 MPa, while the tensile test with concentrated force obtained a value of 1287.33 MPa. The comparison between the two reveals a 0.64% relative difference, which shows that, either using concentrated force or displacement, the output results are very similar. Now that this primary evaluation is confirmed, further studies can proceed.

6.2 Representative Unit Study

As mentioned before, the process to create the representative unit was done with the *Rhinoceros* software. After having the final geometry, the model was, then, imported to the *Abaqus* software, so that the uniaxial tension tests could be simulated. This study is important since it allows obtaining the effective Young's modulus, leading to more accurate results afterwards, instead of just using the constant value characteristic of PP. This difference comes from the fact that the elaborate microstructure built of the complex intersection of PP filaments, seen in Figure 5.1, must provide

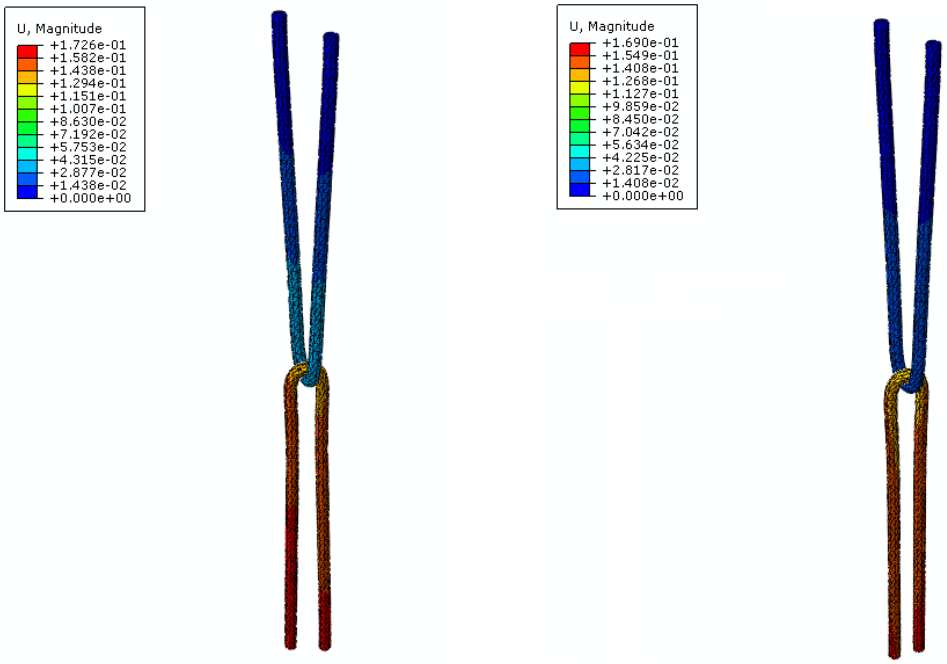


Figure 6.2: Output displacement magnitude obtained from the uniaxial tensile tests using concentrated force (left) and displacement conditions (right) on the simple model.

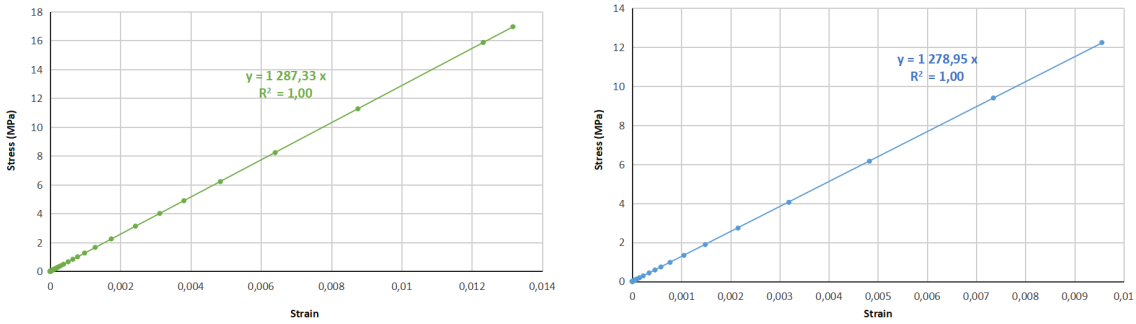


Figure 6.3: Stress-strain curve from the uniaxial tensile tests obtained with concentrated force (left) and displacement conditions (right) of the simple model.

different mechanical properties to the *Restorelle* mesh, when compared to a single straight filament of PP, namely regarding stiffness and the ability to resist to applied stress. As a consequence, the uniaxial tensile tests enable the computation of the effective Young's modulus, which can be further used in the definition of the mesh model properties.

Accordingly, the mechanical properties defining the representative unit model consist of polypropylene's characteristics, as the basic monofilaments are made of this polymer. Thereby, the input Young's modulus for the unit model is the value corresponding to the PP presented before, 1300

MPa, as well as the other constants shown in Table 5.1. As the model has a lot of intersections, the simulation came across contact problems, so there are a few contact conditions to be worked on. Namely, some minor initial overclosures caused by small penetrations, that is, contacting surfaces that overlap at the beginning of the analysis. Since the domain used is general contact, the default method to solve initial overclosures is with strain-free adjustments, appropriate to unintentional overlaps. The positions of the surfaces are automatically adjusted by displacements without stress or strain occurring, in order to remove the overclosures. This is done by defining contact initialization in the initial step. Alongside, the mesh created is made of tetrahedral elements C3D10, and the final result was shown before in Figure 5.2.

As referred in [63], *Restorelle* is assumed to have a bidirectionally isotropic behaviour, as a consequence, the uniaxial tensile tests are made only along the two orthogonal directions, x and y. So, first, the test was made in the y-direction (Figure 6.4 at left, so the upper section was fixated so that there was no movement nor rotation, and the bottom part was pulled down by applying a displacement condition, as it was verified in the previous section. The deformed model and the verified displacement magnitude is represented on Figure 6.4 at the right. The x-direction test is similar, but the bottom portion has displacement in opposite ways, as shown in Figure 6.5 at left. Subsequently, is plotted the resultant displacement magnitude at the right. As expected, the model stretched in y-direction and x-direction accordingly, with a maximum magnitude of displacement of 0.17 mm and 0.10 mm, respectively. The maximum value is higher in the y-direction since the unit has a bigger height than width, and more loose gaps in this direction to lengthen.

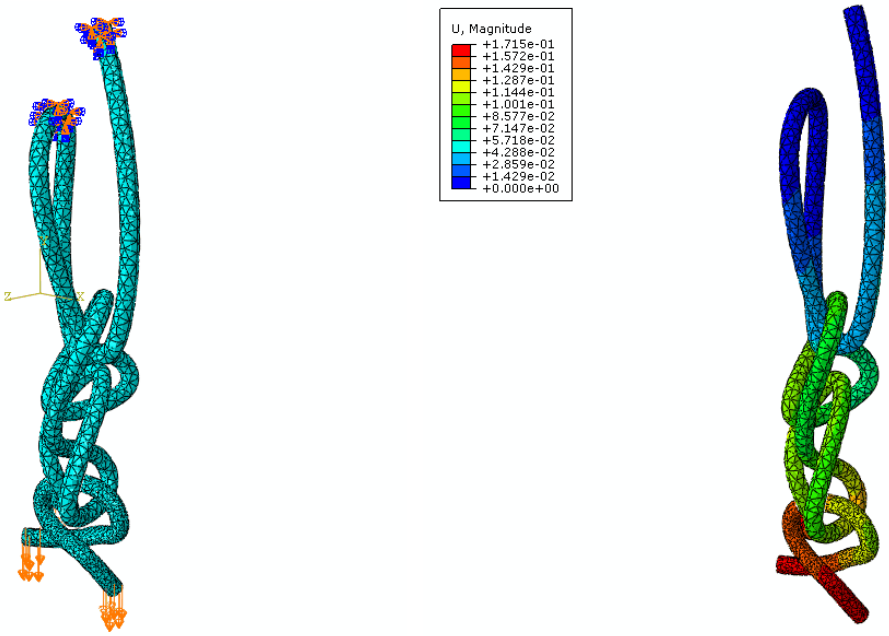


Figure 6.4: Uniaxial tensile test in the y-direction on the representative unit model. Boundary conditions applied (left) and resultant deformed model with the displacement magnitude (right).

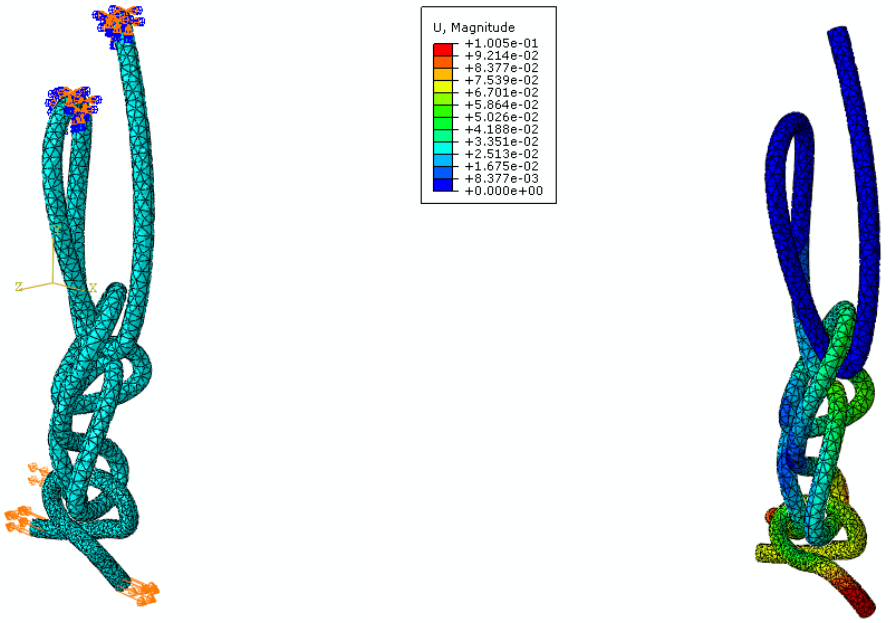


Figure 6.5: Uniaxial tensile test in the x-direction on the representative unit model. Boundary conditions applied (left) and resultant deformed model with the displacement magnitude (right).

Secondly, the stress and strain values of all nodes in the model, in the accordant direction, are extracted to plot the stress-strain curves for each test. The consequent graphics of the stress-strain curves are represented in the Figure 6.6, the blue line corresponds to the y-direction tension test, and the orange one to the x-direction tension test. Indeed, both stress-strain curve evidence a linear behaviour during the simulations made. In both simulations, the model suffered about the same strain, but in the y-direction there was a higher resistance to deformation, so the model is stiffer. Similarly, Young's modulus in the y-direction (Ey) is higher, about 1358.85 MPa, while the value for the x-direction (Ex) is 1203.88 MPa. These are the effective constants that are supposed to truly represent the stiffness behaviour of the mesh in both directions, rather than the simple polypropylene constants. Even though the difference is not enormous, the predominant Young's modulus is the Ey, the one that has the most expression. Hence, if we consider that [63] states that the *Restorelle* synthetic mesh is bidirectionally isotropic, its properties are the same along the two perpendicular directions, so the model can be simply defined by the predominant Young's modulus, the effective Ey can be used as the input mechanical properties of the fundamental unit of the *Restorelle* mesh for further simulations.

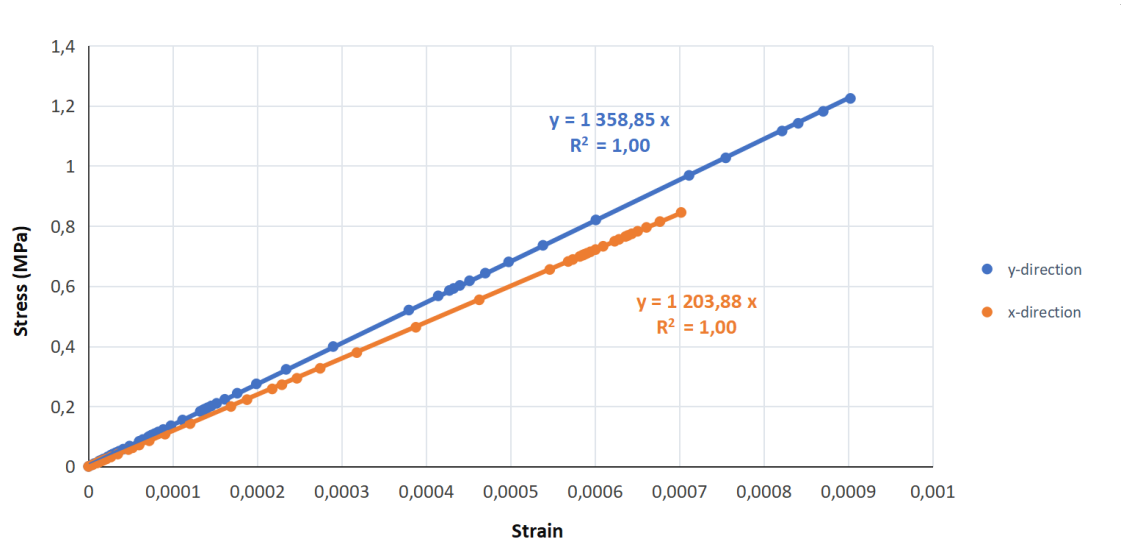


Figure 6.6: Stress-strain curve obtained from the uniaxial tensile test on the representative unit model in the y-direction (blue) and x-direction (orange).

6.3 *Restorelle* Surgical Mesh

The innovative design of the porous *Restorelle* mesh was done with the *Rhinoceros* software. The representative unit was substituted by a straight three-dimensional parallelepiped since this unit was already studied, and it can be simplified as a way of decreasing the computation time of the simulations with the entire mesh. The parallelepiped will be the repeated unit of the entire mesh, building a structure where the empty volume inside corresponds to the pores verified in *Restorelle*, thus introducing the porosity on the model as it is the main value subject of this study.

Briefly, the idea is to introduce the effective Young's modulus on the mesh model properties, obtained from the output of the tensile tests simulations with the representative unit, since the complexity of interactions in the unit would change the normal properties of polypropylene. Thereby, the effective Young's modulus obtained from the unit tensile testing in the y-direction will be considered to define the micro-behaviour of *Restorelle* in a first approach to the topic. Thus, the value of 1358.85 MPa is used in the mechanical properties of the mesh model definition, considering a isotropic material.

Now, to understand if the flat mesh model can represent *Restorelle*'s mechanical properties, uniaxial tensile testing is useful as it is a common assessment in literature. Besides, prolapse meshes mainly undergo uniaxial forces *in vivo*, so evaluating the response to uniaxial tensile tests provides important information on the mesh mechanical behaviour [61]. The after results are compared with the experimental tensile tests made with a specimen of *Restorelle*'s material. These were obtained from a uniaxial tensile test, with boundary conditions standard clamping boundary conditions, that is, the entire top and bottom edges fixed. In the same way, the biomechanical model of *Restorelle* is clamped along the top and bottom, with encastre boundary conditions in the

top and applied displacement in the bottom. In the presented test, applying 5 mm of displacement in the bottom section resulted in the deformed model represented in Figure 6.7.

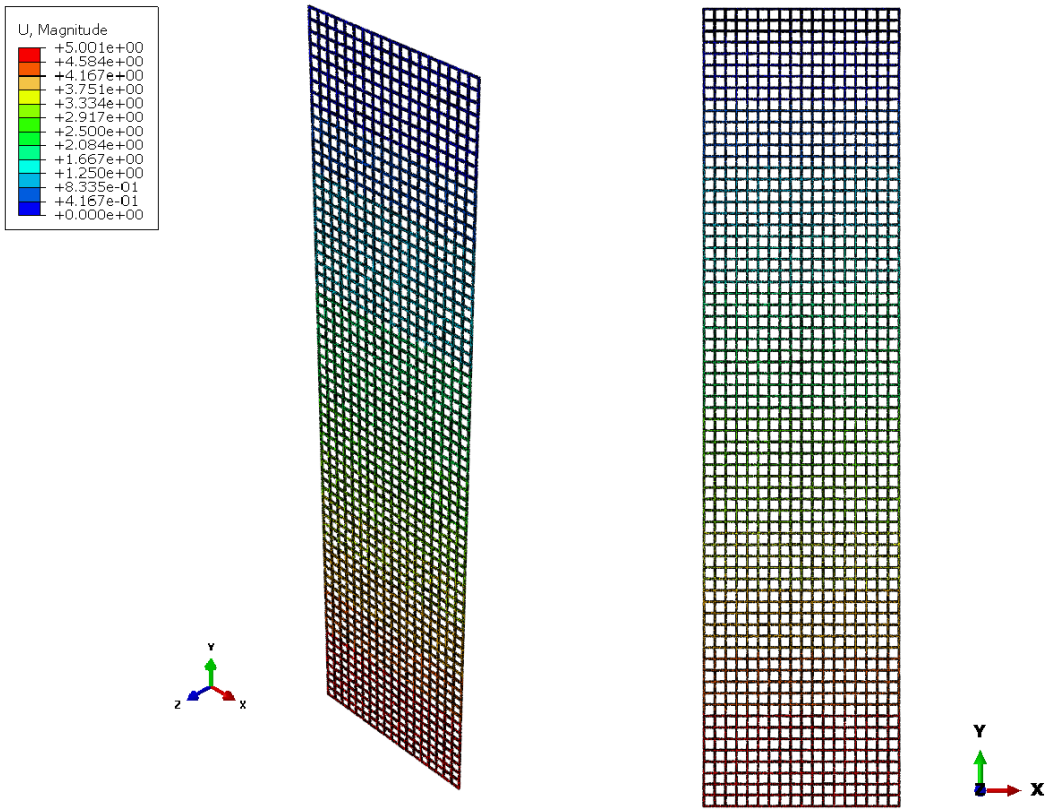


Figure 6.7: The deformed model with the displacement magnitude scale, resulting from the uniaxial tensile test in the y-direction on the porous *Restorelle* model.

In fact, applying 5 mm of displacement on the tensile test simulation reflects on a maximum displacement magnitude of 5 mm, as it is presented in the Figure 6.7, which could mean that the mesh model is fully able to comply with this small applied displacement. Then, the extraction of the stress and strain values in the y-direction of all nodes of the mesh enables the plot of the associated stress-strain curve, represented in Figure 6.8.

After simulating the tensile test on the mesh itself, the results obtained are compared with the experimental data obtained by the work group. The curve represented in Figure 6.9 was obtained experimentally by performing a uniaxial tensile test with a specimen of the mesh *Restorelle*.

In uniaxial tensile testing, there are some properties able to characterize a material, such as stiffness and Young's modulus, that are related to each other. The first constant refers to absolute measures, as it corresponds to the slope of the linear region of the load-extension curve, while Young's modulus is the slope of the stress-strain curve on the elastic region, so it is associated with relative measures. Hence, the stiffness depends on the size of the material, while Young's

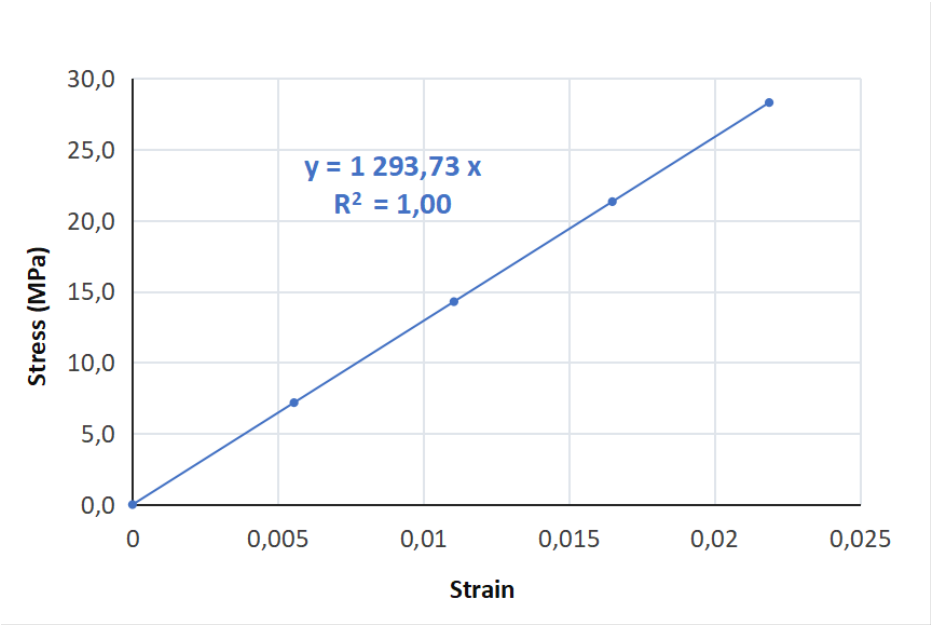


Figure 6.8: Stress-strain curve obtained from the uniaxial tensile test on the *Restorelle* mesh model, using the effective Young's modulus obtained from the tensile tests with the representative unit model.

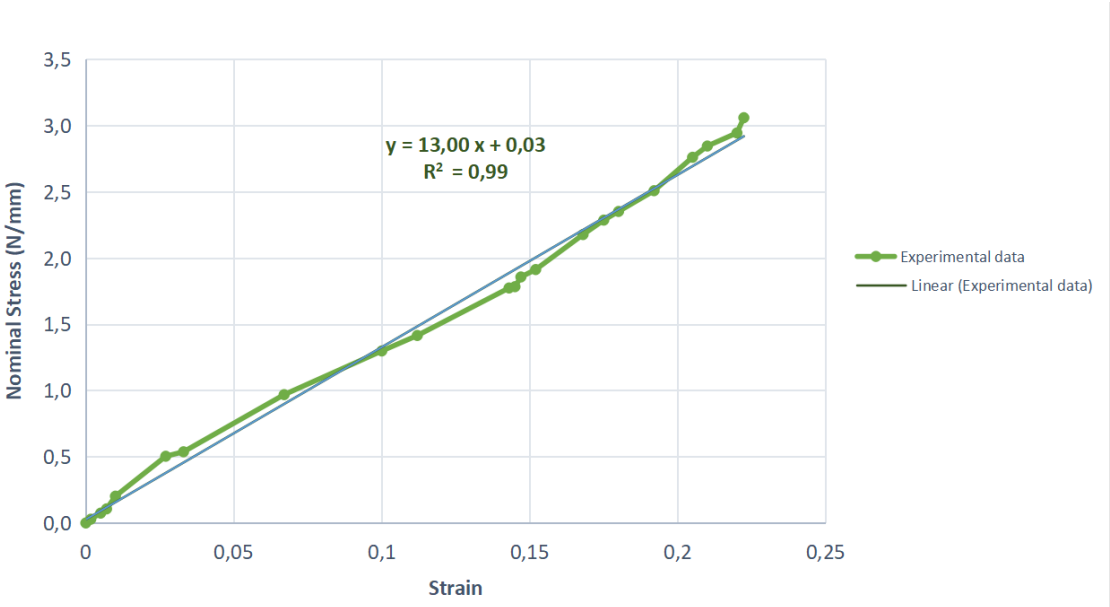


Figure 6.9: Stress-strain curve obtained experimentally from the uniaxial tensile test on a specimen of *Restorelle*'s material.

modulus is constant for the same material. Thereby, as seen in the graphics above, the resultant slopes are very distant, being the slope resulting from the simulation using the effective Young's modulus (obtained from the representative unit test provided) of 1293.73 MPa, almost 100 times

the one from the experimental tensile test (13.00 MPa). Compared with the specimen testing results, the strain observed in the simulation was about 10% of the experimental, meaning that the extension that occurred on the model was smaller, showing that the model is stiffer than reality. Also, considering that the stress required was 10 times the one observed in experimentally emphasizes the fact that the model is not as flexible as desired, it produced less deformation with more applied force per cross-sectional area. On the other hand, the stress-strain curves, and consequently Young's moduli, from this simulation with the entire mesh are in line with the results from the representative unit (Figure 6.6), that is, around the same value, which is expected as the mechanical properties remain the same, regardless of the geometry.

Since the results were not the desired, an alternative emerged. Instead of using the effective Young's modulus obtained previously, the use of the experimental data itself could test the mesh model. So, the data from the graphic on the Figure 6.9 was used as input mechanical properties on the mesh model, to perform a uniaxial tensile test in the y-direction again. The test was made by applying the same displacement as before, 5 mm, and the final deformed model was very similar to the previous simulation, as seen in the Figure 6.10 at the left, as the maximum displacement magnitude verified was also 5 mm. Secondly, the node values were acquired to plot the stress-strain curve seen in the right. The simulation resulted in a slope of 14.30 MPa, which is quite different from the previous simulation with the mesh model. It is, otherwise, in accordance with the experimental testing curve in Figure 6.9.

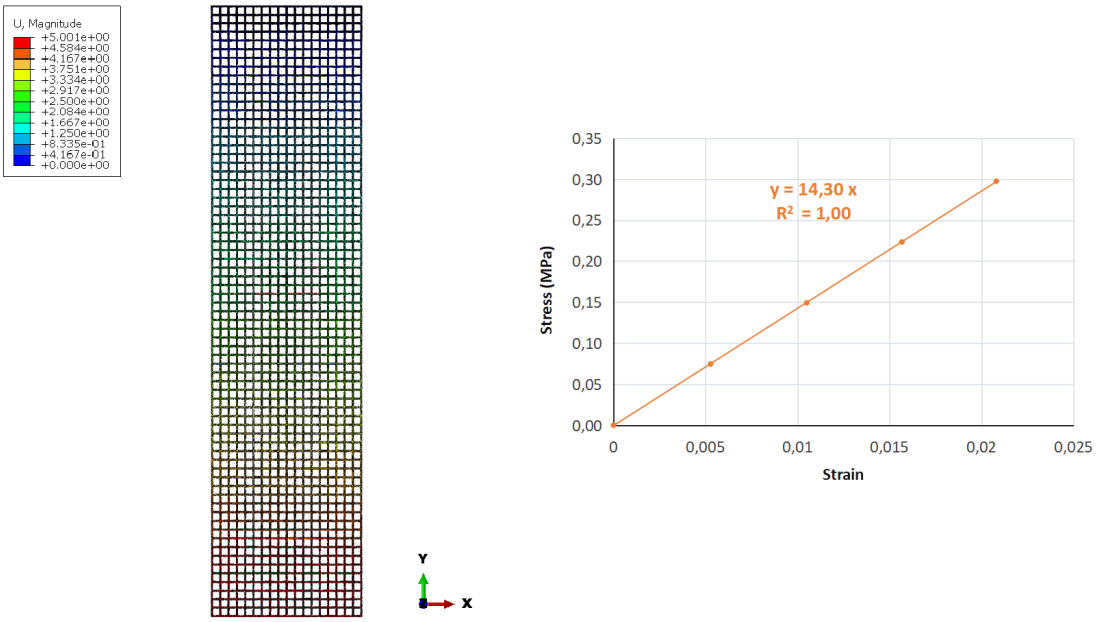


Figure 6.10: Stress-strain curve obtained from the uniaxial tensile test on the *Restorelle* mesh model, using the experimental data obtained from the specimen tensile test.

However, now gathering all results, it is more appropriate to compare values of stiffness, rather than Young's moduli. The estimation of the value of stiffness from Young's modulus is simple, it is based on the following equation:

$$k = E \times \frac{A}{L} \tag{6.1}$$

Where k is the stiffness value, E is the Young's modulus constant, A corresponds to the cross-sectional area, and L is the length of the material put through the tensile testing.

The experimental data with the specimen, present in the Figure 6.9, provided a stiffness value of 2.14 N/mm. According to [64], *Restorelle* has a stiffness value for uniaxial tensile testing of 2.60 N/mm, which is a close value from the one obtained experimentally. Moreover, the simulation with the mesh model using the effective Young's modulus revealed having a stiffness value of 14.75 N/mm, which enhances the former observation that the designed mesh model is much stiffer than it should. On the other hand, the simulation with the experimental data provided a stiffness value of 0.17 N/mm, which is even smaller than the stiffness from the experimental test. As it is clear, the tensile tests done with the mesh model evidence the excessive resistance to deformation, when a load is applied, as the model is quite stiff.

To support loads in cases of prolapse surgical procedures, the stiffness of the mesh should be reasonable but not excessive, as it can cause stress shielding in the surrounding bones, one of the complications reported after prolapse repair. This problem happens when an implant is stiffer than the tissues and, when a load is applied, the implant (in this case, the mesh) removes the typical stress from the bone, causing the impairment and degeneration of the soft tissues. Thus, the mesh stiffness should be lower to better match the properties of the vaginal tissues [61]. The stiffness value reported for the vaginal wall tissues has a wide range due to various experimental methodologies, the variation can go from 0.16 N/mm up to 6.47 N/mm, but a reasonable stiffness value to consider is 1.45 N/mm [65]. Accordingly, the experimental data with the specimen shows a stiffness value closer to the one from the vaginal tissues, yet the two tensile test simulations with the mesh model are far from the value desired.

Chapter 7

Conclusions and Future Work

The pelvic organ prolapse is characterized by the descent of one or more pelvic organ from their natural anatomical positions, such as the vagina, uterus, urinary bladder, rectum, among possible other. The protrusion of the organs against the vaginal wall, in extreme cases, can go even further and result in the exteriorization of these pelvic organs. The main cause of this dysfunction is the loosening and weakening of the supporting structures that normally would strengthen and keep in place the pelvic organs. The weakening of the pelvic floor muscles, pelvic ligaments or fascia compromises the integrity of the female pelvis and induces a PFD. POP has a negative impact on women's lives since it brings pain, discomfort, pressure and can also induce other clinical situations like urinary or fecal incontinence.

To repair prolapses, there are two main methods, conservative and invasive. When the first approach does not correct the problem, the invasive treatment options are required, as they aim to rectify the anatomical positioning of the pelvic organs, correcting and recovering the functionality of these organs. The specific procedure is suited to each clinical case, but often require the use of a synthetic mesh to hold the organ in place. These implants need to be further studied, given that there were complains made by women concerning postoperative complications.

Thus, this dissertation aimed to study a specific synthetic mesh, *Restorelle M Flat Mesh*, a complex monofilament knitted mesh made from polypropylene with square pores. The goal was to understand its elaborate structure and following impact on the mechanical behaviour of the overall mesh. In addition, the distinguishing factor of this dissertation study is the introduction of porosity on a mesh model, as the literature about this topic only handles with continuous mesh models, that do not truly represent the geometry of a porous synthetic mesh. For that reason, to be able to introduce the pores on the model, the approach taken was a multiscale modeling method, due to the fact that the analysis made was across separate space continua, from a study of the complex microstructure to a macro mesh analysis. As such, the biomechanical models of the microstructure, as well as the whole mesh, were developed. These studies were mainly made using uniaxial tensile testing simulations.

The observation of the microstructure of the mesh *Restorelle* reveals a repetitive microstructure of monofilaments interconnected and knitted to build the mesh sheet. This structure was analysed,

first, its biomechanical model was designed, called the representative unit, then, uniaxial tensile tests were made in the y- and x-direction. These simulations revealed that the unit deforms more in the y-direction, but is also a little stiffer than in the x-direction, also given that the Young's moduli obtained were 1358.85 MPa and 1203.88 MPa, respectively. These constants were called effective Young's modulus, as they are supposed to represent better the mechanical properties of the microstructure of *Restorelle*, rather than just using the constant from polypropylene properties. This statement comes from the fact that the microstructure built of the complex intersection of polypropylene monofilaments must provide different stiffness properties to the *Restorelle* mesh, comparing with a single straight filament of polypropylene.

Afterwards, the whole mesh model was developed and further analysed, to evaluate if it is capable of representing the properties of the *Restorelle* sheet. As the meshes *in vivo* essentially suffer uniaxial loading, and that is the main focus of the existent studies done on this topic, the analysis of the mesh model to uniaxial tensile tests provides information on the way the mesh behaves when implanted in tissues. In a first approach, the input mechanical properties were the effective Young's modulus computed previously, namely the one obtained from the y-direction, that is, the 1358.85 MPa value, as it had the biggest expression on the unit tests. The obtained deformed model fulfilled the applied 5 mm of displacement in the bottom region, as its output model had a maximum displacement magnitude of 5 mm as well. However, the model revealed to be too stiff, especially when compared with the experimental curve obtained from the uniaxial tensile testing with a specimen of the material.

So, in a second approach, the mechanical properties used were the experimental data from that specimen. The resultant deformed model was very similar to the previous simulation, but this time the corresponding Young's modulus was 14.30 MPa, with a stress-strain curve similar to the experimental one.

Afterwards, all results were compared using the calculated stiffness value, instead of Young's modulus. The computed stiffness value for the experimental tensile testing was 2.14 N/mm, and literature says *Restorelle* has a value of 2.60 N/mm, so the experimental data provided a consistent stiffness value. Now, the other two simulations with the mesh model had very distant results, the one with the effective Young's modulus gave a stiffness value of 14.74 N/mm, while the one with the experimental data had a 0.17 N/mm constant. These values are concordant with the obtained graphics for the stress-strain curves presented in the previous chapter. Furthermore, the range of stiffness values for the vaginal tissues is wide, but a proper analysis value is 1.45 N/mm, which is, again, close to the experimental test with the specimen. An appropriate stiffness for a prolapse mesh should be reasonable but not too excessive, as it can have complications on the bone tissues surrounding. Thus, the stiffness should be near to the soft tissues of the female pelvic cavity.

In the future, more research should be done with porous biomechanical models, as it is not seen in literature so far. In this case, with the developed model, the main reason why the mesh model did not deform as much as intended is related to the fact that the model is computationally heavy, and applying higher boundary conditions would take excessive time, knowing that the technical resources available for the development of this dissertation were not the most appropriate. So, to

begin with, the present mesh model should undergo a higher applied displacement in the tensile test simulation, to understand extensively its behaviour, and verify if the present model is really too stiff or if it just needed higher displacement values applied.

Afterwards, if the model still does not correspond to the desired response, it emphasizes the importance of future improvement regarding the model characterization, which should be adjusted. In particular, the mechanical properties set should change from isotropic to orthotropic, to better characterize the behaviour of the mesh in all orthogonal directions. Also, changing the element type might improve results, particularly from the tetrahedrons to hexahedrons, as to facilitate the deformation of the model and improve stiffness.

Going further on this research, the deformed model already designed and developed could be implanted in the female pelvic cavity. The simulation of the mesh behaviour connected to the uterus and sacrum under the influence of suitable loads and its impact on the overall model is a very interesting study. Also, introducing the porosity with this model and understand the influence of porosity on the simulation, when compared with the continuous mesh models used in the published research.

More in-depth studies about synthetic meshes should be performed so that these procedures can be safer for women, without the implications of postoperative adversities.

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