Giampiero Campanelli *Editor*

The Art of Hernia Surgery

A Step-by-Step Guide

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Editor
Giampiero Campanelli
University of Insubria, Istituto Clinico, Sant'Ambrogio General Surgery Day Surgery
Milan, Italy

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Foreword

This new hernia book, *The Art of Hernia Surgery: A Step-by-Step Guide*, edited by Professor Giampiero Campanelli, and which I have the honor and the privilege to present, summarizes the maximum knowledge of abdominal wall surgery at this time. It answers all the questions that surgeons, not just hernia surgeons, will find useful in their daily practice both for the benefit of their patients and for extending their own erudition.

As an esteemed hernia surgeon and as Secretary General of the European Hernia Society (EHS) for more than 15 years, Professor Campanelli, with whom I have collaborated for many years on the EHS Board, has seen many changes and many advances and has rubbed shoulders with the world's top specialists in herniology. He appreciated the value of their publications and for this reason chose these top specialists to write the 67 chapters of this book, which provide exhaustive information in the field of hernia surgery.

Although related to general and visceral surgery, surgery of the abdominal wall is now a specialty in its own right. The names of the early pioneers in modern hernia surgery and their books are well known, such as the publications of H. Fruchaud, L. Nyhus, B. Devlin, J.P. Chevrel or R. Bendavid, V.K. Nigam, and C. Avci.

A number of important events have led to abdominal wall surgery becoming a recognized specialty. These events include the creation of the GREPA Research Group on Wall Surgery in France by J.P. Chevrel in 1979, this Group becoming the EHS in 1996. The following year, in 1997, an international journal, *Hernia*, was founded. Also notable are the creation of the American Hernia Society in 1998 in Miami and the creation of the Asia Pacific Hernia Society in 2004.

As well as these important societies, numerous other national hernia societies have been created, leading to a new surgical dynamic. Publication requirements have gradually improved, with detailed statistical evaluations, randomized trials, comparative studies, and so on. All of this activity has led industry to develop, at our request, multiple kinds of prostheses (more than 250), both synthetic and biological, in various materials, textures, shapes, and dimensions. We could also add the invention of many and varied means of fixation—sutures, staples, and glues. Other advances have led to such changes as laparoscopic surgery, robotic surgery, and ambulatory surgery.

The content of the book is the result of all the scientific research, evaluation, and data generated by these societies through their publications.

The originality of this book lies in its short and easy-to-read chapters, with their complete descriptions of current methods and applicable references. The book offers a broad range of subjects that are rarely tackled by other hernia books. Among these topics, we can mention the problems of prevention and emergencies, the new total extraperitoneal repair technique, open abdomen and component separation operations**,** and the Mini- or Less-open Sublay Operation (MILOS) technique; also provided are hernia classifications and guidelines.

In addition, you will find an original presentation of the anatomy of the abdominal wall, as well as detailed descriptions of traditional techniques in the treatment of various types of hernias, including incisional hernias. Improvements in these techniques and their recent results are also described. In short, you will have everything to guide you in the decision-making process.

In summary, it is a huge pleasure for me to introduce this new and complete practical hernia book, which is based on recent publications, clearly presented, and enhanced with significant illustrations.

I am sure that this book will be a reference for any surgeon, beginner or senior, who is looking for information on recent methods and techniques in hernia surgery.

I extend my congratulations to Professor Giampiero Campanelli and his co-authors for this new hernia book, which is sure to become very successful.

Paris, France Jean Henri Alexandre

Preface

Over 100 years ago Edoardo Bassini, the great pride of Italian surgery, wrote about whether it was still necessary to argue about hernia surgery.

Actually, from Hippocrates' time until today, and certainly for decades to come, we will continue to talk about hernia surgery and to discuss this topic.

In the last 30 years, during my succession of personal, academic, and, especially, professional activities, I have had—for more than 15 years—the honor of holding the leadership of the European Hernia Society. This organization has become a great Society, that, with the American Hernia Society, the Asia Pacific Hernia Society, the Afro Middle East Hernia Society, and the Australasian Hernia Society, involves the best international professionals in the field. The members of these Societies, I like to remember, are responsible for the largest numbers of hernia surgeries carried out worldwide.

With the scientific expansion spearheaded by these Societies, technological and material evolution has been such as to arouse the interest of companies, patients, media, and, especially, surgeons.

The fundamental objective in surgery of the abdominal wall is that of a *restitutio ad integrum*; that is, a reconstruction that is as natural as possible and which can achieve a perfect repair in the different wall regions, with, at the same time, a level of recurrences and complications that is as low as possible.

But today this objective is not our only aim.

More important has become the concept of quality of life, which appears in even the most serious and important series as an essential item whose measurement is requested by the individual patient after such surgery.

Essentially, postoperative comfort for the recovery of normal life and work habits, and in some cases the improvement of sports performances, and finally a natural appearance, have become collateral objectives that are increasingly requested and form an essential part of our daily activity.

To this end, we have gradually developed a concept of tailor-made surgery, which, together with the employment of our international guidelines, must permeate the training and daily activity of surgeons who want to dedicate their professional life to this exciting journey, which nowadays is recognized as a super specialization, mostly realized at specific worldwide hernia centers, but also realized in general surgery departments, by general surgeons.

The precise concept behind this book is to give a real guide to expert herniologists and to general surgeons the world over, suggesting different approaches, outlining technological aspects, and providing tips and tricks.

These contributions come from the wide experience of the authors—friends, who, with me, share their passion and daily practices in the journey along this complex, beautiful, and always developing path.

Milan, Italy Giampiero Campanelli

Contents

Part I

General Aspects

1 History and Evolution of Hernia Surgery

Giampiero Campanelli, Piero Giovanni Bruni, Andrea Morlacchi, Francesca Lombardo, and Marta Cavalli

Abdominal wall hernia is very common; the prevalence in the general population is about 5% [1]. Inguinal hernia is the most widespread presenting as a bulge in the groin.

Although the natural course of the disease is relatively slow, it eventually reaches the size that severely impairs with the patient's ability to perform daily activity. Already in antique times, the surgeons and physicians were trying to find the solution for this condition. Even though progress in surgical techniques and new principals allow the patient to resume a normal life in a very short time, up to 150 years ago, this was not possible.

The currently used term "hernia" comes directly from ancient Greece (*hernios*: offshoot or bud) reflecting in part the pathophysiological mechanism of the disease.

The **Egyptian Papyrus of Ebers** (1552 BC) contains an observation on hernias. Pharaoh Merneptah's mummy (1224–1214 BC) showed a scar in the groin as for hernia operation while that of Ramses V of Egypt showed hernia not operated [2].

Hippocrates (400 BC) differentiated between hernia and hydrocele: the former was reducible and the latter transilluminable [3]. He wrote about inguinal hernia in De Morbis and in De Affectionibus, suggesting enema therapy [1].

Aulus Cornelius Celsus (14 BC–AD 50) was one of the first that described surgical approach to the inguinal hernia: "for a medium size swelling one incision is enough, for bigger size two linear incisions are necessary and the cord is removed, vessels are identified, tied and cut." Lack of anatomical knowledge was clear in that age [4].

Galeno (129–199 AD) in De Semine described the correct anatomy of the inguinal canal. He thought that herniation was produced by rupture of the peritoneum with stretching of overlying fascia and muscle [2].

Jumping to the sixth century AD, the Italian **Paolo d'Egina** in his work *De Medicina* described his intervention of inguinal hernia. He suggested the cauterization: ligation and section of sac with the amputation of the testicle.

Guy De Chauliac (1300) wrote *Chirurgia Magna*. He was the first that distinguished inguinal to the femoral herniation. He also developed a method for reducing hernia on patients in the Trendelenburg position [5]. He prescribed a 50-day bed rest after the surgery: nowadays, after seven centuries, hospitalization is reduced to 1 h.

G. Campanelli (✉) · P. G. Bruni · F. Lombardo
M. Cavalli
University of Insubria, Varese, Italy

General and Day Surgery Unit, Center of Research and High Specialization for the Pathologies of Abdominal Wall and Surgical Treatment and Repair of Abdominal Hernia, Milano Hernia Center, Istituto Clinico Sant'Ambrogio, Milan, Italy
e-mail: Giampiero.Campanelli@grupposandonato.it

A. Morlacchi
Surgical Department, Ospedale di Circolo di Varese e Fondazione Macchi, University of Insubria, Varese, Italy

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Lack of knowledge about the anatomy and relying on Galeno's theory of rupture of the peritoneum as pathogenesis, all of these surgeons were limited to the closure of the peritoneal sac resulting inevitable recurrence of the disease.

Guido Lanfranchi (1300) suggested to avoid cord section, but it is necessary to wait until the sixteenth century when surgeons, supported by improved anatomy knowledge, pursued cord preservation during inguinal hernia repair [4].

Girolamo Fabrici d'Acquapendente (1533–1619) described the cord dissection and the division of spermatic vessel from the sac: this one was sutured with golden stitches.

Practica copiosa was the first book about etiology, morphology, and treatment of hernia written by **Caspar Stromayr** in 1559 [6]. Stromayr for the first time made a distinction between indirect and direct hernias and recommended a testis-sparing procedure for the direct type.

In the anatomic era (seventeenth to nineteenth centuries), autopsy and anatomic dissection spread throughout Europe that increased knowledge about groin herniation. Knowledge culminated during the early nineteenth century in a complete anatomic understanding of the inguinal canal.

The great contribution of the surgical anatomist was between the years 1750 and 1865 and was called the age of dissection. The main contributors were Antonio **Scarpa**, a great anatomist, and Sir **Astley Cooper**, who defined the transversalis fascia position, distinguished this layer from the peritoneum, and emphasized this layer as being the first layer to be breached in groin hernia. He also implicated venous obstruction as the first cascade in the circulatory failure of strangulation. One more important contributor was Percival Pott, who described the pathophysiology of strangulation in 1757 and recommended surgical management. He also emphasized that hernia sac was a part of general peritoneal cavity and had not to be ruptured or broken. Franz Hesselbach described the homonymous triangle which is now very important in laparoscopic surgery.

In the same time, Oliver Wendell Holmes and Semmelweis emphasized the importance of hand washing before operating. The application of Lister's principles of providing clean linen and special coats, cleansing sponges soaked in carbolic acid and thymol, and the segregation of postmortem examinations and operating theaters influenced British and European surgeons and decimated postoperative infection rate [7].

A revolution happened on Christmas night of 1889 when Edoardo **Bassini** first operated a patient for hernia with his novel technique, repairing, for the first time, the posterior wall of the inguinal channel. Bassini's merit was to focus the attention of the surgeons on the posterior wall as the real repair location, lowering hernia recurrence rate from about 100% to about 10%.

Bassini created a physiologic reconstruction of the inguinal canal, suturing the conjoint tendon and the transversalis fascia with inguinal ligament. This operation was considered the gold standard for nearly a century [8].

Some modified versions were suggested (Mugnai, Ferrari, Postemski). McVay popularized the Cooper's ligament repair, in which the aponeurosis of the transversus abdominis and internal oblique were sutured to Cooper's ligament, rather than to the inguinal ligament [9].

In the late 1940s, **Shouldice** refined the Bassini inguinal hernia repair by reconstructing the posterior inguinal wall using continuous sutures equalizing tension throughout the suture line; this technique reported a recurrence rate of less than 1% following primary inguinal hernia repair [10].

Although it was a very popular technique, there were several disadvantages such as suture line tension, patient discomfort, prolonged postoperative recovery, and rehabilitation, and recurrence rates are considered too high. The most critical factor in the development of recurrences following all tissue-based hernia repairs was excessive tension on the suture line, hence the introduction of the concept of ***tension-free hernia surgery*** [11].

The first mesh repair was performed by **Usher** in 1958, and in 1960 he described a tension-free technique of inguinal hernia repair using polypropylene mesh.

Many surgical procedures and devices have been marketed in the last 20 years, some of them evolved, and now they are accepted worldwide and used (Lichtenstein technique).

Lichtenstein tension-free hernioplasty, introduced in 1984, is now the most commonly used technique because it does not need a long learning curve to obtain highly acceptable result; recurrence and complication rate are less than 1% [12]. The original technique requires a polypropylene mesh fixed with unabsorbable suture on the inguinal ligament and with absorbable stitch on the conjoint tendon.

Trabucco in 1989 proposed a tension-free sutureless technique: a flat preshaped memory mesh with proper rigidity was placed on the posterior wall of the inguinal canal without suture fixation on the surrounding tissue. The main advantage of a tension-free and sutureless repair was given by the relevant reduction in postoperative chronic neuralgia, which was not an uncommon complication and, depending on its intensity, can also potentially jeopardize a patient's work and social activities [13].

Lichtenstein and Trabucco's techniques are often the first choice by residents and nonexperts because anterior anatomy is more familiar, whereas preperitoneal approach has no widespread success because of their hard performance and feasibleness under local anaesthesia [4].

In the last year, the advent of the laparoscopic technique and success of laparoscopic cholecystectomy let the surgeons focus their attention on other applications of laparoendoscopy. Teorically, advantages of laparoscopic techniques compared to open ones are, early rehabilitation, reduction of acute postoperative pain and better intraoperative vision [14]. Moreover laparoscopic repair allows also to inspect both inguinal regions to repair concurrent contralateral hernias.

Finally, it's indicated for the repair of bilateral and recurrent inguinal hernia, permitting the approach of the groin region by a non-scarred plane. On the other hand laparoscopy requires a general anaesthesia, higher costs and a long learning curve for surgeons and at the end regarding primary inguinal hernia repair, that could be done easily in local anaesthesia and through a mini-invasive open approach can be considered as overtreatment. Currently, the most widely used laparoscopic techniques for inguinal hernia repair are the transabdominal preperitoneal (TAPP) repair, the intraperitoneal onlay mesh (IPOM) repair, and the totally extraperitoneal (TEP) repair [11].

Since laparoscopic technique is introduced, more attention has been focused on the preperitoneal space for mesh placement also during open anterior approach.

Implantation of mesh behind the transversalis fascia via open approach can be achieved through a transinguinal method such as the Rives operation introduced in 1965, a lower midline abdominal incision (Stoppa repair 1967), and a slit made in the broad abdominal muscle (Wantz repair1988). These approaches are limited to repair recurrent inguinal hernia in the hands of a limited number of hernia experts.

Gilbert tried to take advantages from the placement in the preperitoneal space and combined them with a simple anterior approach.

Gilbert created the "Prolene Hernia System," he used bilayer connected device that incorporates two flat polypropylene mesh patches. The two patches were attached by a polypropylene connector which itself sits in the direct hernia defect of the posterior wall or the deep internal ring of an indirect hernia. With the preperitoneal space sufficiently actualized by sponge and/or finger dissection, the entire PHS device was inserted into the preperitoneal space [15].

Modern advantages in hernia repair are credited with reduced recurrence rate and chronic pain after hernia surgery. A systematic

review reports that 11% of patients suffer chronic pain, but estimates in literature range from 0 to 53% [15].

Chronic pain is defined as pain arising 3 months after hernioplasty; it is a significant complication that can compromise the patient's quality of life. The risk of chronic pain after laparoscopic hernia repair is lower than after open hernia repair and is lower after mesh repair than suture repair [15].

Today there is no consensus opinion about the cause and treatment of chronic postoperative pain. What is clearly important is the prevention: performing local anesthesia, identifying three nerves of the region, leaving nerves in the position if possible, limiting sutures and fixation devices, and, in case of nerve injury, doing selective neurectomy [16].

Choosing the proper biomaterial can determine the success of an operation. The most frequently used prosthetic materials for hernia surgery can be grouped into absorbable and nonabsorbable materials. Absorbable materials can be divided into synthetic and biological materials. All absorbable biomaterials are totally replaced by the host tissue. Nonabsorbable materials can be grouped in base on pore size.

Today the gold standard for primary inguinal hernia repair is an open tension-free technique performed in local anesthesia in day surgery unit or laparoscopic TAPP approach.

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2 Teaching Hernia Surgery: The Experience of the Italian School

Paolo Negro, Linda D'Amore, Elena Annesi, Francesca Ceci, and Francesco Gossetti

2.1 Introduction

Inguinal and ventral/incisional hernia repair is one of the most common operation in surgical practice [1]. Each year 20 million groin hernia repairs are performed worldwide, 800,000 cases of which are only in the USA. Mention must also be made of the frequency of ventral/incisional hernia surgery, 400,000 repairs yearly in the USA, with a projected annual growth rate [2]. The numbers are mostly similar in all countries, in relation to the population size.

Basically herniorrhaphies and the majority of abdominal wall repairs are performed as a part of a broad-based general practice, often delegated to general surgery residents, since they are considered as easy to learn and to perform at the technical level. However, in last decades hernia surgery has become more complex, due to the spread of new surgical approaches, as laparoscopic repair, innovative open techniques, as component separations, and continuous increasing number of available prosthetics or medical devices. Moreover today success rate does not only depend on recurrence indicator but also on other equally important concerns, such as patient satisfaction, quality of life, and costs. Furthermore patient population also has become more complex, due to the increasing age, comorbidity, and challenging mesh-related complications, including recurrence following prosthetic repair. The guidelines of the European Hernia Society recommend that a hernia specialist perform complex inguinal hernia [3]. At the same way, complex incisional hernia repair requires specialization, due to high failure rate, which increases exponentially with subsequent repairs [4]. Cases like these should be treated with a tailored approach by surgeons keeping up to date with the latest developments in hernia surgery. Only specialized surgeons or those who have developed a special interest in hernia surgery can properly be faced with this new hernia surgery era. That's why there is a need for comprehensive hernia centers, in which surgeons with high volume experience work together with a multidisciplinary team [5, 6]. It is paramount to create specialized or expert hernia surgeons. Current methods to train general surgeons could be not sufficient [1], and further evaluation of hernia education should be considered [7]. Based on these considerations, in 2008 the Italian School of Hernia and Abdominal Wall Surgery was created, first in Europe, as an educational branch of the Italian Society of Hernia and Abdominal Wall Surgery (ISHAWS), and in 2009 it was officially presented to the international community [8]. The purpose of the school was to create a new generation of expert surgeons through a comprehensive hernia education program focused on the funda-

P. Negro (✉) · L. D'Amore · E. Annesi · F. Ceci
F. Gossetti
Abdominal Wall Surgery Unit, Department of Surgery, Sapienza University of Rome, Rome, Italy
e-mail: linda.damore@uniroma1.it; gossetti@tiscalinet.it

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mentals of hernia disease and its clinical and surgical tailored management.

Actually hernia surgery teaching was already proposed in Italy some years before. In 1992, inspired by the question discussed in those years "*…must we specialize herniorrhaphy for better results?"* [9], some of us (PN, FG) established an annual academic postgraduate course on groin and ventral hernias of abdominal wall under the patronage of the Ministry of Public Education [10]. Five editions were delivered, up to the end of 1997 when the course was suspended. During the same period, a similar postgraduate course was held in Milan, promoted by P. Pietri and G. P. Campanelli. A training program was also proposed by Palumbo in 2001 [11]. Since then, the interest in this topic has grown in Europe. The fourth Joint Hernia Meeting of the American Hernia Society (AHS) and European Hernia Society (EHS) dedicated a special session to specialization and hernia teaching surgery focusing on the usefulness and the principles of hernia surgery training [12]. The German Hernia Society (DHG) in collaboration with the Federal Association of German Surgeons (BDC) developed the project of a German Hernia School, starting its first basic training course in 2011. Recently, the experience gained to date by DHG has been evaluated and discussed [5].

2.2 Italian School of Hernia and Abdominal Wall Surgery

The Italian School of Hernia and Abdominal Wall Surgery was developed to meet the need of education and training in modern surgical approaches and to improve results in hernia surgery. The Italian Society of Hernia and Abdominal Wall Surgery strongly supported this innovative idea also through the creation of the Alliance for Hernia, a corporate alliance of industries involved in hernia surgery, which contributes to the costs of the training courses. This cooperation offers product specialists the opportunity to participate in the basic sessions of the school. The school is governed by the Educational Board and the Director. Both these administrative bodies are designated by the ISHAWS Board, every 3 years.

The first course of the Italian School of Hernia and Abdominal Wall Surgery was held in 2010 in Rome, which later became the stable seat of the school. From the beginning it was addressed to residents in surgery and surgeons interested to develop a special knowledge in hernia surgery. The comprehensive program, which was first worked out in 2009, is structured in interrelated segments: (a) a basic training course, of 30 h, in 3 days, ending with a final exam consisting in a standardized multiple-choice test to set up participants' improved knowledge; (b) clinical stages for a minimum of 15 h of hands-on training in accredited regional centers under the supervision of expert surgeons and high volume of activity in hernia repair; and (c) documented active research in hernia surgery and participation to national and international scientific meetings. At the end of this track, participants are awarded an ISHAWS certificate of Expert in Hernia Surgery.

The 3-day basic course was initially limited to 35 participants. In the following years, this number was progressively increased to meet the increasing demand involving not only surgery residents but also surgeons interested in renewing and updating their curriculum in hernia surgery. The eighth course involved 80 participants (32 surgeons, 48 surgery residents) and 18 product specialists. Every year, at the end of the classes, all participants are asked to give a detailed feedback to evaluate all aspects of their experience, as organization, appraisal of lectures, faculty, and relevance of discussed topics (Table 2.1). The program is then yearly updated on the basis of the answers to this feedback form, adding or reducing some learning elements, inviting different experts, and inserting a live-surgery session. The faculty is composed of at least 30 surgeons and scientists with remarkable curricula.

The basic course begins the evening before its opening with "guest lectures" on biomaterials and the tissue reparation/regeneration after prosthetic repair, the state of the art, and the history of hernia surgery. On the first day, the anatomy of the inguinal canal and the abdominal wall is explained both theoretically and through film clips registered and commented with special emphasis on anatomic classification. The course program goes

Table 2.1 Feedback form

1. How do you evaluate this basic training course?
(a) *Very well*
(b) *Well*
(c) *Sufficient*
(d) *Insufficient*
2. Do you consider appropriate the duration of this course?
(a) *Yes*
(b) *No*
3. Do you consider the topics to be considerable for your updating in the hernia surgery?
(a) *Very cosiderable*
(b) *Considerable*
(c) *Not considerable*
4. Are you satisfied with the whole organization?
(a) *Very satisfied*
(b) *Satisfied*
(c) *Sufficiently satisfied*
(d) *Not satisfied*

Table 2.2 Key points of the basic course

– Historical aspects of hernia surgery and its state of the art
– Prosthetic materials in hernia surgery and the biology of repair process
– Anatomy of the groin abdominal wall
– EHS classification of groin and abdominal wall hernias
– Open and laparoscopic surgery in groin hernias
– Postoperative complications and chronic pain
– Biological implants
– Open and laparoscopic surgery and component separations in ventral hernia repair
– Pre- and postoperative management in complex abdominal wall hernias
– Umbilical hernias
– Parastomal hernia repair
– Abdominal compartment syndrome (ACS) and open abdomen
– Plastic surgeon's keynotes

on with the description and analysis of the different meshes, both synthetic and biologic, available on the market, carefully evaluating pros and cons of each material. Then standardized surgical procedures for groin, umbilical, and ventral hernia repairs are described step-by-step. The most performed open and endoscopic techniques are shown with the help of a large number of film clips, particularly focusing on the need of standardization and reproducibility of procedures, in order to minimize complications and recurrences. These subjects will be discussed in the following topics together with medicolegal issues.

The second day is entirely dedicated to a live-surgery session with expert surgeons demonstrating some of the previously described open and laparoscopic techniques, directly from the operative room, using a Visera 4 K UHD system that allows a ultrahigh definition and visualization of the procedures. During each operation, different technical options and devices are shown with a special emphasis on the reasons leading to the final selection. A continuous interactive communication between audience and operating surgeons is strongly stimulated.

The third day is dedicated to particular aspects of hernia surgery, as pre- and postoperative management, hernia in sportsmen, parastomal hernias, open abdomen and complex abdominal wall repairs, panniculectomy, and plastic and reconstructive techniques (Table 2.2).

During the course, industries involved in the Alliance for Hernia are invited to give short presentations regarding new techniques or incoming materials and devices. Industries' sponsorship does not influence any teaching or planned subjects neither the choice of devices to be implanted in the live-surgery session. Teachers and participants are encouraged to have meals together to promote their relationships and offer a further chance of discussion.

Since the beginning of this experience (2010–2017), a total of 396 surgeons and surgery residents have attended the basic course (Table 2.3). Results were monitored through participants' response to the feedback form, and some contents were accordingly updated. Each edition of the course recorded a high level of customers' and teachers' satisfaction increased over the years (Tables 2.4, 2.5, 2.6 and 2.7).

A critical analysis of this experience reveals that the Italian School should definitively be improved with the implementation of practical activities. A weak point seems to be the lack of hands-on exercise with anatomy specimens, to improve knowledge in anatomy of the groin. This is the reason why a cadaver lab has been recently organized to integrate the basic course, in spite of

Table 2.3 (**a**) Courses participants 2010–2017. (**b**) Courses participants 2010–2017

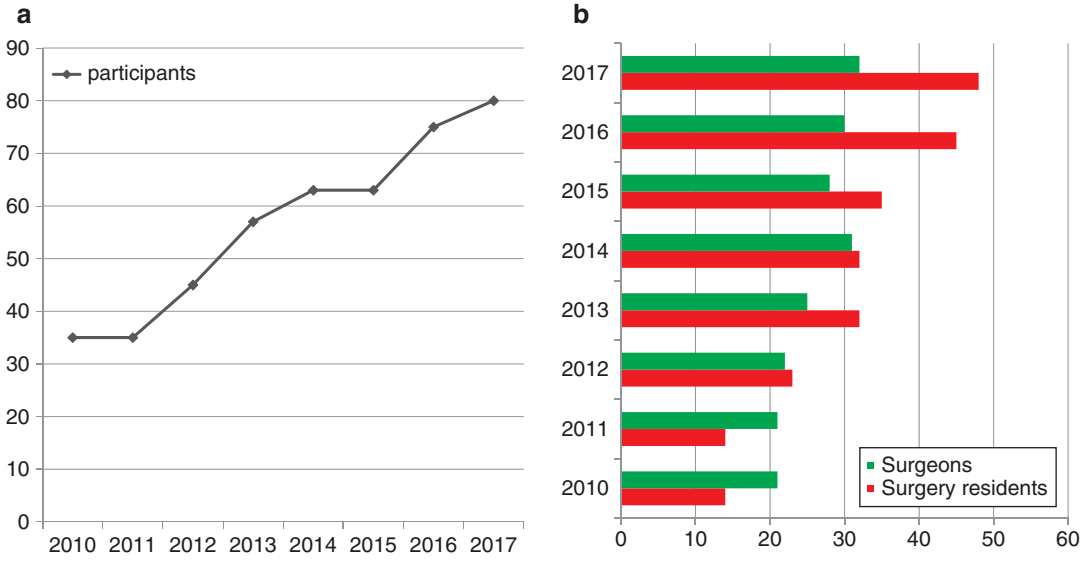


Table 2.4 How do you evaluate this basic training course?

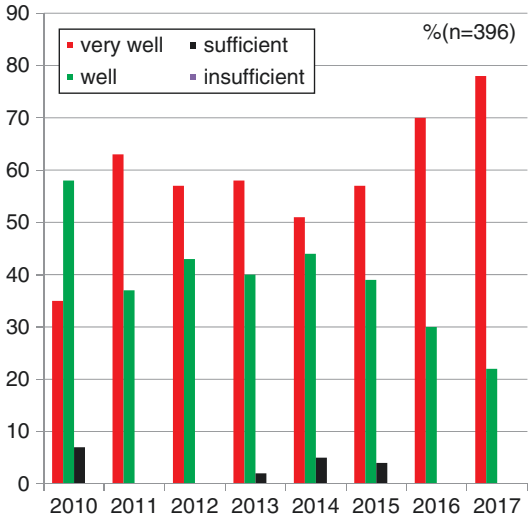
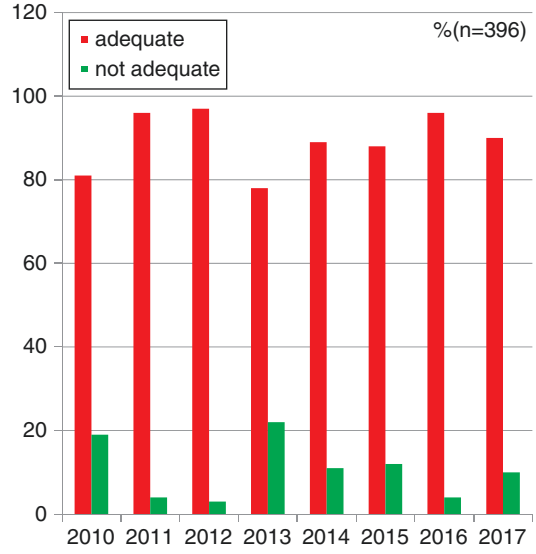


Table 2.5 Do you consider appropriate the duration of this course?



the high costs of cadavers and, therefore, the respective fees.

Only few participants have undergone clinical stages in accredited hernia centers, probably due to economic problems and working distance. A more active participation of trainee surgeons in the operating table should improve their skills with appropriate learning curve under the supervision of experienced surgeons. This is particularly true when performing laparoscopic repair, whose learning curve is undoubtedly longer than open procedures. Besides costs, difficulties lay in the selection of the training centers. In a recent paper [5], the need was stressed to identify hospital units and referral centers accredited in abdominal wall reconstruction in Italy, with suitable

Table 2.6 Do you consider the topics to be considerable for your updating in the hernia surgery?

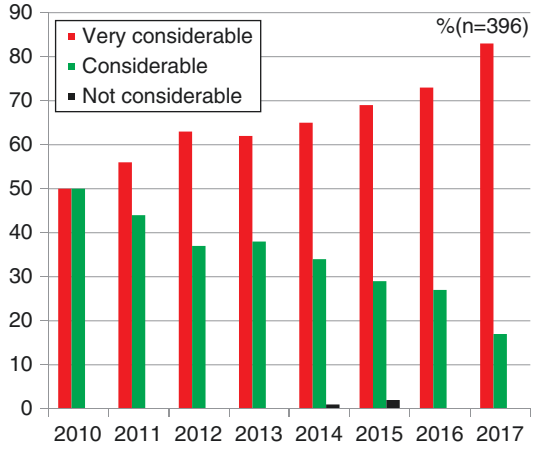
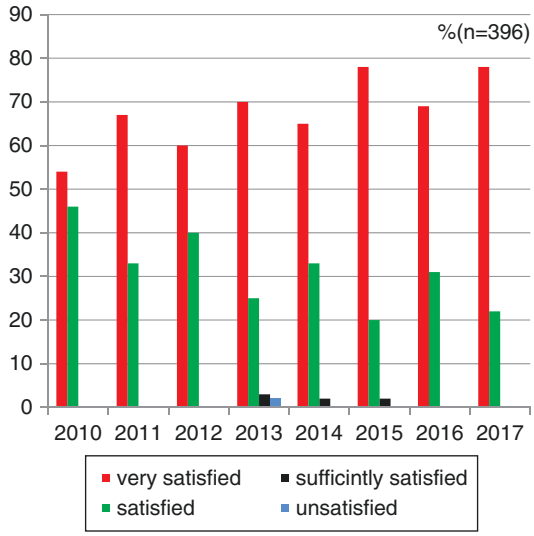


Table 2.7 Are you satisfied with the whole organization?



structural and organizational features and quantitative and qualitative standards, useful also in the educational training of hernia surgeons. In order to be more competitive, these centers should have more than one seat in different areas of the country and provide adequate human, structural, and technological resources, with a sufficient yearly number of procedures, the skill of training surgeons to perform all laparoscopic and open techniques for hernia repair with a low rate of complications and adequate follow-up, and a theoretical and updated knowledge in hernia field.

At the moment, the Italian School seems to have contributed to the continuous learning and education of Italian surgeons, with the regular review of basic hernia care, and the knowledge of new techniques, updating also materials and devices, to ensure that hernia patients receive "tailored" care, leading to excellent outcomes. It has been highlighted the need that expert surgeons with particular skill in hernia surgery actively train and educate a new generation of surgeons.

A systematic, standardized, and widespread educational program of continuing training is strongly advisable with the creation and the development of local training courses in each European country. The excellent experience of the German-Austrian Hernia School [13] together with the know-how of the Italian School should perform as a model to promote the awareness of standardized groundwork, updating surgeons' knowledge and skills in hernia surgery, according to the suggestion of the EHS.

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3 Alterations of the Extracellular Matrix of the Connective Tissue in Inguinal Herniogenesis

Gemma Pascual and Juan M. Bellón

3.1 Introduction

Inguinal hernia is still one of the most frequently performed procedures by general surgeons. Their socio-health and labor costs are important. In the USA, this pathology has a cost of approximately three billion dollars a year [1]. Its etiology and pathogenesis are complex, with multiple factors contributing to its development, including individual predisposition and some congenital alterations such as peritoneal-vaginal duct persistence. Positive familial susceptibility to inguinal hernia development has been demonstrated, suggesting the role of genetic contribution in the etiology of the disease, but site-specific familial factors might exist [2]. Studies of families with inguinal hernia propose a genetic trait for both primary and recurrent inguinal hernias [3]. Mutations in different collagen genes have been recently suggested to be associated with the development of inguinal hernia [4], and four novel inguinal hernia susceptibility loci have been identified, showing an important role for two of these genes (EFEMP1 and WT1) in connective tissue maintenance and homoeostasis [5].

From a general point of view, the integrity of the abdominal wall at the level of the inguinal region depends on the oblique orientation of the inguinal canal, a sphincter-like structure that forms part of the deep inguinal ring and the transverse fascia (TF) [6]. The latter structure, which constitutes the posterior wall of the inguinal canal, is the one that finally prevents hernia formation and, in a special way, direct hernias. Some authors [7], after performing mechanical studies, attribute to the integrity of TF, a containment mechanism that would prevent the formation of both direct and indirect type hernias.

The development of hernias at the abdominal wall level and its recurrence has been shown to occur more frequently in patients with connective tissue disorders, not to mention some other important factors such as smoking [8]. It has been suggested that defective connective tissue metabolism is involved in the pathogenesis of both the indirect and the direct types of inguinal hernia. In diseases with connective tissue alterations, the incidence of inguinal hernia is higher, such as patients with aortic aneurysm, Marfan and Ehlers-Danlos syndromes, cutis laxa, osteogenesis imperfecta, and congenital dislocation of the hip [9, 10].

G. Pascual
Department of Medicine and Medical Specialties, Faculty of Medicine and Health Sciences, Networking Biomedical Research Centre on Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), University of Alcalá, Madrid, Spain

J. M. Bellón (✉)
Department of Surgery, Medical and Social Sciences, Faculty of Medicine and Health Sciences, Networking Biomedical Research Centre on Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), University of Alcalá, Madrid, Spain
e-mail: juanm.bellon@uah.es

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An important database study [11] including a large number of patients operated on inguinal hernia has been published some years ago showing that patients with direct or recurrent inguinal hernias are at a higher risk of developing ventral hernia repair compared to patients with indirect inguinal hernia. This fact was supported by previous studies demonstrating that the more important connective tissue alterations are found in these patients suffering direct or recurrent inguinal hernia, suggesting future research that reveals the specific alterations of the connective tissue.

This review paper aims to collect the experience and previous results of our group in the study of the constituents of the abdominal wall extracellular matrix of connective tissue, in the development of inguinal herniogenesis.

3.2 Role of the Extracellular Matrix in Hernia Pathology

The extracellular matrix is a complex integrated system developing a structural network that supports and surrounds cell populations within the connective tissue. It includes a set of tissue fibers such as collagen and elastic fibers that are present in variable amounts depending on the structural needs or function of the connective tissue. In addition this matrix contains a variety of proteoglycans, multiadhesive glycoproteins, and glycosaminoglycans that constitute the ground substance.

The mechanisms of the development of the inguinal hernia involve changes in the expression of different components of the extracellular matrix detectable at the TF level, such as collagen turnover (collagen I/III ratio) and metalloproteinases (MMPs). In the same way, the elastic component that forms part of the extracellular fibrillar matrix may contribute to the development of this pathology.

The biological factors, proposed by the Read group, involved in the development of hernia have gained acceptance in recent years, conferring a particularly relevant role to metabolic factors in the development of inguinal hernia [12–14]. Other groups such as Jansen et al. [15] have located inguinal hernias in the context of a condition generated by an abnormal composition of the extracellular matrix.

Patients with inguinal hernia show some alterations in collagen metabolism and significantly altered collagen types I/III ratios [16, 17], but few data are known about the elastic component of the extracellular matrix and factors involved in tissue remodeling that may affect the metabolism of elastin.

The extracellular matrix is a very complex integrated system, responsible for the mechanical properties of the connective tissue. The different constituents of the matrix interact with each other, and any alteration of one of them may lead to a disorganization of the extracellular matrix and the development of different pathologies such as inguinal hernia (Fig. 3.1).

Among the most studied different constituents of the extracellular matrix in relation to hernia pathology, collagen and MMPs are found. However, it has been demonstrated by our group that other soluble mediators, such as certain growth factors or enzymes related to the cross-linking of the matrix fibrillar proteins, may be altered in patients suffering from hernias [18, 19].

Following, we will review the most studied extracellular matrix constituents in relation to the pathology of inguinal hernia, with special emphasis on the findings obtained by our research group.

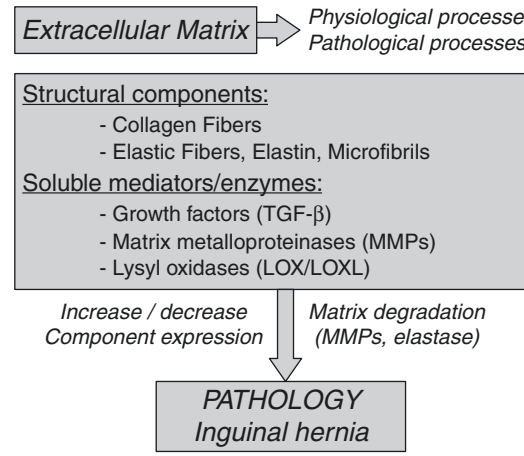

Fig. 3.1 Scheme of the different constituents of the extracellular matrix as a complex integrated system and its disorganization in the development of different pathologies such as inguinal hernia

3.2.1 Collagen Fibers

Collagen is the main and most abundant fibrillar protein in the extracellular matrix. This protein is mainly synthesized by connective tissue fibroblasts. In the process of collagen formation, important hydroxylation reactions occur at the intracellular level to form hydroxylysine and hydroxyproline, which are essential in the synthesis process and confer stability to the collagen molecule. This molecule is formed by three polypeptide α chains assembled at the intracellular level in the form of a triple helix. It is secreted into the extracellular matrix in the form of procollagen, which after a process of cleavage of its terminal uncoiled ends by procollagen peptidases, will become tropocollagen, assembling in the form of collagen fibril in the extracellular space [20]. This cross-linking is mediated by enzymes of the family of lysyl oxidases that promote the formation of highly resistant covalent bonds between lysine and hydroxylysine residues and provides strength and stability to collagen fibril, which are highly organized polymers that further associated with each other to form larger collagen fibers. Some groups [21] have shown a decrease in proline hydroxylation in TF accompanied by a significant decrease in the content of proline and hydroxyproline in the rectus sheath [22] of patients with direct inguinal hernia, indicating a compromised collagen stability at the level of the fascia.

The α chains that constitute the helix are not all the same; to date at least 42 types of α chains encoded by different genes have been identified. There are more than 28 genetically different types of collagens that have been categorized on the basis of the combination of α chains [23]. Type I collagen is the most resistant, widely distributed in the human body, including the fascia, the integumentary system, the ligaments, and the fibrous tissue. Type III collagen is found in small amounts in the same tissues and in greater proportion in the initial stages of tissue repair and wound healing [8, 23]. Type I confers mainly tensile strength, while type III is related to a temporal matrix during the tissue remodeling process. Therefore, a change in the ratio of collagen in favor of the type III would results in a loss of resistance of the structures involved.

Several studies reported an imbalance between type I collagen and type III collagen [16, 17]. When the collagen content in tissue samples is analyzed, the result is frequently quantified by the ratio of collagen type I:III. This collagen ratio has been found that was significantly decreased in the TF of patients with indirect inguinal hernia compared to controls [24]. In contrast, other studies have shown an increase in type III collagen but do not report statistically significant differences in the collagen I: III ratio in TF between patients with inguinal hernia and controls [21, 25]. Other authors [7] have shown that TF of patients with direct hernia shows higher levels of immature type III collagen and that the total amount of collagen is lower in direct hernia than in indirect hernia [26]. Ultrastructural studies using transmission electron microscopy have focused on the study of the collagen and interfibrillar matrix of the connective tissue of patients with this pathology, showing the absence of alterations in the diameter of the collagen fibers in the TF of patients with inguinal hernia [27].

Our group [21], examining the TF ultrastructure of patients with direct and indirect hernia, observed that there were no differences in the uniformity of collagen fibrils nor in their characteristic banding pattern; however, the interfibrillar matrix was more abundant in direct hernias, showing a large amount of small particles with high electrodensity (Fig. 3.2). In this same work, and by using biochemical studies, the degree of hydroxylation of the lysine and proline, essential in the process of synthesis and stability to the molecule of collagen, was analyzed. No differences were observed in proline hydroxylation in different types of hernia, and only a small decrease in lysine hydroxylation was detected in patients with direct hernia of more than 40 years (Fig. 3.3). The ratio of collagen type I:III studied by immunoenzymatic analysis did not show statistically significant differences between controls and patients with hernia pathology (Fig. 3.4).

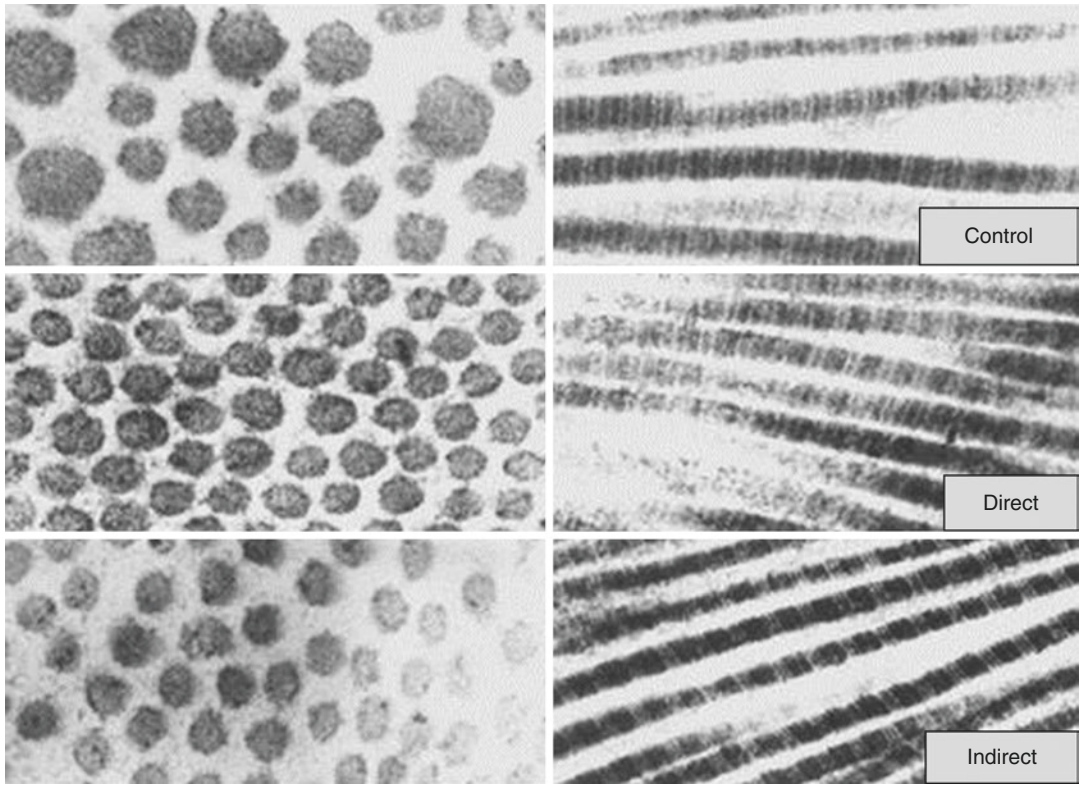

Fig. 3.2 Transmission electron microscopy images of the connective tissue of the transversalis fascia showing absence of ultrastructural alterations of the collagen fibers in the different study groups. Lead citrate and uranyl acetate staining (Magnification 85,000×)

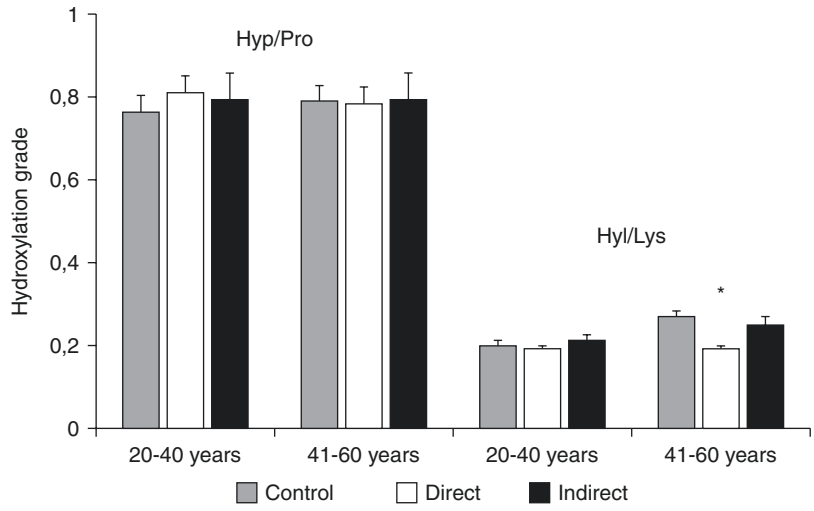

Fig. 3.3 Hydroxylation of proline and lysine in the transversalis fascia of the control groups and direct and indirect inguinal hernias, depending on the age factor of the population. A significant decrease in lysine hydroxylation was observed in the direct hernias of the older group compared to the rest of the study groups ($^{*}p < 0.05$) (Hyp/Pro, Hydroxyproline/Proline ratio; Hyl/Lys, hydroxylysine/lysine ratio)

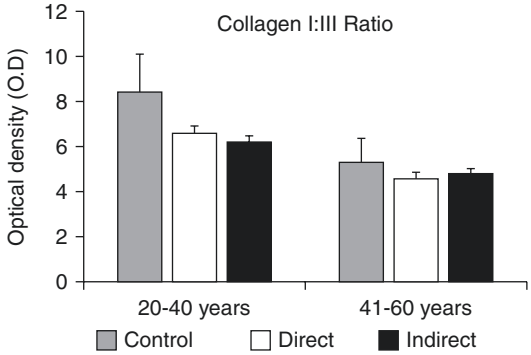

Fig. 3.4 Collagen I:III ratio observed in the different study groups, taking into account the age factor of the population. No significant differences were observed between the different groups of patients (*OD* optical density)

3.2.2 Matrix Metalloproteinases (MMPs)

Matrix metalloproteinases (MMPs) are a family of zinc dependent important proteins involved in extracellular matrix remodeling, which is subjected to a constant dynamic balance between its synthesis and degradation by the action of these enzymes. The MMPs are known to regulate the synthesis and degradation of collagen, but also of many other components of the extracellular matrix, such as proteoglycans, elastin, fibronectin, etc. There are about 23 different types of human MMPs that are grouped into collagenases, gelatinases, stromelysins, matrilysins, membrane MMPs, and other MMPs [28]. The classical MMPs include collagenases like MMP-1, MMP-8, and MMP-13, involved in the degradation of type I, II, and III collagens, and the MMP-2 and MMP-9 gelatinases involved in the degradation of denatured type IV collagens and proteoglycans. However, MMP-2 is also capable of degrading native type I, II, and III collagens [29, 30]. Collagenases and gelatinases are probably the most important MMPs in relation to hernia formation.

In general MMPs are expressed at very low level; however, their expression may be induced as a consequence of different pathological mechanisms. Pro-inflammatory cytokines, growth factors, and hormones are important regulators of MMPs expression. The proteolytic activity of these enzymes, latently secreted, is mainly controlled by the activation of tissue inhibitors of MMPs known as TIMPs [29, 31]. It has been shown that doxycycline administration, as MMPs inhibitor, results in significantly improved strength of repair fascial interface tissue along with a remarkable increase in collagen I, II, and III ratios [32, 33].

Experimental studies performed by different groups have shown that there are no significant differences in the levels of the MMP-1, MMP-9, and MMP-13 enzymes in the TF of patients with direct or indirect hernia compared to controls [34, 35]. Unlike other studies that found significantly higher values of MMP-1, MMP-2, and MMP-9, in inguinal hernia cases [36]. Other authors have found significantly elevated levels of MMP-2 in patients with direct inguinal hernia compared to indirect hernia or control, accompanied by a significant decrease in their inhibitor TIMP-2 [37, 38].

The degradation of the extracellular matrix by the effect of MMPs on the TF has also been the objective of our investigations. Four different types of MMPs (MMP-1, MMP-2, MMP-3, and MMP-9) were analyzed by our group in tissue sections, using immunohistochemical techniques with specific monoclonal antibodies. However, we found only significant differences in the protein expression of MMP-2 [21], where a significant overexpression of the enzyme was observed in the direct hernias of the young patients group with respect to the rest of the groups (Fig. 3.5).

After this study we carried out a second in vitro phase [39], using fibroblasts, in order to check whether the overexpression of MMP-2 observed in tissue was maintained in the cultured cells obtained from TF. The results obtained with immunocytochemical, immunoblotting, and zymography techniques corroborated that MMP-2 would be involved in the degradation process of the TF matrix in patients with direct hernia. The persistence of alterations in MMP-2

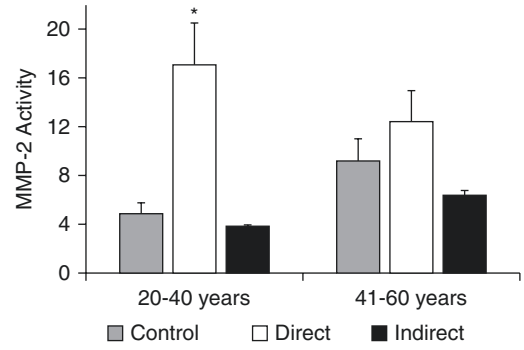

Fig. 3.5 Immunohistochemical staining images for the detection of MMP-2 in tissue sections of transversalis fascia. An increase in expression may be observed in the group of direct inguinal hernia (Magnification 200×). Quantification of MMP-2 activity in the different study groups, depending on the age of the population. A significant ($^{*}p < 0.05$) increase in expression was observed in direct hernias in the group of patients younger than 40 years

levels in cell cultures seems to suggest a genetic defect or irreversible change as the origin of this pathology rather than environmental factors that may later be involved in the development of the disease (Fig. 3.6). These works were the first in the literature to implicate MMP-2 in the pathogenesis of a type of hernia, namely, direct hernia in patients under 40 years of age, where this hernia is often bilateral.

Our research group has even more previous experience [40] related to MMP-2 and its modulators, using human skin biopsies obtained from patients suffering inguinal hernia repair. In this study immunocytochemical and immunoblotting techniques were used in intact tissue and fibroblast cell cultures, as well as zymography techniques to analyze the degradative activity of MMP-2. These results indicate an overexpression of the active form of MMP-2 in the group of direct hernias that could point to an abnormal systemic metabolism as a risk factor for the development of this type of hernia.

3.2.3 Growth Factors

Cytokines or growth factors like TGF-β (transforming growth factor beta) are involved in remodeling processes of different types of tissues. TGF-β is a multifunctional secretion protein that regulates many aspects of cellular function, including cell proliferation, differentiation, and metabolism of the extracellular matrix, [41] through its binding to specific cellular receptors. Five different isoforms have been described, and three of them are found in all species of mammals. TGF-β1 is most widespread and is a 25,000 Kd molecular weight homodimeric protein composed of two identical 12.5 Kd proteins linked by a disulfide bridge [42, 43]. A wide vari-

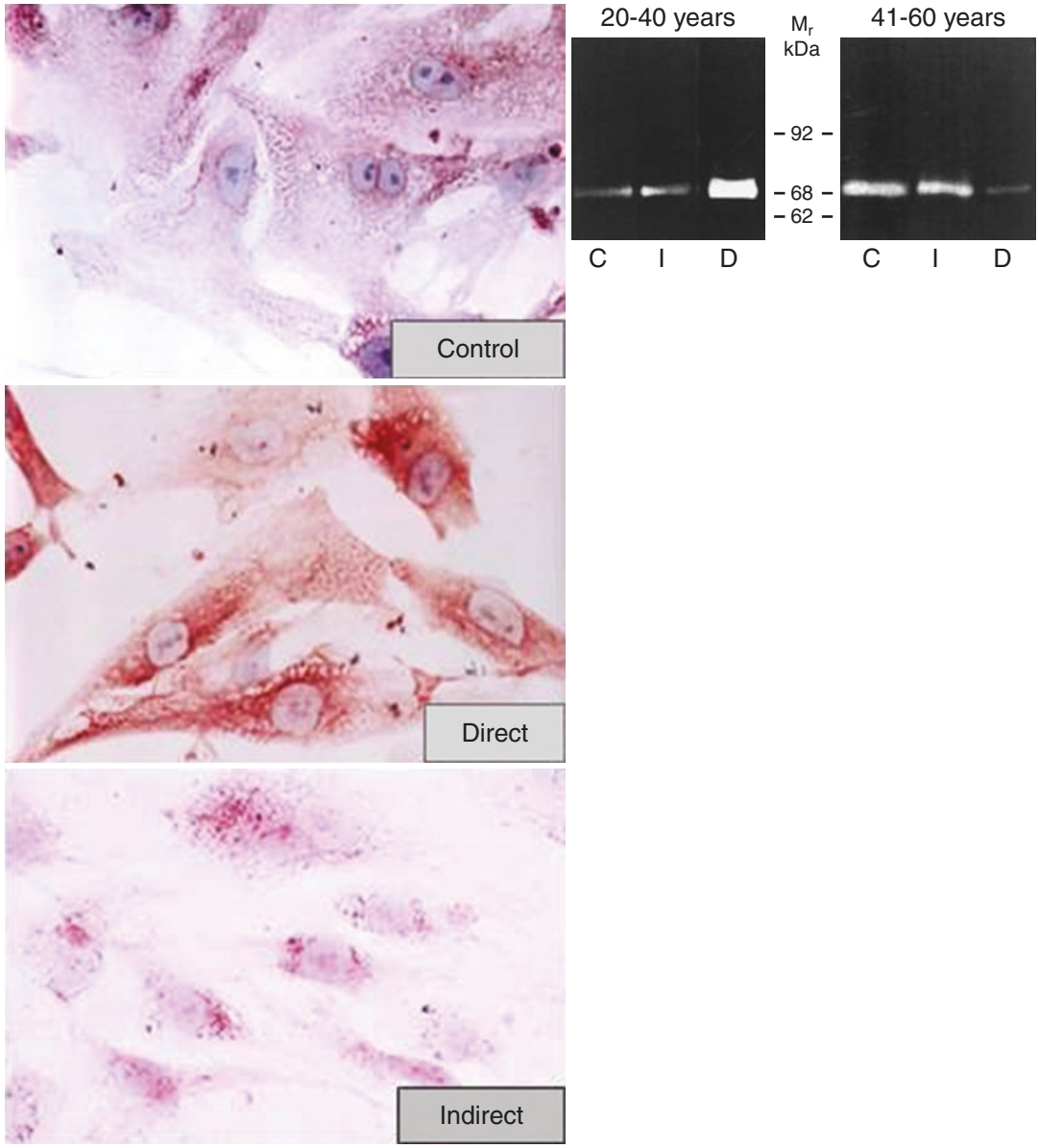

Fig. 3.6 Images of fibroblasts obtained from the transversalis fascia of the different groups of patients, submitted to immunocytochemical techniques for the detection of MMP-2. Higher levels of the enzyme were observed in the group of direct hernias (Magnification 1000×). Gelatinolytic activity determined by zymography techniques in the different study groups, showing an increased degradative band in the group of direct hernias of the younger age group (*C* control, *I* indirect hernias, *D* direct hernias, *Mr* molecular weight)

ety of potential clinical applications have been suggested for this growth factor, including increased scar tissue, control of chronic inflammation associated with fibrosis, and suppression of autoimmune diseases. TGF-β is a pleiotropic factor that can stimulate, inhibit, or modulate cellular events in a time- and concentration-dependent manner. It is a crucial peptide in the control of healing, attracting cells to the wound, but especially promoting the subsequent deposition of collagen and matrix [42]. It has also been identified as a potent modulator of MMPs

expression. Some authors have stated that this growth factor regulates the expression of MMP-2 in several cell types such as fibroblasts and endothelial cells [44, 45].

Our group has carried out different studies in order to evaluate the expression of different growth factors in tissue affected by inguinal hernia [18] and on the integration tissue after the implantation of different types of prosthetic materials in hernia repair [46]. Accordingly, a protein analysis of the distribution and levels of the active and latent form of TGF-β1 was performed, using immunohistochemical and western blot techniques. No significant differences were found in the expression of the latent form of TGF-β1 (LAP-TGF-β1); however, the results of our study indicated an overexpression of the TGF-β1 active form in TF of young patients with direct inguinal hernia (Fig. 3.7). This overexpression of TGF-β1 correlated with the previously described overexpression of MMP-2, in the same group of patients, which could be interpreted as an attempt to counteract the process of degradation of the extracellular matrix observed in this type of hernia.

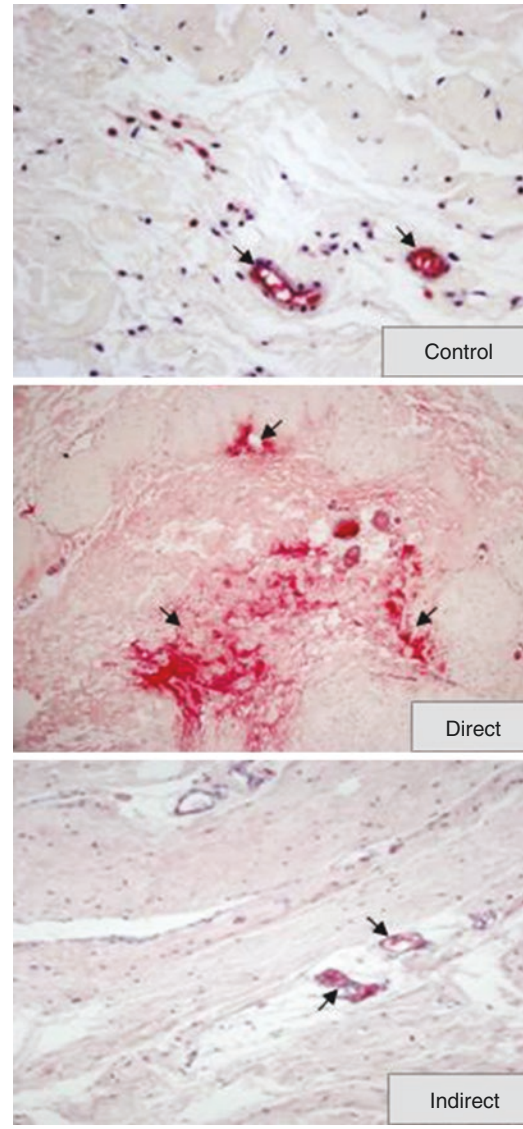

Fig. 3.7 Histological images of the immunohistochemical technique performed on tissue sections of transversalis fascia of healthy patients and patients with direct and indirect inguinal hernias to detect active MMP-2. Overexpression of active enzyme levels on the tissue corresponding to patients with direct hernia can be observed (Magnification 200×)

3.2.4 Elastic Fibers

Elastic Fibers are large fibrillar extracellular matrix structures that provide recovery to tissues undergoing repeated stretching. Elastic fibers are formed by two main components, elastin and microfibrils, that are assembled in a spatial and temporal certain way [47]. Elastin is encoded by a single gene and is the main constituent of the mature fiber. This polymer with a molecular weight of 72 kDa with great capacity of expansion is formed through the cross-linking of tropoelastin (TE) monomers on a support of microfibrils which consist mainly of fibrillin [48] but also associated with proteins such as fibulins, microfibril-associated glycoproteins (MAGPs), and EMILIN-1 [47]. In this crosslinking process, the enzyme lysyl oxidase (LOX) plays a key role. LOX is a family of copper-dependent enzymes that play a critical role in the cross-linking of different extracellular matrix proteins. Some authors [49] have proposed a selective role for LOXL-1 (lysyl oxidase like-1) in the metabolism of elastin, by which elastin deposition is stabilized in a spatially defined manner, as a prerequisite for the formation of functional elastic fibers [50]. One of the most important degradative enzymes of the

elastic system is elastase, which is capable of degrading elastin and elastic fibers, which together with collagen determines the mechanical properties of the connective tissue.

Structural alterations in elastic fibers, related to age, including a considerable reduction in the number of microfibrils leading to a loss of tensile strength and elasticity of transverse fascia tissue have been previously described [51]. This fact could explain the high incidence of inguinal hernia observed from the 50 to 60 years of age.

As we have already mentioned, patients with inguinal hernia show some abnormalities in collagen metabolism and alterations of the MMPs system [16, 17], but there is not much knowledge about the elastic component of the extracellular matrix and the factors involved in tissue remodeling that could affect the elastin metabolism.

Therefore, some studies that aimed to examine in the TF affected by inguinal hernia, the expression of the elastin precursors, tropoelastin (TE), LOXL-1, the enzyme responsible for the cross-linking of elastin polymer and elastase, the main enzyme that causes the degradation of elastin, were performed. Protein analysis techniques such as immunohistochemistry and western blot were used, as well as molecular biology techniques for gene expression analysis. A deficiency in the metabolism of elastin was demonstrated in patients with inguinal hernia that could contribute to the failure of TF [19]. This deficiency was reflected by the insufficient production of LOXL-1 (Fig. 3.8), which plays a selective role in elastin cross-linking, as well as by the overproduction of elastase, one of the most important enzymes involved in the degradation of the elastic component. The findings indicated similar

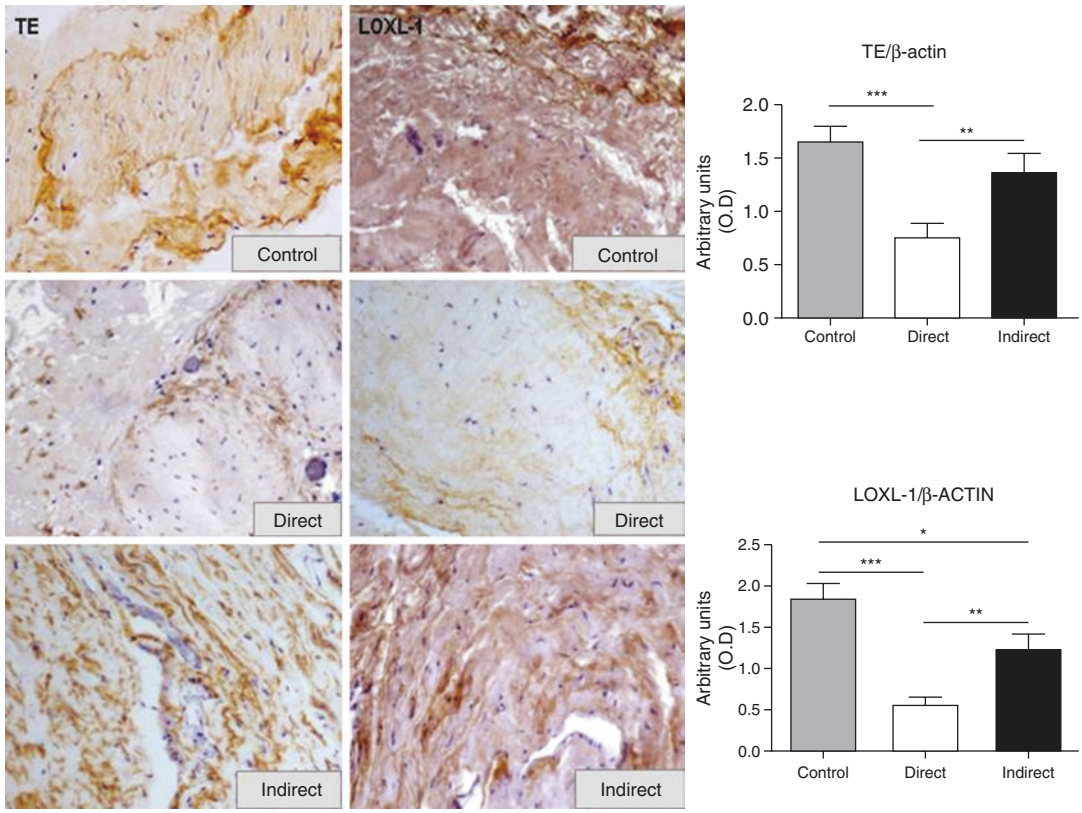

Fig. 3.8 Immunohistochemical detection and levels recorded in the different study groups revealed by western blot analysis of TE and LOXL-1 on transversalis fascia tissue (Magnification 200×). Significantly lower levels were detected in both constituents for the direct hernia group compared to the rest of the groups ($^{*}p<0.05$; $^{**}p<0.01$; $^{***}p<0.001$)

amounts of mRNA encoding for TE in fibroblasts isolated from TF from patients with direct and indirect inguinal hernia. But messenger levels for LOXL-1 showed significantly decreased expression in cell cultures obtained from patients with direct inguinal hernia.

Both elastic fiber fragmentation and reduction of its number in spite of an increase in the extracellular matrix have been observed by other groups [52], in patients with hernia. Other studies have reported a decrease in the total amount of elastic fibers in connective tissue in remote locations to the site of the hernia, such as the rectus sheath, supporting the theory of a global connective tissue disorder [53].

3.3 Discussion

Throughout all this review, we have been able to verify in inguinal herniogenesis that the TF is formed by a connective tissue with an altered extracellular matrix, mainly in those patients with direct inguinal hernia. The ultrastructural analyses did not show alterations in the density and diameter of the collagen fibers that justify the formation of hernias [21]. Other groups, according to these findings have reported similar results [54], but some of them have observed some alterations that have been attributed to the age factor and not to the hernia condition [51]. Hydroxylation of the amino acids proline and lysine of the collagen molecule is an essential process in the formation and stabilization of the collagen triple helix. Our results showed no proline hydroxylation differences, as did other authors [22] in patients with hernia. However, a significant decrease in lysine hydroxylation was observed in direct inguinal hernia of patients of the older age group. This could indicate alterations in the cross-linking of collagen that could affect the interaction with other components of the extracellular matrix [18].

Alterations in the collagen I:III ratio have been described by some authors [16, 55], in contradiction with our group that has not demonstrated significant differences in this ratio in TF between different types of hernias. A literature review [8] performed by the group of Henriksen, on collagen alterations in abdominal wall hernia, states that there is evidence of a significant increase in type III immature collagen with respect to mature type I collagen, resulting in the corresponding loss of biomechanical resistance of the repair area. It suggests that these alterations may be due to variations in the process of synthesis, maturation, or degradation of the collagen matrix by MMPs, in combination with other processes or independently. The authors of this review conclude that both the development of primary hernia and its recurrence are associated with a decrease in the collagen I:III ratio.

After the study involving the collagen component, our interest was centered in the analysis of different MMPs. We found only significant differences in the expression of MMP2, whose main substrates are different types of collagens and other extracellular matrix components such as fibronectin, elastin, and proteoglycans [56]. Our results with MMP-2 demonstrated that this enzyme is overexpressed in direct hernias at the tissue level and in cell cultures obtained from the TF of these patients [21, 39]. These results were corroborated by investigations of other groups showing an increase in MMP-1, MMP-2, and MMP-9 in inguinal hernia, stating that these enzymes play a very important role in the development of this pathology [36].

Other groups [57] have subsequently shown dysregulation of the extracellular matrix degradation process in patients with inguinal hernia, showing a significant increase of MMP-2 and 9, accompanied by a decrease in their endogenous inhibitors (TIMPs). The results of this study suggest problems in collagen metabolism that could be the underlying pathophysiological mechanism of inguinal hernia formation.

There is scarcely any bibliography to analyze the importance of growth factors in the development of inguinal hernia. TGF-β1 has been described as an important modulator of MMPs [41]. In our study overexpression of TGF-β1 was correlated with the overexpression of MMP2 in patients with direct hernia. Other authors have shown selective regulation of MMP-2 by TGF-β1 in transcriptional and posttranscriptional lev-

els in fibroblast cultures [58]. Other research work [59], according to this regulation, maintain the possibility that under the pathophysiological conditions, the digestion of the extracellular matrix by the MMPs could induce the TGF-β-mediated tissue reaction released by the connective tissue. All these results are in agreement with our findings in the TF of patients with hernia pathology.

In a model of experimental hernia in rat, some authors [60] have shown that the local application of this growth factor does not increase the biomechanical resistance of the abdominal wall. However, another research group [61], also using an experimental rat model, states that treatment with TGF-β2 prevents the development of hernias, stimulating the mobilization of macrophages and fibroblasts, as well as an increase of collagen deposition in the wound area.

Regarding the elastic component, a genetic mutation has been described by the group of Junqueira et al. [62] involving the elastic tissue and its dysfunction at the TF level. Our studies have shown a disorganization and reduction in the number of elastic fibers in the TF of patients with direct inguinal hernia, which corresponded with the minimal expression of LOXL-1, which would prevent normal cross-linking of TE and with the greater expression of elastase, which degrades the elastic components. These results emphasize the importance of LOXL-1 to avoid the loss of elasticity of tissues in which elastic fibers are essential for the correct functionality.

According to our results, other groups [52] have also observed in inguinal hernia both elastic fiber fragmentation and reduction of its number with an increase in the extracellular matrix. A decrease in the total amount of elastic fibers in connective tissue of remote locations to the site of the hernia have been also reported, supporting a global connective tissue disorder [53]. Conversely, some studies [19] have shown a significant increase of elastic fibers in the fascia of patients with direct inguinal hernia. Other papers using immunohistochemical evaluation showed no statistically significant differences in the amount of elastic fibers and collagen I and III among patients with inguinal hernia when compared with subjects without hernia [63].

There are very few published reports in the literature relating inguinal hernia to the analysis of the enzymes involved in elastin and collagen cross-linking. These include a study by Kayaoglu et al. [64] in which significant lower plasma and hernia sac copper levels were detected in patients with direct hernias than those with indirect hernias. Given that copper is an essential cofactor for lysyl oxidase, the authors proposed that patients with direct hernia could show impaired collagen and elastin synthesis because of the deficient activity of LOX. Other studies [65] evaluating copper and zinc levels in hernia formation have showed significantly lower tissue levels compared to control, which might reflect excessive consumption or dysfunction of lysyl oxidase as playing a role in the etiology of hernias.

The amounts of collagen and elastic fibers in the TF determine its tensile strength and elasticity. Significant biomechanical changes in the TF of patients with hernia have been reported by Pans et al. [7] Some other authors [66], according to our results and in a search for possible relationship between hernia and abdominal aneurysm, have described elevated levels of elastase and significantly higher prevalence of inguinal hernia in these patients with aneurysm suggesting systemic fiber degeneration. Other authors [67], also in agreement, have reported significantly higher circulating serum elastinolytic activity in patients with direct hernia.

Taking into account our findings and those of other authors, in relation to the biological factors involved in herniogenesis, we could conclude that the different elements of the connective tissue extracellular matrix play an important role in the genesis of inguinal hernias, and especially in one type, the direct hernia.

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4 Classification of Inguinal and Abdominal Wall Hernia

Diego Cuccurullo and Stefano Reggio

4.1 Inguinal Hernia Classification

Since 1840, when Hesselbach used the inferior epigastrics vessels as the defining boundary between indirect and direct hernias, surgeons have always tried to classify the inguinal hernias. This first classification resisted for years; nowadays the interest in a more accurate and scientific classification of groin hernias is increasing. The general opinion is that one standardized system must be adopted, and since 2009 the EHS recommended that its classification system should be used [1]. The primary objective of any classification system is to stratify the pathology in study (groin hernia) for severity in order to allow reasonable comparisons between treatment strategies [2]. Moreover, a classification must be simple and easy to use. Several operative techniques with their variations for herniorrhaphy have been described, but no one classification system can satisfy all presently. The EHS overpass this problem, developing a brand new classification system by consensus [2–9]: in effect an expert panel analyzed the known systems to date and proposed classification that resembles largely the Aachen classification [10]. This latter makes a distinction between the anatomical localization (indirect or lateral vs. direct or medial) and the size of the hernia orifice defect in cm (<1.5, 1.5–3, >3 cm) (Table 4.1). Moreover Miserez et al. [2] decided to modify to some minor aspects this classification, proposing the "index finger" rule as the reference in open surgery (normally the size of the tip of the index finger is mostly around 1.5–2 cm). This size is also identical to the length of the branches of a pair of most laparoscopic graspers, dissector, allowing the surgeon to use the same standardized classification during minimally invasive procedures [11, 12]. For recurrent hernias, a detailed description could be used as proposed by Campanelli et al. [13]. The recurrent hernias are divided into three types:

- Type R1: first recurrence "high," oblique external, reducible hernia with small (<2 cm) defect in nonobese patients, after pure tissue or mesh repair

Table 4.1 EHS groin hernia classification

EHS groin hernia classification		Primary	Recurrent		
	0	1	2	3	×
L					
M					
F					

D. Cuccurullo (✉) · S. Reggio
AO dei Colli, Ospedale Monaldi, U.O.C. di Chirurgia Generale, Centro di Chirurgia Laparoscopica e Robotica, Naples, Italy
e-mail: diego.cuccurullo@ospedalideicolli.it

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- Type R2: first recurrence "low," direct, reducible hernia with small (<2 cm) defect in non-obese patients, after pure tissue or mesh repair
- Type R3: all other recurrences or anyway not easily included in R1 or R2, after pure tissue or mesh repair (femoral, big defects, multirecurrent, non-reducible, obese patient)

For now, the classification system for groin hernia is mired in some controversy and disagreement; one disadvantage could be that the EHS system was not developed to classify hernia types preoperatively; moreover a flow chart to inform decision-making about the complex cases would be helpful. However, the EHS system as classification system is supported by several available evidence and expert opinion; but the major objective to achieve is to convince all surgeons performing hernia surgery to report the class of the groin hernia systematically in the operative report. Ideally, these data should be collected in a prospective nationwide registry securing patient and surgeon anonymity (http://www.herniaweb.org/).

4.2 Primary and Incisional Abdominal Wall Hernia Classification

Since 2000, several authors have proposed classification for incisional hernias, but none of them are widely accepted in literature [11, 12]. After the publication, in 2007, of a simple classification for groin hernias by EHS [2], in 2009 Muysoms et al. [13] proposed a classification of primary and incisional abdominal wall hernias. The classification allows to describe hernias in a standardized way, improving the possibility of comparing different studies and their results. We all speak the same language which is easier to collect different results of several techniques described in literature, in order to develop evidence-based guidelines using this classification. The first question was to reach the agreement on separating "primary abdominal wall hernias" (the ventral hernias, non-incisional) and other "incisional abdominal wall hernias"; a consensus has been found on avoiding the word "primary incisional hernia" that should not be used. Moreover, there was a consensus to exclude "parastomal hernias" from this classification: they make up a distinct group, with specific properties and treatment options [14].

4.2.1 Classification of Primary Abdominal Wall Hernias

For these hernias there is agreement on the use of localization and size as two variables.

Localization of the hernia: Two midline (epigastric and umbilical) and two lateral hernias (spigelian and lumbar) are identifiable entities with distinct localizations.

Size of the hernia: Cutoff values of 2 and 4 cm were chosen to describe three subgroups according to size: small, medium, and large.

Taxonomy: nominative description (epigastric, umbilical, small, medium, large) (Table 4.2).

4.2.2 Classification of Incisional Abdominal Wall Hernias

Definition: "any abdominal wall gap with or without a bulge in the area of postoperative scar perceptible or palpable by clinical examination or imaging" [12].

Localization: The abdomen was divided into a medial or midline zone and a lateral zone.

Medial or midline hernias: The borders of this area are defined as cranially the xyphoid, caudally the pubic bone, and laterally the lateral margin of the rectal sheath. An easily memorable

Table 4.2 EHS classification for primary abdominal wall hernias [Muysoms]

EHS primary abdominal wall hernia classification	Diameter cm	Small <2 cm	Medium ≥2–4 cm	Large ≥4 cm
Midline	Epigastric			
	Umbilical			
Lateral	Spigelian			
	Lumbar			

classification from M1 to M5 going from xyphoid to pubic bone was proposed (Fig. 4.1).

- M1: subxyphoidal (from the xyphoid till 3 cm caudally)
- M2: epigastric (from 3 cm below the xyphoid till 3 cm above the umbilicus)
- M3: umbilical (from 3 cm above till 3 cm below the umbilicus)
- M4: infraumbilical (from 3 cm below the umbilicus till 3 cm above the pubis)
- M5: suprapubic (from pubic bone till 3 cm cranially)

If hernias are extending over more than one M zone, it was decided to mark every zone in which the hernia was located when using the grid for incisional hernias (Fig. 4.1). Different hernia defects caused by one incision will be considered as one hernia. If the different defects were caused by two different incisions, they should be considered two different hernias.

Lateral hernias: The border of this area is defined as cranially the costal margin, caudally the inguinal region, medially the lateral margin of the rectal sheath, and laterally the lumbar region. Thus, four L zones on each side are defined as (Fig. 4.2):

1. L1: subcostal (between the costal margin and horizontal line 3 cm above the umbilicus)

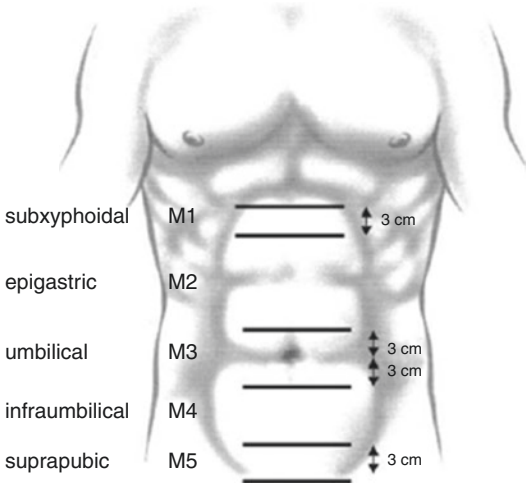

Fig. 4.1 Five zones were defined to classify midline incisional hernias

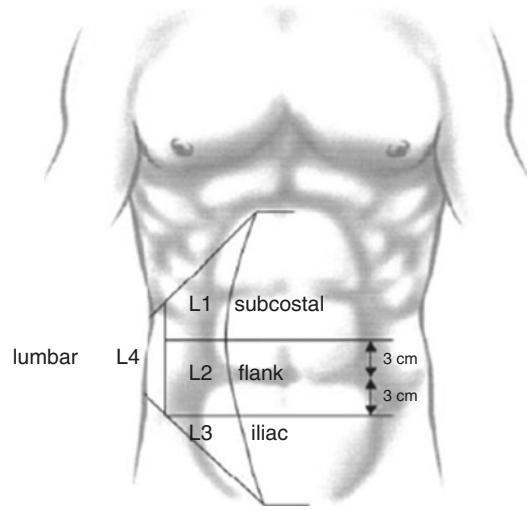

Fig. 4.2 Four zone lateral of the rectal muscle sheaths were defined to classify lateral incisional hernias

2. L2: flank (lateral to the rectal sheath in the area 3 cm above and below the umbilicus)
3. L3: iliac (between a horizontal line 3 cm below the umbilicus and the inguinal region)
4. L4: lumbar (laterodorsal of the anterior axillary line)

Size of the hernia: The width of the hernia defect alone was insufficient to describe the hernia defect size adequately. Muysoms [13] proposed that width and length should be used. The width was defined as the greatest horizontal distance in cm between the lateral margins of the hernia defect on both sides. In case of multiple hernia defects, the width is measured between the most laterally located margins of the most lateral defect on that side (Fig. 4.3). The length of the hernia defect was defined as the greatest vertical distance in cm between the most cranial and the most caudal margin of the hernia defect. In case of multiple hernia defects from one incision, the length is between the cranial margin of the most cranial defect and the caudal margin of the most caudal defect (Fig. 4.3).

Taxonomy: To avoid confusion with primary abdominal wall hernias (small, medium, large), a coded taxonomy was chosen instead of a nominative description:

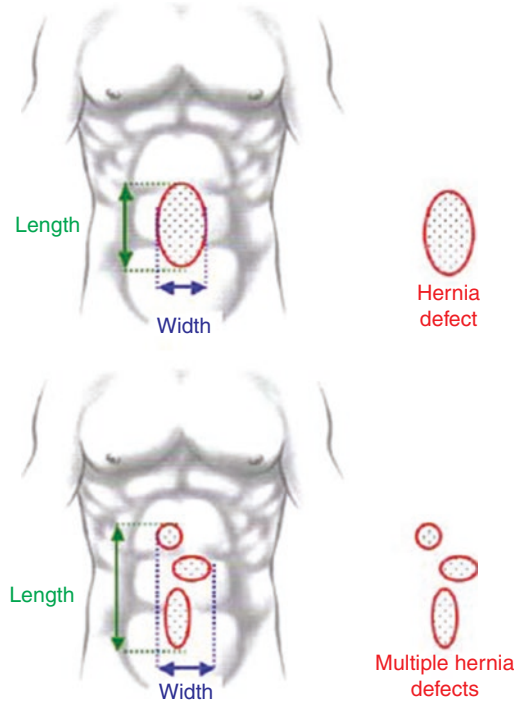

Fig. 4.3 Hernia defect surface can be measured by combining width and length in a formula for an oval, thus trying to make an estimation of the real surface in cm^2

- W1 < 4 cm
- W2 ≥ 4–10 cm
- W3 ≥ 10 cm (Table 4.3)

Table 4.3 EHS classification for incisional abdominal wall hernias

EHS incisional hernia classification					
Midline	Subxyphoidal	M1			
	Epigastric	M2			
	Umbilical	M3			
	Infraumbilical	M4			
	Suprapubic	M5			
Lateral	Subcostal	L1			
	Flank	L2			
	Iliac	L3			
	Lumbar	L4			
Recurrent incisional hernia		Yes	O	No	O
Length:	cm	Width:		cm	
Width cm	W1	W2		W3	
	<4 cm	≥4–10 cm		≥10 cm	
	O	O		O	

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Diagnostic Tools in Hernia Disease

5

Paul Tenzel, Jordan Bilezikian,
and William W. Hope

5.1 Introduction

Most inguinal and ventral hernias can be diagnosed using a thorough history and physical examination. Patients are usually referred to a surgeon for diagnosis confirmation and a discussion of treatment options. However, additional diagnostic imaging may be necessary to identify an occult hernia or to plan the operation. In this case, the surgeon has many choices depending on the hernia type or clinical problem and the information that is needed. In general, additional diagnostic tools include ultrasound, computed tomography (CT) scanning, and magnetic resonance imaging (MRI) with other adjuncts for inguinal hernias including herniography. Each imaging modality has strengths and weaknesses. Imaging choice is impacted by the local hospital environment and radiology department.

5.2 History and Physical

Patients with a hernia often complain of feeling a bulge. In this case, the surgeon should confirm hernia presence with a physical examination (Fig. 5.1). In some cases, an occult hernia (one that is difficult to detect) is present. This can be due to the small hernia size or other patient characteristics such as obesity. In this case, additional diagnostic imaging should be obtained.

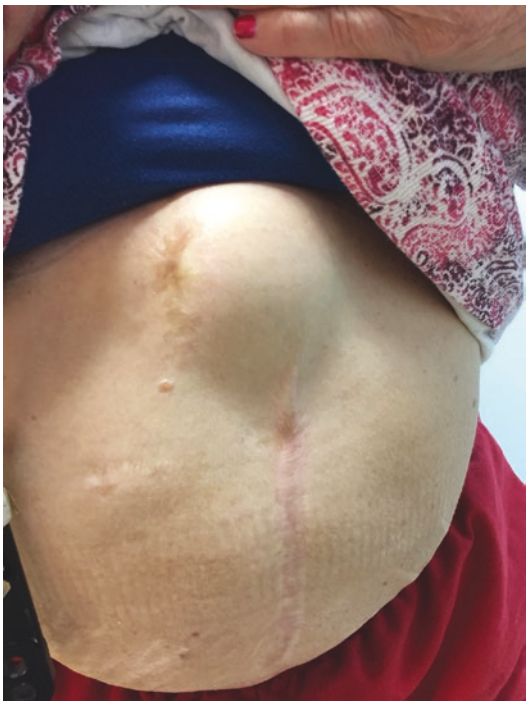

Fig. 5.1 Ventral hernia shown on physical exam

P. Tenzel, M.D. · J. Bilezikian, M.D.
W. W. Hope, M.D. (✉)
Department of Surgery, New Hanover Regional Medical Center, Wilmington, NC, USA
e-mail: William.hope@nhrmc.org

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5.3 Diagnostic Tools for Inguinal Hernia

5.3.1 Imaging in Inguinal Hernias

In most cases, a history of groin pain and an obvious inguinal bulge are all that are required to diagnose an inguinal hernia. In this case, the next step is operative repair. Diagnosis is less clear when there are no physical exam observations consistent with inguinal hernia. An occult inguinal hernia can be too small to detect on physical exam but can produce symptoms consistent with a groin hernia such as a feeling of a bulge or pain. Without physical exam evidence, imaging is crucial in diagnosis, because there are many causes of pain that should not be treated using surgery.

5.3.2 Ultrasound

Ultrasound is usually the first modality used to diagnose occult inguinal hernias because it is easily accessible and relatively inexpensive. An inguinal hernia ultrasound with and without Valsalva maneuver (Fig. 5.2), not a pelvic ultrasound, will provide the best information for accurate diagnosis of an occult inguinal hernia. The patient can be moved into different positions such as lying down and standing which can often aid in diagnosis of the hernia; as in some positions, the protrusion through the hernia defect may be more pronounced (Fig. 5.3). Although the dynamic nature of ultrasound is a distinct benefit, this characteristic also makes its accuracy operator dependent.

Although ultrasound is the first-line imaging option for diagnosing an inguinal hernia, it is far from perfect. A recent meta-analysis comprised of five ultrasound studies totaling 716 patients showed that ultrasound had a sensitivity of 86% and specificity of 77% [1]. Though these numbers may seem reasonable for diagnosis, two recent studies reported that ultrasound has a low positive predictive value after the patient is evaluated in the operating room. The first study contained 116 patients who underwent surgery after a positive ultrasound and yielded only a 74% positive predictive value [2]. This correlated with another study of 118 patients who at the time of

Fig. 5.2 Ultrasound image showing of right groin showing fat protruding through a hernia defect that is more pronounced with Valsalva

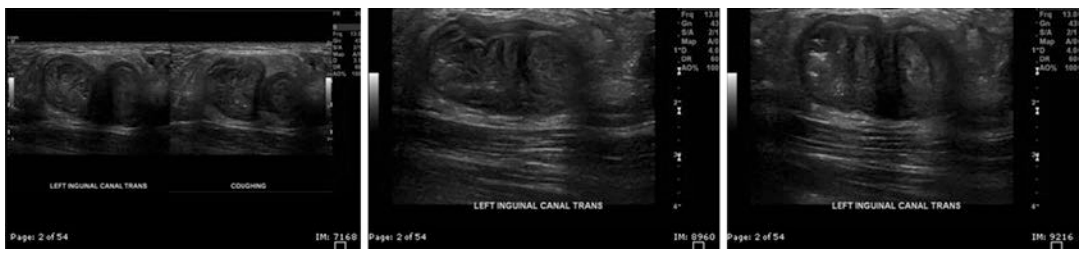

Fig. 5.3 Ultrasound image showing bowel protruding through a left inguinal hernia

operation had a 70% positive predictive value for presence of a hernia. The same study followed 141 patients with a negative groin ultrasound for a median of 3 years, and no patients were later diagnosed with a hernia [3]. The most recent study on the subject by Miller showed a sensitivity of 0.33 and specificity of 0.0 [4]. These data indicate that ultrasound may be a better imaging method to help rule out a hernia diagnosis than to determine the need for surgery.

5.3.3 CT Scan

CT scan is also used to diagnose occult inguinal hernias. It is widely available, and many surgeons are accustomed to reading CT scans, which is not the case with most other imaging options. A CT scan facilitates evaluating the entire abdomen, which can occasionally identify other causes of pain or abnormalities. In a study comparing CT and herniography, CT identified bone spurs as the cause of pain in 2 of the 51 patients evaluated [5].

Despite these advantages, the usefulness of CT for inguinal hernia diagnosis is very limited. Studies using CT show a fairly low sensitivity and specificity but a fairly high positive predictive value for patients that undergo surgery. Recent data on the subject showed a sensitivity of 0.54, a specificity of 0.25, but a positive predictive value of 86% in 39 patients who underwent CT and subsequent surgery [4]. Another study evaluated 158 patients with groin pain. In these patients, 49 hernias were diagnosed via CT, and the patients were taken to surgery for evaluation and hernia repair. This study showed a positive predictive value of 92% and a negative predictive value of 96% [6]. These data indicate that CT is not the best option for the initial diagnosis of an occult hernia; however, when a hernia is identified on CT, the patient can proceed to surgery for hernia repair.

Although CT may not be the best option for the diagnosis of occult inguinal hernias, it can be useful for inguinal hernias in certain clinical circumstances such as when other intra-abdominal pathology is suspected or cases of difficult to diagnose hernias such as femoral and obturator hernias (Figs. 5.4, 5.5, and 5.6).

Fig. 5.4 Computed tomography scan showing portal venous gas from incarcerated right femoral hernia causing a bowel obstruction

Fig. 5.5 Computed tomography scan showing pneumatosis from incarcerated right femoral hernia causing a bowel obstruction

Fig. 5.6 Computed tomography scan showing incarcerated right femoral hernia causing a bowel obstruction which lead to ischemic intestine, pneumatosis, and portal venous gas

5.3.4 MRI

MRI is useful in diagnosing occult inguinal hernias; however, it is not without disadvantages. It is more expensive than ultrasound or CT and also takes the most time to complete. Generally, surgeons are not as skilled at reading MRIs compared with reading CTs; however, MRI has several benefits. Like CT, MRI can be used to evaluate the entire pelvis. Because of the ability to closely assess the bones and soft tissues in the pelvic region, MRI is useful to diagnose hernias and other musculoskeletal etiologies for groin pain (Figs. 5.7 and 5.8).

There is increasing evidence that MRI should be the initial study to evaluate suspected occult inguinal hernias. A study by Miller compared the use of CT, ultrasound, and MRI in 34 patients and determined that MRI was the best option for diagnosing occult inguinal hernias. The study yielded a sensitivity and specificity of 0.91 and 0.92, respectively [4].

5.3.5 Herniography

Ducharne first described herniography, also known as peritoneography, in Canada in 1967 [7]. Herniography consists of injecting iodinated contrast into the peritoneum and imaging the area with X-ray or CT to evaluate possible hernia defects. This imaging modality is the most invasive of the options discussed. Because this procedure is done with X-ray or CT, it exposes the patient to radiation. Despite these negatives, it is considered one of the most accurate tests used to diagnose hernias; however, it is not widely used probably because of the lack of comfort and familiarity with the study both by surgeons and by the radiology teams that would perform them

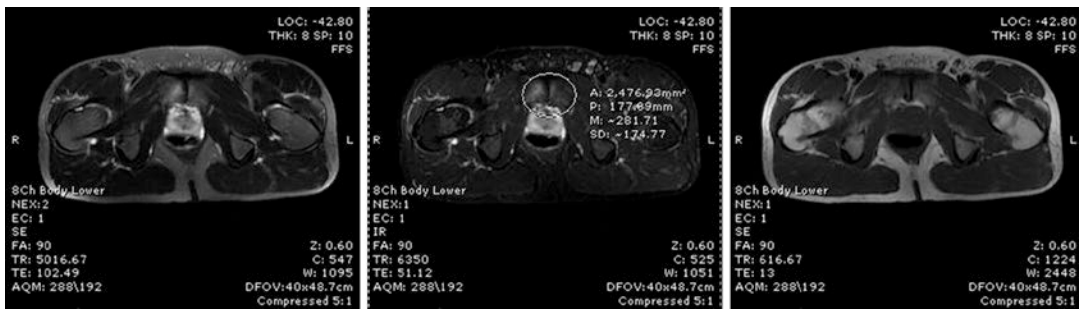

Fig. 5.7 MRI for chronic groin pain in a runner revealing mild degenerative changes of the pubic symphysis with parasymphyseal bone marrow edema suggestions stress/reactive edema due to repetitive stress

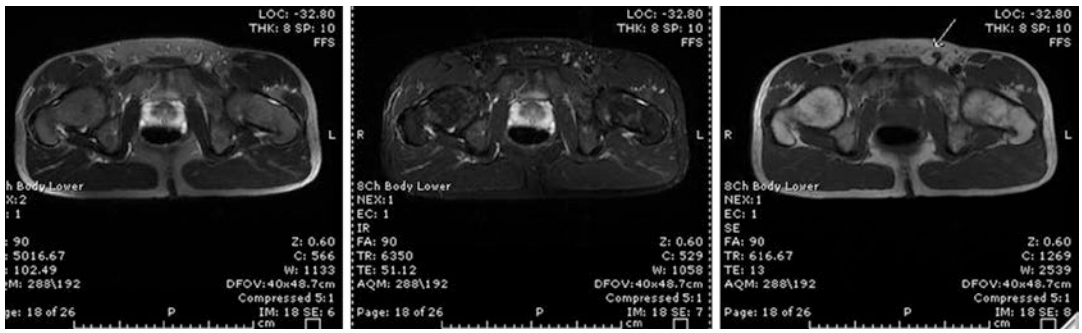

Fig. 5.8 MRI showing small fat containing left inguinal hernia