Aus der Klinik für Visceral- Thorax- und Gefäßchirurgie
Direktor: Prof. Dr. med. Detlef K. Bartsch
des Fachbereichs Medizin der Philipps-Universität Marburg

In Zusammenarbeit mit dem Universitätsklinikum Gießen und Marburg GmbH
Standort Marburg

Titel der Dissertation:

Transabdominal preperitoneal (TAPP) versus totally extraperitoneal (TEP) repair of inguinal hernia

Inaugural-Dissertation zur Erlangung des Doktorgrades
der gesamten Humanmedizin
der Philipps-Universität Marburg
vorgelegt von

Stavros Athanasios Antoniou
aus Amarousio, Athen

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Διήλθομεν διά πυρός και ὕδατος,

καί ἐξήγαγες ἡμᾶς εἰς ἀναψυχήν

(Ψαλμ. ξε΄ 12)

We went through fire and through water,
but You brought us to the place of abundance

(Psalms 66:12)

Wir gingen durch Feuer und Wasser,

doch Du hast uns in die Freiheit hinausgeführt

(Psalmen 66:12)

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Preface

An holistic perception of medicine in Ancient Greece presupposed a dual philosophical and humanistic approach of the suffering person and the disease. The "father of Medicine" Hippocrates was recognized not only as a physician, but also as an outstanding philosopher. He claimed that *"the physician must insert wisdom in medicine"*,[1] whereas the Hippocratic Oath denounced the technocratic aspect of medical science. Another Greek philosopher, Antisthenes, asserted *"ἀρχὴ σοφίας ἡ τῶν ὀνομάτων ἐπίσκεψις"*,[2] meaning *"the origin of wisdom lies within the insight of the words"*. In order to support the philosophical basis of a scientific hypothesis, one must be acquainted with the terminological background, the history, the meaning and the very substance of the words. This approach allows an holistic evaluation of the past, the present and the future perspectives of medical science.

The first part of the present work is thus dedicated to the investigation of the terminological origins and the history of the words *endoscopy* and *laparoscopy*, and a brief historical approach of the evolution of open and laparoscopic inguinal hernia repair.

The second part constitutes a statistical approach of current scientific evidence on the clinical outcomes of endoscopic and laparoscopic inguinal hernia repair. Special care was taken to identify and meta-analyze high-quality clinical data, whereas non-randomized studies were not disregarded, since they often derive from centers with limited experience in minimally invasive surgery or low volume centers, and may thus reflect the current surgical practice in many medical institutions around the world. Finally, a critical approach of the results of the statistical analysis was attempted, highlighting implications on current surgical practice and future perspectives.

FIRST PART

1.1 Terminology and historical evolution of the words *endoscopy* and *laparoscopy*

The invasive character of surgical therapy has been elegantly highlighted by Hippocrates, aphorizing *"Ὁκόσα φάρμακα οὐκ ἰῆται, σίδηρος ἰῆται [...]"*, meaning "What medicines do not heal, the lance will […]".[3] The introduction of minimally invasive techniques in surgery has signaled a new era, substantiating the diachronic efforts to minimize surgical trauma. The evolution of laparoscopy may be observed as a further step towards investigating human body cavities, efforts which have begun as early as in the 5th century BC, when the first endoscopic examinations of the rectum and the vagina were performed by the Hippocratic school.[4,5] The terminological origins of the words *laparoscopy* and *endoscopy*, however, are traced further back in history. The value of modern medical nomenclature lies in its close relationship with medical history, the pioneers of the medical profession, and its continuous enrichment through time.[6]

Etymology of the terms *endoscopy* and *laparoscopy*

Endoscopy refers to the action of investigating a hollow organ or cavity of the body using special instruments. The word *endoscopy* derives from the Greek word *ἐνδοσκόπησις* (endoscópesis), which is a compound word consisting of *ἐνδο-/ἔνδον* (endo-/éndon), which means *inside, into, within*, and *σκοπεῖν* (scopeín), which means *to watch carefully, to observe*. The word *ἐνδο-* corresponds to the Latin derivative *endo-, indu-*. It is suggested, that the original *ἐνδο-* consists of the preposition *ἐν (en)*, corresponding to the latin *in*, and the suffix *–το* (–to).

Laparoscopy is the action of visualizing the abdominal cavity through a small opening of the abdominal wall. *Laparoscopy* is also a compound word, consisting of the words *λαπάρα* (lapára), which means *abdomen* or *abdominal wall*, and *σκοπεῖν* (scopeín). The word *λαπάρα*, which is supposed to be the ionic type of the word *λαπάρη* (lapáre), derives from the adjective *λαπαρός* (laparós), which means *soft, flexible* **(Figure 1)**. It is obvious, that the word endoscopy embodies the meaning of laparoscopy, as the latter refers to a human cavity.

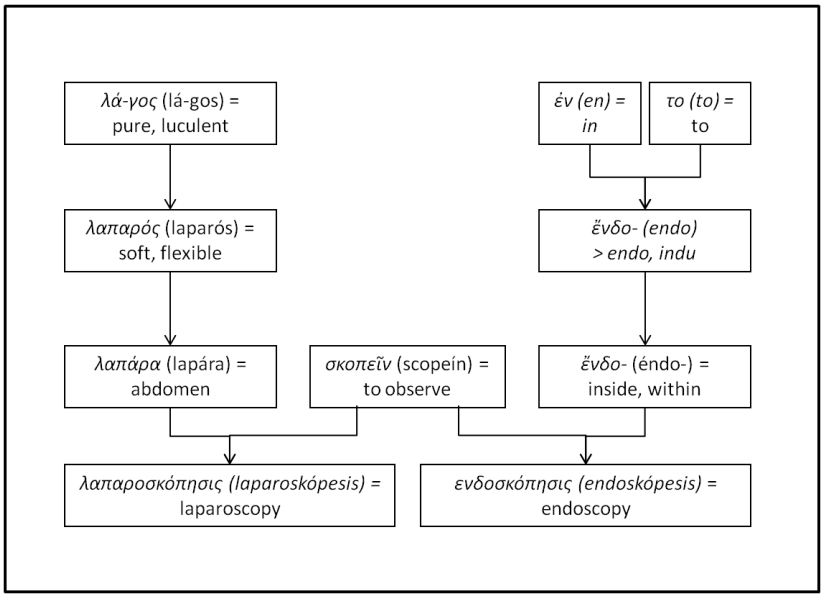


Figure 1. Etymological origins of the words *endoscopy* and *laparoscopy*.

Historical origin and evolution

The word *λαπάρα* may be traced back to the Linear B syllabic script of the Mycenaean and the Minoan civilizations of Peloponnese and Crete (17^{th} -13^{th} century BC), respectively.[7-9] Homer (8^{th} century BC) repeatedly uses the word *λαπάρα* in his lyric descriptions of fights during the Trojan war **(Figure 2)**. In rhapsody *Z*, verse 64, the Perse fighter Atreus, having been caught by Menelaus, promises "treasure of gold, bronze and wrought iron", if he was left to follow the ships of the Achaeans as a captive. However, Agamemnon reminds Menelaus of the misfortune having being caused by the Trojans; then, Menelaus thrust Atreus from him, *"τὸν δὲ κρείων Ἀγαμέμνων οὖτα κατὰ λαπάρην ὃ δ' ἀνετράπετο"*, meaning, whereon King Agamemnon struck him in the flank, and he fell. Then the son of Atreus planted his foot upon his breast to draw his spear from the body.[10] In another fighting scene, Antilohus, the first son of Nestor, King of Pylos, *"λαπάρης δὲ διήλασε χάλκεον ἔγχος"*, "pierces the coppery shaft through his flanks".[11] It is noteworthy, that English translations of Homer's Iliad, refer to *lapára* as the flank. Similarly, translations of the manuscript in modern Greek, use the word *λαγόνι* or *λαγγόνι* (laggóni) as translation of *lapára*. *Λαγόνι* is the Greek word for the lateral abdominal wall, whereas *λαγόνιον ὀστοῦν* (lagónion ostoún) is the iliac bone. It is speculated, that both words originate from the common stem *la-*, deriving from the adjunctive *λά-γος* (lá-gos), which means pure, luculent, soft.[12]

Figure 2. The Athenian hoplite Aías (Ajax) is dueling with a Persian warrior during the Trojan war. Goddess Athena is standing behind Aías, as his protector.

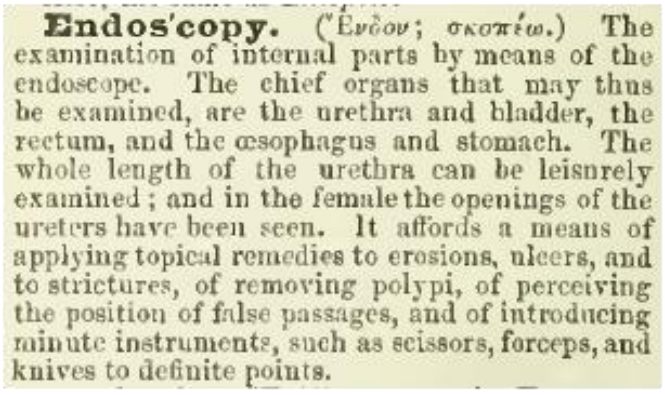
5th century BC:	*endoscopic examinations of the rectum and the vagina by the Hippocratic school*
1st century AC:	*Agathinos of Lakedaimonia describes resections of the prolapsed uterus using a speculum*
2nd century AC:	*Galen uses rectal and vaginal dilators*
10th century AC:	*Arab physician Albukasim developes a speculum based on the concept of camera obscura*
16th century AC:	*Italian physician Giulio Cesare Aranzi performes rectal examinations using a speculum illuminated by light reflectors*
18th -19th century AC:	*Physicians struggle with the use of natural and artificial light for the purposes of endoscopy*
1879:	*The lemma "endoscopy" is included in "The New Sydenham Society's lexicon of medicine and the allied sciences"*
1911:	*Hans Christian Jacobaeus (1879-1937) is accredited with having performed the first laparoscopic examination in humans. He first uses the term "Laparothorakoskopie"*
1980:	*The first laparoscopic appendectomy is performed by the gynecologist Kurt Semm*

Figure 3. Schematic review of historical steps towards the evolution of endoscopic techniques.

Furthermore, the "father of History" Herodotus (5th century BC) refers to the process of embalmment *"[...] μετὰ δὲ λίθῳ Αἰθιοπικῷ ὀξέι παρασχίσαντες παρὰ τὴν λαπάρην ἐξ ὧ εἶλον τὴν κοιλίη πᾶσαν, [...]"*, that is, "then, using Ethiopian sharp stones, they cut through the abdominal wall and remove the contents".[13] Similarly, the words

lapára and *laparós* are found in the manuscripts of the historian Xenophon (5th century BC), the philosopher Aristotle (4th century BC) up to the Byzantine period, in the scripts of Gregorios Alexandrinos (9th century AC).[14-16]

Efforts to explore natural body orifices have begun in the early classical period of ancient Greece **(Figure 3)**, with the development of special instruments for visualization of the rectum and the vagina, not very different from modern endoscopic instruments. Hippocrates (460-377 BC) referred to the use of a speculum in order to visualize and excise rectal condylomata.[17] Agathinos of Lakedaimonia (60-100 AD) described the resection of the uterus in case of prolapse using a vaginal speculum.[18] Galen (129-201 AC) also used rectal and vaginal dilators, according to archaeological findings of the 18th century. There is a paucity of archaeological and written evidence on the use of endoscopic instruments during the Middle Ages. At the same time, the rising Arabic medical school was constrained by the contemporary religion, which forbid endoscopic examinations of the rectum and the vagina. However, during the Medieval period in Europe, the Arab physician Albukasim (980-1037) and later the Italian Giulio Cesare Aranzi (1530-1589) developed a speculum illuminated by a set of light reflectors.[19] Until the 19th century AC, however, no evidence on the use of the term *endoscopy* may be found in the literature. The modern pioneers of endoscopy, Bozzini (1773-1809), Antoine Jean Desormeaux (1815-1894) and Johann Mikulicz



Endos'copy. (Ἔνδον; σκοπέω.) The examination of internal parts by means of the endoscope. The chief organs that may thus be examined, are the urethra and bladder, the rectum, and the œsophagus and stomach. The whole length of the urethra can be leisurely examined; and in the female the openings of the ureters have been seen. It affords a means of applying topical remedies to erosions, ulcers, and to strictures, of removing polypi, of perceiving the position of false passages, and of introducing minute instruments, such as scissors, forceps, and knives to definite points.

Figure 4. The lemma *endoscopy* in the New Sydenham Society's lexicon of medicine and the allied sciences, 1879.

(1850-1905), among others, struggled with the use of natural and artificial light illumination in order to visualize human orifices. The evolution of novel instruments using artificial light and the dissemination of techniques for endoscopic examinations

led to the wide use of the term *endoscopy*, which was first included as a lemma in "The New Sydenham Society's lexicon of medicine and the allied sciences" in 1879 **(Figure 4)**.[20]

Hans Christian Jacobaeus (1879-1937) of Stockholm is accredited with having performed the first laparoscopic examination in humans, whereas he was the first to use the term *Laparothorakoskopie*. His work was published in the review journal *Münchener Medizinische Zeitschrift* in 1911.[21] Nevertheless, publications in the following years used the terms *peritoneoscopy* or *coelioscopy*. *Peritoneoscopy* is a compound word, consisting of *περιτόναιον* (peritónaeon) and skopeín. Furthermore, peritónaeon is a compound word from *περί* (peri), which means *around* and *τείνω* (teíno), meaning *to extend, to stretch* or *to lean*. Similarly, *coelioscopy* is a compound word consisting of *κοιλία* (coelia), which means abdomen, and skopeín. The word *coelia* derives from the adjective *κοῖλος*, meaning *concave*. During the following years, the terms *peritoneoscopy* and *coelioscopy* have been gradually almost completely replaced by the term *laparoscopy* in the medical nomenclature. In the modern surgical literature, the word *laparotomy*, a compound word consisting of *lapára* and *τέμνειν* < *τομή* (témnein < tomé), which means *to incise* or *to cut*, is used to describe the action of incising the abdominal wall and exploring the peritoneal cavity.

The 20th century has found a wide dissemination of endoscopic and laparoscopic examinations, interventions and procedures with the advent of television chips, fiberoptic cameras and flexible endoscopes.[22] The word *endoscopy* has been registered as a surgical diagnostic technique, and *laparoscopy* as an endoscopic technique in the Medical Subject Headings Database of the National Library of Medicine. In the rise of the 21st century, novel terms are expected to generate after the advent of natural orifice transluminal techniques, single-incision laparoscopic procedures and robotic technologies in the field of minimally invasive surgery.[23,24] Whereas the universality of medical terminology facilitates international exchange of scientific information, the originality of the background of simple compound words allows the convenience of this communication. It is therefore not difficult to envision the use of terms such as monotomic or amphiluminal laparoscopic surgery,

pleiostrophic endoscopes, or even multiaxonic or polyceratic laparoscopic instruments in the near future.

The origins of the words *laparoscopy* and *endoscopy* are traced back to the archaic period and later to the classical years of ancient Greece. The everlasting semantic of these origins is revisited in the 21st century, as minimization of surgical trauma with the aid of modern technology substantiates the diachronic objective "*to do no harm*".

1.2 Historical note on the evolution of surgery of groin hernia

The first historical reports on abdominal wall hernia are found in the texts of a 14th century B.C. Egyptian papyrus[25] and later in Hippocratic manuscripts of the 2nd century B.C.; however, Praxagoras of Kos was the first to consider hernia as a surgical disease.[26] Galen (2nd century AD) provides a classification of inguinal hernias in his writings, whereas during the Byzantine Period (330-1653 A.C.) Aetius of Amida (~ 5th century A.C.) describes a technique of dissection of the hernia sac, ligation and excision of the prolapsed peritoneum. Paul of Aegina (7th century A.C.) proposes, among conservative treatments, reduction of the hernia contents and suturing of the abdominal wall defect with cross sutures.[27,28]

There are virtually no surgical advances in the surgical anatomy and the treatment of inguinal hernia during the obscure Middle Ages.[29] Along with other scientific disciplines, the rise of surgery came during the Renaissance period in Europe. During the 18th and the 19th century A.C., numerous monograms, anatomical and surgical manuscripts are published, and distinct types of inguinal hernia are described by Richter, Scarpa, Littré and Astley Cooper.[30] However, septic complications predominated during this period, with devastating consequences on surgical outcomes and on hernia recurrence rates. Contemporary trends supported ligation of the hernia sac and thermal or chemical cauterization of the inguinal area, which was left to heal by secondary intention, in order to promote formation of scar tissue.[29,31] The introduction of antisepsis by Lister allowed for the modern era of inguinal hernia repair to rise.

The era of modern surgical repair of inguinal hernia (late 19th–21st century A.C.) may be divided into two sections, according to the anatomical approach of the repair.[31] Reconstruction of the anterior wall of the inguinal canal characterizes the first short period of the modern era of inguinal hernia repair. The principle of the anterior repair consisted largely on reduction of the hernia sac and narrowing of the external ring, an approach proposed by Vinzenz von Czerny in 1890.[32] Recurrence rates as high as 30% suggested that the anterior approach cannot effectively prevent hernia recurrence.

The landmark for the posterior repair of the inguinal canal was the introduction of the transection of the external oblique aponeurosis by Just Lucas-Championniére in 1892.[33] It may be suggested, that this revolutionary approach of the anatomy of the hernia defect was the first step to the basic principles of groin surgery. Immediately after this innovation, Bassini described reinforcement of the posterior inguinal wall with the internal oblique muscle, the transverse abdominal muscle and the transversalis fascia, using multiple interrupted sutures.[34] Furthermore, he suggested entering of the preperitoneal space after division of the transversalis fascia and high ligation of the hernia sac. His reports led many predominant surgeons of his time to adopt his repair, many of those, however, failed to achieve low recurrence rates. It has been suggested, that inconsistencies between the text and the figures, as well as a poor translation of the original work of Bassini by his student, Attilio Catterina, resulted in a limited reproducibility of his work.[31] We would speculate, however, that Bassini himself modified his approach during his surgical curriculum, which may have resulted in this misinterpretation of his work.

Whereas several modifications of the Bassini's procedure were reported, Edward Earle Shouldice (1890-1965) was the first to highlight the importance of the transversalis fascia in the pathogenesis and in the surgical treatment of inguinal hernia.[35] In his original publication, Shouldice performed reinforcement of the posterior wall using the cremaster muscle and the internal spermatic fascia, whereas a duplication of the external oblique aponeurosis is advocated. One report on the Shouldice's technique describes the currently performed practice of transection and sutured duplication of the transversalis fascia, with subsequent anchoring of the internal oblique muscle to the inferior surface of the external oblique aponeurosis.[36]

Although the Bassini technique resulted in a significant reduction of recurrence rates, it soon became clear that postoperative pain and recurrence may occur due to tension on the pubic end of the repair. The significance of tension-free hernioplasty was recognized by Berger and Wölfler, who introduced a relaxing incision to the anterior rectus sheath.[37,38] Other investigators used autogenous and heterogenous grafts, such as the external oblique aponeurosis, the fascia lata, deer and kangaroo tendons.[39-42] These grafts were, however, expendable due to the phagocytic reaction which they induced.

The evolution of alloplastic materials have radically changed the approach to the posterior repair, facilitating reinforcement of the inguinal floor with a durable material, without the need to reconstruct the transversalis fascia. Polypropylene, polyester, polytetrafluoroethylene (PTFE) and expanded PTFE (ePTFE) are available from the 1940s'. Lichtenstein introduced the tension-free repair with an oval-shaped polypropylene mesh, which was placed on the floor of the groin and sutured to the pubic tubercle medially, to the inguinal ligament laterally and the conjoint tendon medio-cephalad, with a slit at the lateral end to encircle the emerging spermatic cord.[43] The excellent results of Lichtenstein's technique soon led to the wide popularization of tensionless hernia repair. During the same period, Stoppa proposed complete dissection of the preperitoneal spaces of Retzius and Bogros, and placement of a giant mesh to cover the myopectinal orifices.[44] The latest advantage of open inguinal hernia repair was introduced by Arthur Gilbert and later by Rutkow and Robbins, with the use of an umbrella-shaped polypropylene plug into the deep inguinal ring, in order to prevent recurrence of indirect hernias.[45,46]

The first laparoscopic attempts to repair inguinal hernia diverged from the basic surgical principles of open hernia surgery. Ralph Ger examined the effectiveness of closure of the neck of the hernia with metal clips during laparotomy for other pathologies and, after a laparoscopic clipping device had been developed, he performed an experimental study on 15 canine models.[47,48] Upon completion of the study he initiated his clinical trial.[49] Some years later, the endoscopic transabdominal and preperitoneal approaches of groin hernia with the use of a mesh were introduced by Arregui and Dulucq.[50,51]

The transabdominal preperitoneal repair (TAPP) requires entrance into the abdominal cavity with standard pneumoperitoneum of 12-14mmHg through a subumbilical incision, either with the open or the Hasson's technique. A 10-12mm port and a 10mm 30-degree optic is introduced through the subumbilical incision. The patient is brought to the Trendelenburg position, in order to visualize the lower abdominal cavity and the deep inguinal ring on both sides. This allows a first evaluation of the presence of hernia and the expected complexity of the procedure. A 10mm working trocar is then introduced in the right lower abdomen, on the convergence of the intertubercular line and the midclavicular line. Care is taken to

avoid the inferior epigastric vessels, running in this region; diaphanoscopy is therefore essential. A 5- or 10mm working port is introduced symmetrically on the left side. The peritoneum is grasped below the anterior superior iliac spine and a ca. 7cm horizontal incision is performed. The upper part of the incised peritoneum is freed from the preperitoneal fatty tissue to an extent of about 2cm. Similarly, the lower part of the peritoneum is freed blunt or sharp from the preperitoneal fat, the testicular vessels and the spermatic cord. The hernia sac is grasped and pulled cranially in order to reduce the hernia contents, which are dissected from further structures of the inguinal canal. In case of a direct hernia, the herniated peritoneum is dissected from the underlying preperitoneal fat. The dissection continues toward the pubic tubercle. Adequate space is essential in order to place the mesh. The latter is introduced through the right 10mm working port and placed against the abdominal wall, over the deep inguinal ring, the spermatic cord and the testicular vessels, up to the pubic tubercle. Fixation may be performed using tacks or staples, introduced through the right 10mm working port. Fixation is carried on to the abdominal wall (i.e. the upper part of the mesh). The peritoneum is then sutured using continuous or interrupted absorbable, non-absorbable sutures, or clips. Contralateral defects may be repaired using the same technique. The pneumoperitoneum is released and the incisions are sutured.

For the totally extraperitoneal repair (TEP) a subumbilical incision is fashioned and the anterior rectus sheath is incised. The rectus abdominis muscles are retracted laterally and a 10mm optic trocar is introduced without entering the abdominal cavity. Field is created toward the pubic symphysis using either the tip of the optic, a thin swab, or a balloon, and pneumoperitoneum is applied to the preperitoneal space. After adequate preperitoneal field is created, two 5mm working ports are introduced under visualization directly above the pubic symphysis and in the midline between the latter and the subumbilical port. The symphysis is prepared and dissection proceeds laterally to the anterior superior iliac spine. The epigastric vessels are identified and preserved. The peritoneum is pulled as low as possible using sweeping motions. The hernia sac is reduced bluntly and dissected free from other structures. A mesh is introduced through the optic trocar and placed against the abdominal wall. The pneumoperitoneum is released and the incisions are sutured.

SECOND PART

2.1 Clinical question

Both the transabdominal preperitoneal and the totally extraperitoneal repair have gained wide popularity throughout the surgical community. Despite this rapid widespread of minimally invasive techniques, recent guidelines issued by the International Endohernia Society noticed the lack of high-quality comparative evidence between endoscopic and laparoscopic inguinal hernia repair.[52] A meta-analytical comparison of the two techniques, which was undertaken by the Cochrane Collaboration in 2005, has demonstrated higher incidence of visceral injuries and increased risk for port-site hernia after TAPP repair.[53] The power of this analysis was however limited by the low quality of the included studies, and the authors emphasized the need for randomized trials in order to compare the outcome between endoscopic and laparoscopic hernia repair.

In view of the wide dissemination of minimally invasive techniques for inguinal hernia repair and the high prevalence of this surgical disease, evaluation of currently available high quality comparative evidence of contemporary modalities is essential. A systematic review and meta-analysis of randomized trials, quasi-randomized studies and prospective non-randomized studies comparing the transabdominal with the preperitoneal approach of inguinal hernia repair was undertaken, with the objective to evaluate the outcomes of the two techniques, as expressed by the incidence of recurrence, operative morbidity, chronic pain, and the time to resume to normal activities.

2.2 Material and methods

Eligibility criteria and study selection

An *ad hoc* protocol was established in order to predetermine the inclusion criteria and analytical methods **(Figure 1)**. Randomized controlled trials (RCTs), quasi-randomized studies (i.e. without strict random assignment to either study arm), and prospective non-randomized studies comparing the TAPP with the TEP repair were considered for inclusion. No restrictions were applied with regard to the number of defects (unilateral/bilateral disease), site of defect (inguinal/scrotal/femoral/ obturator hernia), type of hernia (direct/indirect/combined hernia), prior hernia repair (primary/recurrent hernia), hernia status (reducible/strangulated/incarcerated hernia), type of intervention (elective/emergency surgery), size of the study population, demographical data (gender, age, health status), follow-up time, or examined measures of outcome. Relative risk of recurrence was the primary outcome measure of treatment effect in the present meta-analysis, whereas secondary outcome measures included intra-operative complications, in-hospital morbidity, long-term pain or sensory deficits, operative time, early postoperative pain (within 24-48 hours following surgery), length of hospitalization and recovery time.

Search strategy

The electronic databases of the National Library of Medicine (Medline; provider Ovid, from 1966 to April 2012), Excerpta Medica (EMBASE; provider Elsevier, from 1980 to April 2012) and the Cochrane Central Register of Controlled Trials were searched, in order to identify relevant articles. No language restrictions were applied, and abstracts of articles in other than the English language were translated. The Medical Subject Headings (MeSH terms) “laparoscopy”, “endoscopy” and “inguinal hernia”, and the terms “TAPP”, “preperitoneal”, “properitoneal”, “TEP”, “totally extraperitoneal”, “total extraperitoneal” were used in combination with the Boolean operators AND or OR **(Figure 2)**. A second-level manual search included the

Methods

Study design:

Meta-analysis of RCTs, quasi-randomized trials and prospective non-randomized studies.

Study characteristics:

a. Literature search strategy:

•Search of the electronic databases:

•The National Library of Medicine (Medline; provider Ovid, from 1966 to July 2011)

•Excerpta Medica (EMBASE; provider Elsevier, from 1980 to July 2011)

•The Cochrane Central Register of Controlled Trials

•Language restrictions: none

•Search terms: Medical Subject Headings (MeSH terms) "endoscopy", "laparoscopy" and "inguinal hernia", and the terms "TAPP", "preperitoneal", "properitoneal", "TEP", "totally extraperitoneal", "total extraperitoneal" in combination with the Boolean operators AND or OR.

•Eligibility assessment: Independently in an unblinded standardized manner by two reviewers. Disagreements between reviewers will be resolved by consensus.

b. Inclusion criteria

1. RCTs
2. Quasi-randomized trials and
3. Prospective non-randomized studies

comparing TAPP with TEP

c. Exclusion criteria

1. Retrospective studies
2. Study population less than 10 patients

d. Data required

1. Year of publication
2. Study design (single blinded/double-blinded/non-blinded RCT, quasi-randomized trial, prospective non-randomized study)
3. Number of participating institutions (single-center/multi-centric RCT)
4. Number of participating patients
5. Number of patients having completed the follow-up period
6. Duration of follow-up time
7. Type of follow-up evaluation of treatment effect (physical examination, telephone interview)
8. Demographical data of participants (age, gender, concomitant diseases)
9. Inclusion and exclusion criteria
10. Pain scoring system
11. Site of hernia (unilateral/bilateral hernia)
12. Site of defect (inguinal/scrotal/femoral hernia)
13. Type of hernia (direct/indirect/combined hernia)
14. Presence of prior hernia repair (primary/recurrent hernia)
15. Hernia status (reducible/strangulated/incarcerated hernia)
16. Prosthetic material used
17. Method of mesh fixation
18. Operative time
19. Amount of blood loss
20. Intraoperative complications
21. Postoperative complications
22. Pain score within 24-48 hours post surgery
23. Length of hospitalization
24. Time to resume to normal activities
25. Number of patients suffering from long-term pain or sensory deficits

•Data collection

Data collection from the manuscript, tables and figures of published articles. In case of missing data, electronic communication with the study authors for retrieval.

•Data processing

Ad hoc designed electronic database (Microsoft Office Excel 2007 Ink., Microsoft Corporation). Statistical analysis using Comprehensive Meta Analysis Version 2.0 (Biostat, Englewood, NJ).

Figure 1. Study protocol

No.	Search term
1	laparoscopic (abstract or text)
2	hernia, inguinal (abstract or text)
3	TAPP (abstract or text)
4	preperitoneal (abstract or text)
5	properitoneal (abstract or text)
6	TEP (abstract or text)
7	totally AND extraperitoneal (abstract or text)
8	total AND extraperitoneal (abstract or text)
9	3 OR 4 OR 5
10	6 OR 7 OR 8
11	1 AND 2 AND 9 AND 10

Figure 2. Search strategy.

bibliography of the included articles. The last search was run on August 3, 2012. Eligibility assessment was performed independently in an unblinded standardized manner by two reviewers. Disagreements between reviewers were resolved by consensus.

Data collection and indexing

An electronic data extraction sheet was developed and refined accordingly. One review author extracted the data from included studies and a second author checked the extracted data. The latter included: year of publication, country of origin, study period, study design (single blinded/double-blinded/non-blinded RCT, non-randomized prospective study), number of participating institutions (single-center/multi-centric RCT), number of participating patients, number of patients having completed the follow-up period, duration of follow-up time, type of follow-up

evaluation (physical examination, telephone interview), demographical data of participants (age, gender, concomitant diseases), inclusion and exclusion criteria, pain scoring system, disease characteristics of the examined patient populations, including site of hernia (unilateral/bilateral hernia), site of defect (inguinal/scrotal/femoral hernia), type of hernia (direct/indirect/combined hernia), prior hernia repair (primary/recurrent hernia), hernia status (reducible/strangulated/incarcerated hernia), prosthetic material used, method of mesh fixation, and study outcome measures, including operative time, amount of blood loss, intraoperative complications, postoperative complications, pain score within 24-48 hours post surgery, length of hospitalization, time to resume to normal activities, number of patients suffering from long-term pain or sensory deficits. Outcome data were collected upon completion of the follow-up period in all studies. The authors of studies fulfilling the inclusion criteria were formally contacted by electronic mail; they were informed about the purpose of the study and were asked to provide missing data and/or follow-up results of their study.

Quality assessment

The Jadad score was calculated for each study, in order to assess methodological quality of eligible randomized trials. This 5-point scoring system takes into account the randomization process, the blind assessment of investigated treatments, and reporting of dropouts.[54] If a study reached a Jadad score of 1-2 it was considered of poor quality, with a score of 2-3 the quality was considered fair, whereas a score of 4-5 indicated good methodological quality. Assessment of methodological quality of non-randomized trials was undertaken using the Effective Public Health Practice Project Quality Assessment Tool for Quantitative Studies.[55] This scale has been developed to assess the quality of studies using a global rating scale consisting of individual scoring of selection bias, study design, confounders, blinding, data collection methods, withdrawals and dropouts, intervention integrity and analyses.

Methods of analysis

The OR and 95% CI for combined studies were calculated using the fixed effects model of meta-analysis, unless evidence of between study heterogeneity existed, in which case the random effects model proposed by DerSimonian and Laird was used.[56] Weighted mean differences (WMD) with 95% confidence intervals (CI) were calculated to assess the size of the effect of each type of procedure on continuous variables. Pooled odds ratios (OR) with 95% CI were calculated to measure the effect of each type of procedure on categorical variables. Heterogeneity among the trials was assessed using the I^2-statistic; an I^2 value of 50% or more indicated the presence of heterogeneity. Risk of bias was evaluated by constructing funnel plots, in which the effect for each trial was plotted by the inverse of its standard error. Funnel plot asymmetry implied that results were subject to reporting or publication bias. Sensitivity analyses were undertaken to investigate potential effect of individual variables on outcome. Review Manager software (RevMan© v. 5.0.16) provided by The Cochrane Collaboration was used for data management and statistical analyses. The present meta-analysis conformed to the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) statement standards, a methodological protocol with items considered essential for transparent reporting.[57]

2.3 Results

Search results and selection of studies

The literature search of the databases returned a total of 355 records. After electronic exclusion of duplicate records, a total of 240 unique results were available for evaluation. The first-level search of the title and abstracts identified 40 relevant, potentially eligible articles.[58-97] Some 200 articles were excluded for the following reasons: reviews, 47 articles; retrospective studies, 21 articles; case series, 54 articles; case reports, 14 articles; editorials, letters, or comments, 11 articles; experimental studies, 2 articles; not relevant were 51 articles. The full texts of the 40 articles were screened. Twenty three articles were excluded due to the following reasons: retrospective studies, 6 articles; failure to report whether the studies were prospective or retrospective, 9 articles; failure to address outcome measures of the present analysis, 8 articles; not relevant articles, 4. An additional eligible study was identified through the manual search of the bibliography of the included articles.[98] Finally, a total number of 18 articles were included for further analysis **(Figure 3)**.[85-98]

Characteristics of included studies

The selected studies were published in the English language. The year of publication ranged between 1995 and 2012 **(Table 1)**. Four studies were published from 1995 to 1998[95-98] and the remaining studies from 2006 to 2012.[85-94] There was a paucity of data between 1999 and 2005. Ten studies were randomized trials[85-93,98] and 8 were prospective case-control studies.[94-97] One RCT was double-blinded[91] and another single-blinded,[88] whereas the remaining RCTs did not indicate whether a blinding approach was applied. Inclusion and criteria varied among studies, however, emergency surgery for strangulated or incarcerated hernia was almost commonly considered as exclusion criterion. The median Jadad score of the randomized trials was 2 **(Table 2)**. Of the prospective case-control studies, 2 were of weak and another 2 of moderate quality.

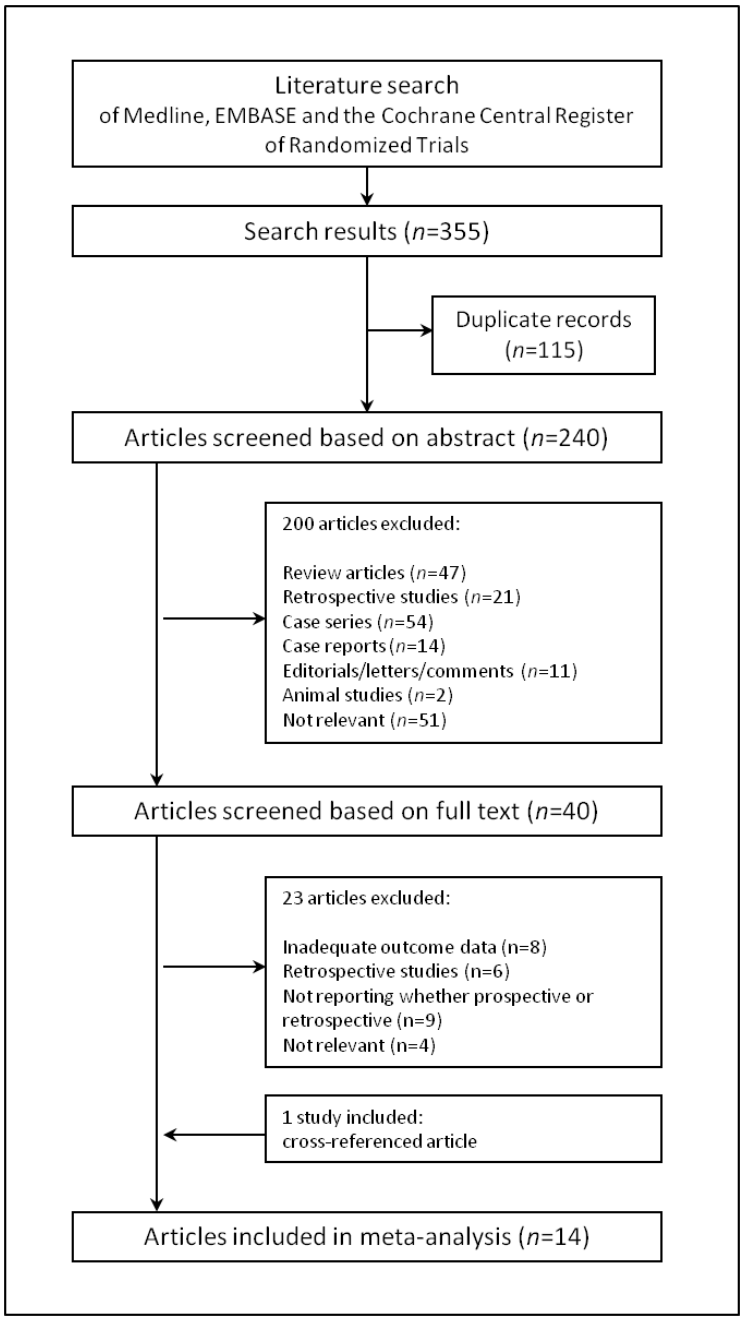


Figure 3. Flow chart of search history

Outcome variables also varied among studies, including, most commonly, morbidity, recurrence rate and postoperative pain **(Table 3)**. Polypropylene meshes were used by most author teams.[85-88,90-92,95-98], and mesh fixation was facilitated either by tacker or stapler,[87,88,92,96,97] whereas some authors did not fixate the mesh both in TAPP and TEP,[85] or exclusively in TEP repairs.[95] Duration of follow up time ranged between 3

Author	Year of publication	Type of study	Inclusion criteria	Exclusion criteria	Jadad score / EPHPP score
Krishna[85]	2012	RCT	primary inguinal hernia	previous surgery of the lower abdomen, irreducible, strangulated or recurrent hernia, coagulopathy, poor surgical candidates, diabetes, hypertension	3
Mesci[86]	2012	RCT	NR	NR	1
Gong[87]	2011	RCT	men 30-70 years old, ASA 1 or 2, primary unilateral inguinal hernia	Need for emergency surgery, previous surgery of the lower abdomen, irreducible, giant, bilateral or recurrent hernia	1
Hamza[88]	2010	RCT	male gender, primary inguinal hernia Nyhus I-III	recurrent, irreducable or obstructed hernia, previous operation of the lower abdomen, coagulopathy, COPD, constipation, obstructive uropathy	2
Zhu[89]	2009	RCT	NR	recurrent or bilateral hernia, history of lower abdominal surgery, severe cardiovascular or pulmonary disease, contraindication for laparoscopic surgery	1
Pokorny[90]	2008	RCT	age 19-85, unilateral primary inguinal hernia	unfit for general anesthesia, incarcerated, recurrent, bilateral, femoral hernia	2
Butler[91]	2007	RCT	primary unilateral inguinal hernia	NR	4
Günal[92]	2007	RCT	ASA I and II, Nyhus 1, 2, 3A and 3B, primary unilateral inguinal hernia	NR	1
Dedemadi[93]	2006	RCT	recurrent inguinal hernia	ASA II or IV, coagulation disorders, previous abdominal or pelvic surgery, irreducible hernia, ascites, previous laparoscopic repair	3
Schrenk[98]	1996	RCT	elective surgery, unilateral inguinal hernia	recurrent or incarcerated inguinal hernia	2
Lepere[94]	2008	prospective case-control	hernia size >4cm	BMI >40kg/m^2, psychiatric disease, bilateral hernia, previous endoscopic inguinal hernia repair	moderate
Van Hee[95]	1998	prospective case-control	NR	NR	weak
Kald[96]	1997	prospective case-control	NR	previous surgery or radiotherapy of the lower abdomen	moderate
Fitzgibbons[97]	1995	prospective case-control	NR	age >12 years, pregnancy, severe obesity, poor surgical candidates, intraabdominal infection, bowel obstruction, local infection, depressive neurosis or psychotic reaction	weak

RCT indicates randomized control trial
NR indicates not reported
ASA indicates American Society of Anesthesiologists score
COPD indicates chronic obstructive pulmonary disease
BMI indicates body mass index
EPHPP indicates Effective Public Health Practice Project

Table 1. Study characteristics

Author	Study described as randomized?	Randomization method described?	Randomization method appropriate?	Study described as double blind?	Method of double blinding described?	Method of double blinding appropriate?	Description of withdrawal/dropouts?	Jadad score
Krishna[85]	Y	Y	Y	N	NA	NA	Y	3
Mesci[86]	Y	N	NA	N	NA	NA	N	1
Gong[87]	Y	N	NA	N	NA	NA	N	1
Hamza[88]	Y	Y	Y	N	NA	NA	N	2
Zhu[89]	Y	N	NA	N	NA	NA	N	1
Pokorny[90]	Y	N	NA	N	N	N	Y	2
Butler[91]	Y	N	NA	Y	Y	Y	Y	4
Günal[92]	Y	N	NA	N	NA	NA	N	1
Dedemadi[93]	Y	Y	Y	N	NA	NA	Y	3
Schrenk[98]	Y	Y	Y	N	NA	NA	N	2

NA, not applicable

Table 2. Quality assessment of randomized controlled trials according to the Jadad scoring system

Author	Outcome measures	Mesh material	Method of fixation	Follow up time*	Pain scoring	Type of follow-up	Diagnosis of recurrence
Krishna[85]	Complications, postoperative pain	PP	no fixation	29.5 months	VAS score	NR	NR
Mesci[86]	Postoperative pain, muscle function	PP	NR	NR	VAS score	NR	NR
Gong[87]	Age, type of hernia, morbidity, recurrence, operating time, bleeding, postoperative pain at 24h and 1 week, hospital stay, time to resume to normal activities, costs	PP	Tacker	15.6±9.9 (TAPP) 15.6±7.7 (TEP)	5-point system	Physical examination at 1 week and 1 month, then phone interview	NR
Hamza[88]	Operative time, postoperative pain, hospital stay, time to resume to normal activities	PP	Stapler	24 weeks	VAS score	2, 12 and 24 weeks	Physical examination
Zhu[89]	Hemodynamic and respiratory function	NR	NR	NR	VAS score	NR	NR
Pokorny[90]	Recurrence at 3-year follow up, intraoperative complications, morbidity	PP	NR	3 years	NR	Physical examination at 2-4 weeks, 3 months and yearly thereafter	Physical examination, ultrasound
Butler[91]	Postoperative pain, duration of convalescence, operative costs	PP	NR	NR	VAS score	7-day intervals until patients returned to work	NR
Günal[92]	Expression of TNF-α, IL-6, postoperative pain, morbidity, recurrence	PP	Stapler	87.4 months	VAS score	Phone interview	NR
Dedemadi[93]	Postoperative pain, time to resume to normal activities, operative time, morbidity, duration of analgesic consumption, recurrence	NR	NR	3 years	VAS score, amount of consumed analgesics	Physical examination at 7 days, 1, 3, 6, 12, 24 and 36 months	Physical examination
Schrenk[98]	Postoperative pain, analgesic consumption, cosmetic result, duration of convalescence	PP	NR	3 months	VAS score, amount of consumed analgesics	Physical examination at 3 months	Physical examination
Lepere[94]	Recurrence, postoperative pain	CCP	Absorbable clips	1 year	NR	NR	NR

Table 3. Outcome measures, operative and follow-up characteristics

Van Hee[95]	NR	PP	Stapler (TAPP) no fixation (TEP)	17.0 months	NR	NR	NR
Kald[96]	Learning curve, morbidity, recovery time	PP	Various	23 months (TAPP) 7 months (TEP)	NR	Physical examination, questionaire	Physical examination
Fitzgibbons[97]	NR	PP	Stapler	23 months	NR	NR	NR

*mean values
NR indicates not reported
PP indicates polypropylene
CCP indicates collagen-coated polyester
TAPP indicates transabdominal preperitoneal repair
TEP indicates totally extraperitoneal repair

Table 3 (continued). Outcome measures, operative and follow-up characteristics

months and 7 years, with a median follow up time of 20 months. The visual analogue score (VAS) was used by authors which measured postoperative pain, except from one study which used a modified 5-point system.[87] Data on pain scoring from this study were converted to the VAS, in order to homogenize and include them in the meta-analytical model. Physical examination was most commonly performed at follow-up, and diagnosis of recurrence was performed by these means.

The cumulative study population consisted of 1288 patients with a total of 1303 hernia defects **(Table 4)**. The male-to-female ratio was 20:1 and the mean age was 53 years.

Author	No. of patients		No. of hernia defects		Male / female	Age*	Hernia characteristics
	TAPP	TEP	TAPP	TEP			
Krishna[85]	47	53	47	53	99 / 1	49	direct, *n*=44; indirect, *n*=78
Mesci[86]	25	25	25	25	NR	48.3	direct, *n*=15; indirect, *n*=24; recurrent, *n*=10
Gong[87]	50	52	50	52	102 / 0	56.5	indirect/scrotal, *n*=72; direct, *n*=20; combined, *n*=10
Hamza[88]	25	25	25	25	50 / 0	35.8	NR
Zhu[89]	20	20	20	20	39 / 1	61.3	NR
Pokorny[90]	93	36	93	36	121 / 8	48.7	NR
Butler[91]	22	22	22	22	44 / 0	NR	NR
Günal[92]	39	40	39	40	NR	24.0	NR
Dedemadi[93]	24	25	24	25	NR	NR	Nyhus II, *n*=30; Nyhus IIIa, *n*=15; Nyhus IIIc, *n*=5
Schrenk[98]	28	24	28	24	46 / 6	40.6	direct, *n*=15; indirect, *n*=37
Lepere[94]	48	28	48	28	NR	NR	NR
Van Hee[95]	33	58	37	69	89 / 2	58.6	direct, *n*=26; indirect, *n*=61; combined, *n*=9; recurrent, *n*=9
Kald[96]	339	87	339	87	394 / 32	56	direct, *n*=207; indirect, *n*=256; combined, *n*=17
Fitzgibbons[97]	NR	NR	562	87	NR	NR	NR

*mean values
TAPP indicates transabdominal preperitoneal repair
TEP indicates totally extraperitoneal repair
NR indicates not reported
n indicates absolute number of patients

Table 4. Demographic and hernia characteristics

Synthesis of results and outcome

A summary of outcome data of the included studies is presented in **Tables 5 and 6**, whereas **Table 7** presents a summary of outcome measures.

Author	Duration of surgery, *min*		Bleeding, *ml*		Intraoperative complications, *n*	
	TAPP	**TEP**	**TAPP**	**TEP**	**TAPP**	**TEP**
Krishna[85]	72.3±25.9	62.1±20.6	NR	NR	0 (0%)	0 (0%)
Mesci[86]	62.4	76.0 TEP	NR	NR	NR	NR
Gong[87]	76±16	79±13	19±7	19±9	0 (0%)	0 (0%)
Hamza[88]	36.1±22.5	77.4±43.2	NR	NR	0 (0%)	0 (0%)
Zhu[89]	34.5±9.3	32.6±9.9	NR	NR	NR	NR
Pokorny[90]	66*	78*	NR	NR	7 (8%)	0 (0%)
Butler[91]	59	NR	NR	NR	NR	NR
Günal[92]	87.59±2.77	87.20±1.1	NR	NR	3 (8%)	2 (5%)
Dedemadi[93]	55±12	56±9	NR	NR	2 (8%)	0 (0%)
Schrenk[98]	46.0±9.2	42.3±13.9	NR	NR	0 (0%)	0 (0%)
Lepere[94]	NR	NR	NR	NR	0 (0%)	0 (0%)
Van Hee[95]	85±14	73±18	NR	NR	2 (6%)	5 (9%)
Kald[96]	80±32	80±41	NR	NR	NR	NR
Fitzgibbons[97]	NR	NR	NR	NR	NR	NR

Data are reported as mean values ± standard deviation, unless otherwise indicated
*median values
TAPP indicates transabdominal preperitoneal repair
TEP indicates totally extraperitoneal repair
NR indicates not reported
min indicates minutes
ml indicates milliliters
n indicates absolute number of events

Table 5. Operative data

Author	In-hospital morbidity, *n*		Duration of hospital stay, *d*		Recovery time, *d*		Postoperative pain†		Recovery time, *d*		Long-term pain or sensory deficits, *n*		Recurrence, *n*	
	TAPP	**TEP**	**TAPP**	**TEP**	**TAPP**	**TEP**	**TAPP**	**TEP**	**TAPP**	**TEP**	**TAPP**	**TEP**	**TAPP**	**TEP**
Krishna[85]	0 (0%)	0 (0%)	1.1±0.21	1.0±0.13	NR	NR	1.83±0.43	1.09±0.30	NR	NR	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Mesci[86]	3 (12%)	1 (4%)	1.0	1.0	5.2	6.4	1.8	1.8	5.2	6.4	NR	NR	NR	NR
Gong[87]	6 (12%)	7 (14%)	3.4±1.7	3.6±1.6	6.6±1.7	6.6±1.5	3.2±1.4	3.4±1.4	6.6±1.7	6.6±1.5	NR	NR	0 (0%)	0 (0%)
Hamza[88]	2 (8%)	0 (0%)	NR	NR	9.8±6.1	7.5±3.7	4.1±1.1	4.0±4.4	9.8±6.1	7.5±3.7	1 (4%)	0 (0%)	1 (4%)	1 (4%)
Zhu[89]	NR	NR	3.5±0.8	3.2±0.5	NR	NR	3.0±1.5	2.7±1.4	NR	NR	NR	NR	NR	NR
Pokorny[90]	27 (32%)	6 (17%)	5*	4*	NR	NR	NR	NR	NR	NR	5 (6%)	7 (21%)	4 (5%)	2 (6%)
Butler[91]	NR	NR	NR	NR	12	12	NR	NR	12	12	NR	NR	1 (5%)	1 (5%)
Günal[92]	2 (5%)	3 (8%)	NR	NR	NR	NR	3.25±1	3.3±1.2	NR	NR	NR	NR	1 (3%)	0 (0%)
Dedemadi[93]	5 (21%)	4 (16%)	0.78±0.38	0.77±0.26	14±9	13±8	1*	1*	14±9	13±8	3 (13%)	6 (23%)	2 (8%)	2 (8%)
Schrenk[98]	1 (4%)	1 (4%)	3.7±1.4	4.4±0.9	5.9±0.7	6.5±0.7	NR	NR	5.9±0.7	6.5±0.7	3 (11%)	1 (4%)	1 (4%)	0 (0%)
Lepere[94]	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	0 (0%)	0 (0%)
Van Hee[95]	2 (6%)	3 (5%)	4.9	3.7	13.6±5.8	12.9±4.7	NR	NR	13.6±5.8	12.9±4.7	3 (8%)	7 (10%)	1 (3%)	2 (3%)
Kald[96]	31 (9%)	7 (8%)	1±2	0.5±1	12±12	8±10	NR	NR	12±12	8±10	NR	NR	7 (2%)	0 (0%)
Fitzgibbons[97]	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	28 (5%)	0 (0%)

*median values
†according to the visual analogue scale
NR indicates not reported
d indicates days
n indicates absolute number of patients
TAPP indicates transabdominal preperitoneal repair
TEP indicates totally extraperitoneal repair

Table 6. Postoperative data

Hernia recurrence The incidence of hernia recurrence was 3.5% for the laparoscopic repair, and 1.4% for the endoscopic repair (OR 2.00, 95% CI 0.92–4.35; p = 0.08). There was low evidence of between study heterogeneity (I^2 = %), and low evidence of publication bias **(Figures 4 and 5)**.

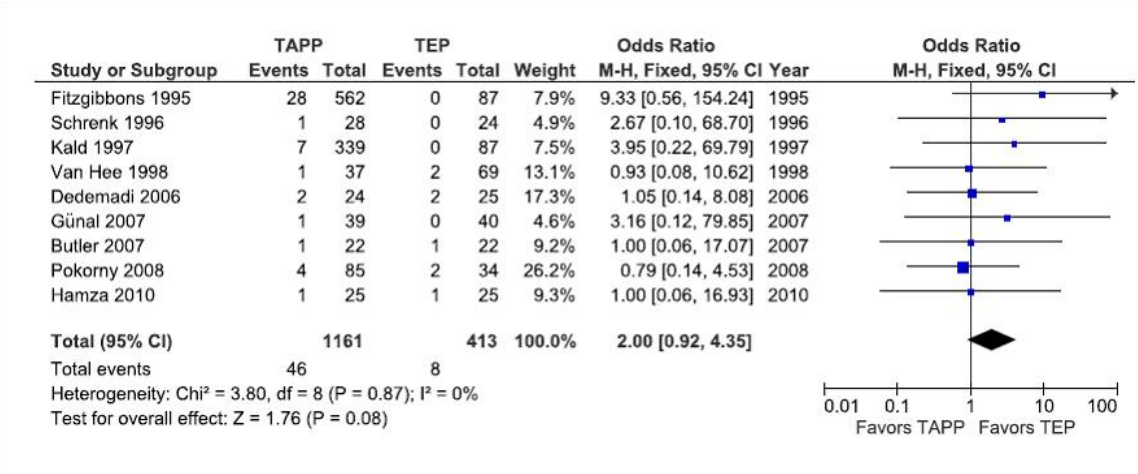


Figure 4. Forest plot shows a comparison of the odds ratios (OR) and 95% confidence intervals (95% CI) of the recurrence rate.

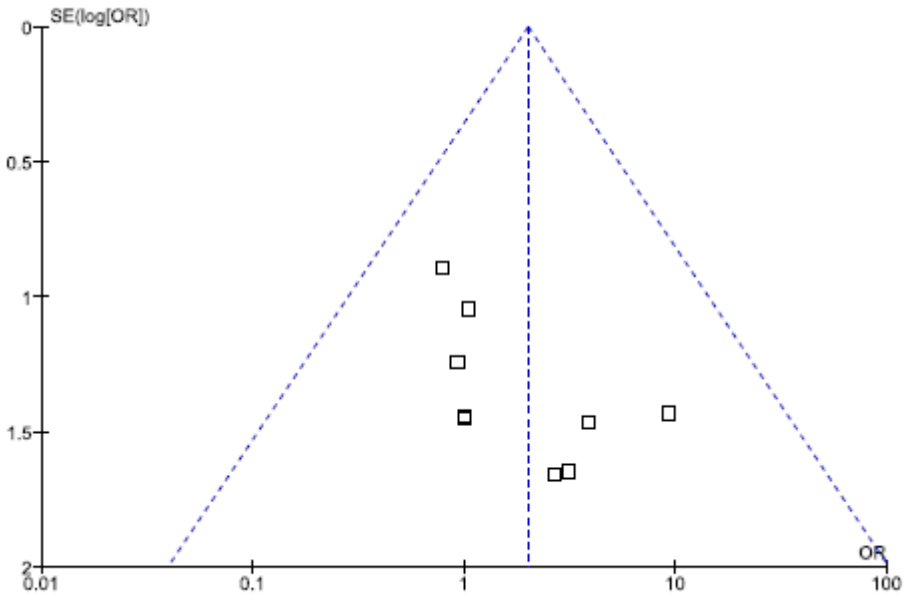


Figure 5. Funnel plot assessing the data on the incidence of recurrence presented in Figure 3.

Intraoperative complications

Intra-operative complications occurred in 3.6% of laparoscopic repairs and 2.0% of endoscopic repairs (OR 1.90, 95% CI 0.73–4.96; p = 0.19). No significant heterogeneity among studies existed (I^2 = 0%) and the likelihood of publication bias was low **(Figures 6 and 7)**.

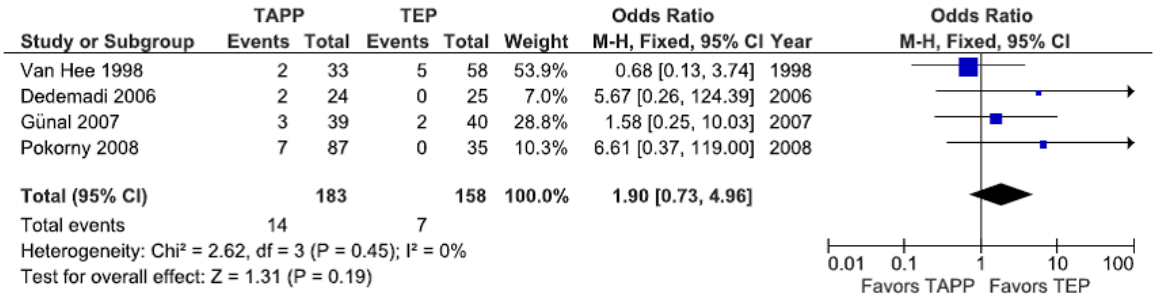


Figure 6. Forest plot shows a comparison of the odds ratios (OR) and 95% confidence intervals (95% CI) of the incidence of intra-operative complications.

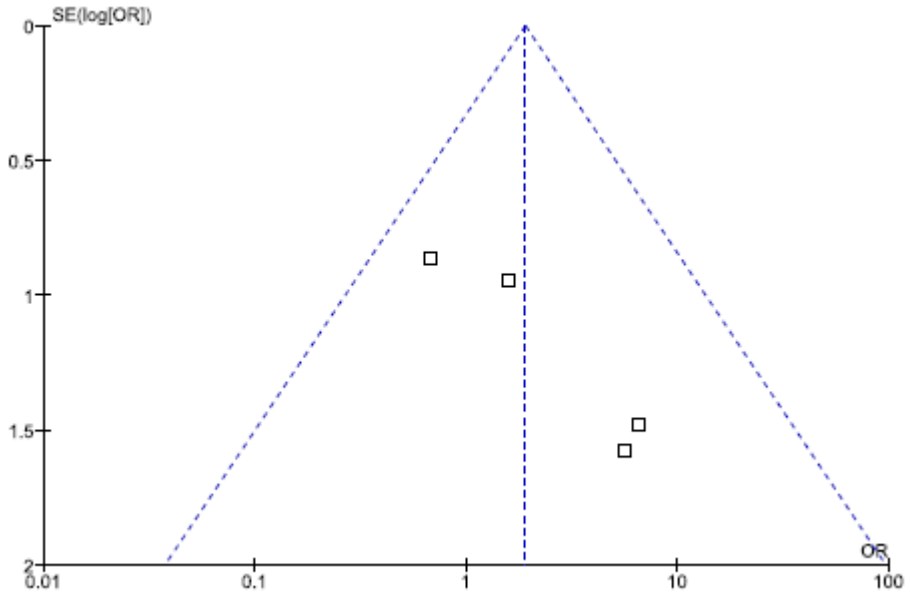


Figure 7. Funnel plot assessing the data on the incidence of intra-operative complications presented in Figure 5.

In-hospital morbidity The morbidity rate was 11.2% for the laparoscopic repair and 7.3% for the endoscopic repair (OR 1.39, 95% CI 0.88–2.20; p = 0.16). No significant heterogeneity among studies was identified (I^2 = 0%) and the likelihood of publication bias was low **(Figures 8 and 9)**.

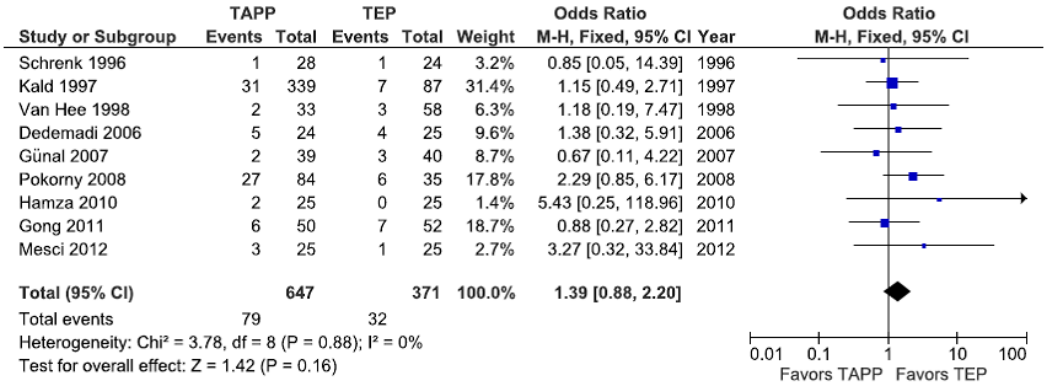


Figure 8. Forest plot shows a comparison of the odds ratios (OR) and 95% confidence intervals (95% CI) of in-hospital morbidity.

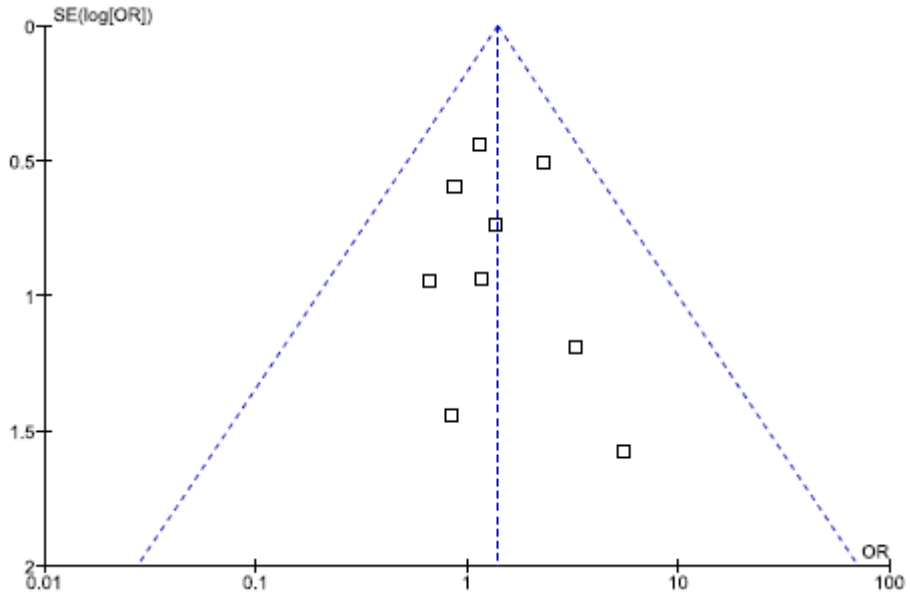


Figure 9. Funnel plot assessing the data on the incidence of in-hospital morbidity presented in Figure 7.

Long-term pain or sensory deficits The incidence of long-term pain or sensory deficits was 6.1% for the laparoscopic group and 9.1% for the endoscopic group (OR 0.54, 95% CI 0.26–1.13; p = 0.10). Low-level heterogeneity was detected among studies (I^2 = 20%), and publication bias was low **(Figures 10 and 11)**.

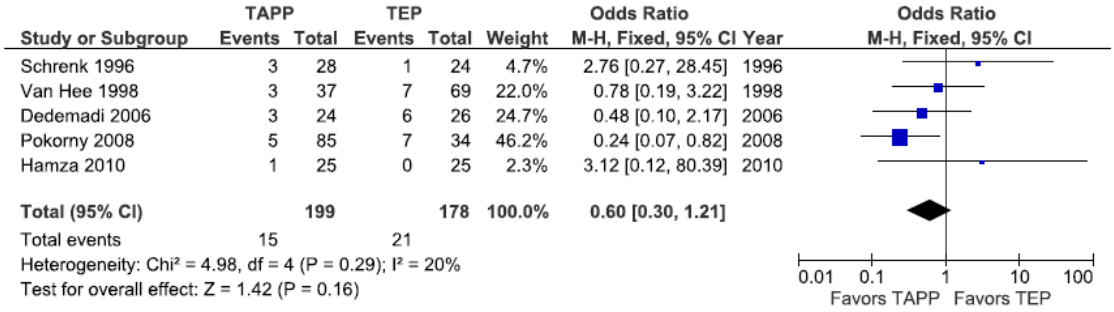


Figure 10. Forest plot shows a comparison of the odds ratios (OR) and 95% confidence intervals (95% CI) of long-term pain or sensory deficits.

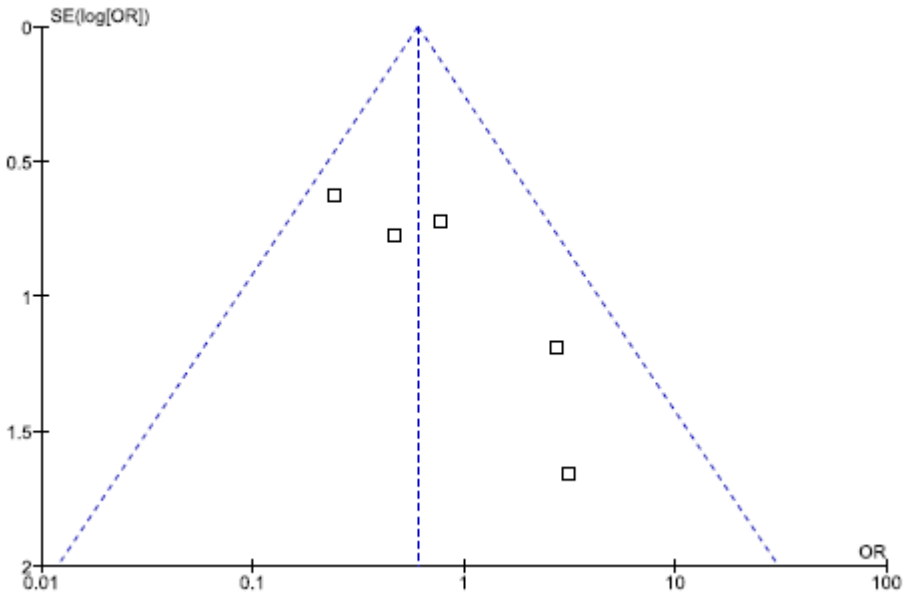


Figure 11. Funnel plot assessing the data on the incidence of long-term pain or sensory deficits presented in Figure 9.

Operative time The mean length of surgical time was 73.0 minutes for the laparoscopic group and 70.9 minutes for the endoscopic group (WMD 0.35, 95% CI -0.53–1.23; p = 0.43). Between-study heterogeneity was high (I^2 = 84%), whereas the likelihood of publication bias was high **(Figures 12 and 13)**.

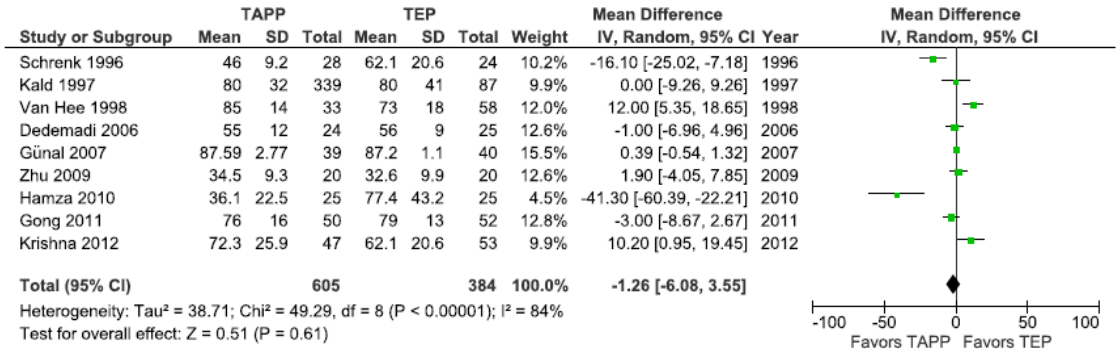


Figure 12. Forest plot shows a comparison of the odds ratios (OR) and 95% confidence intervals (95% CI) of operative time.

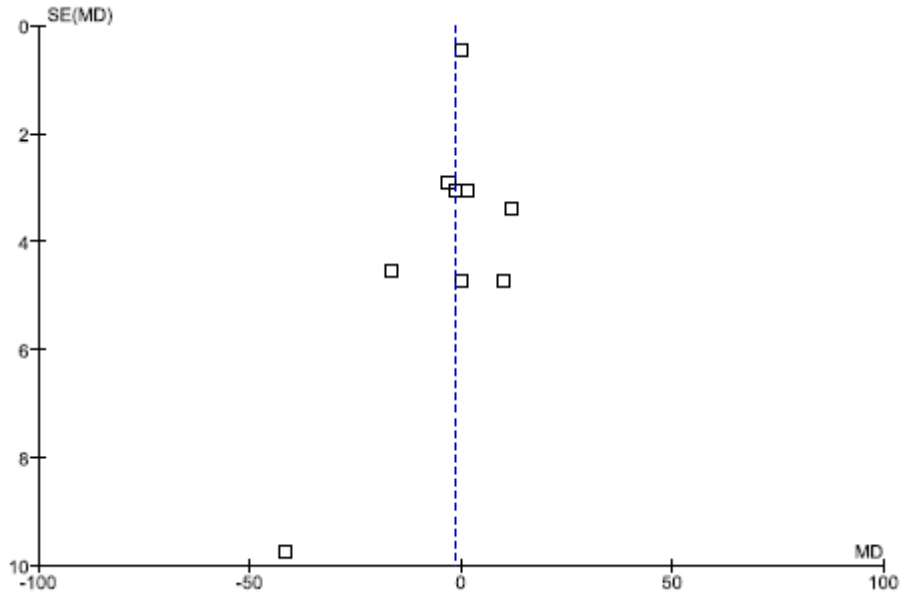


Figure 13. Funnel plot assessing the data on operative time presented in Figure 11.

Postoperative pain

The mean adjusted VAS was 2.4 for the TAPP repair and 2.2 for the TEP repair (WMD 0.74, 95% CI -0.31–0.76; p = 0.42). Heterogeneity among the studies was high (I^2 = 88%), whereas the likelihood of publication bias was high **(Figures 14 and 15)**.

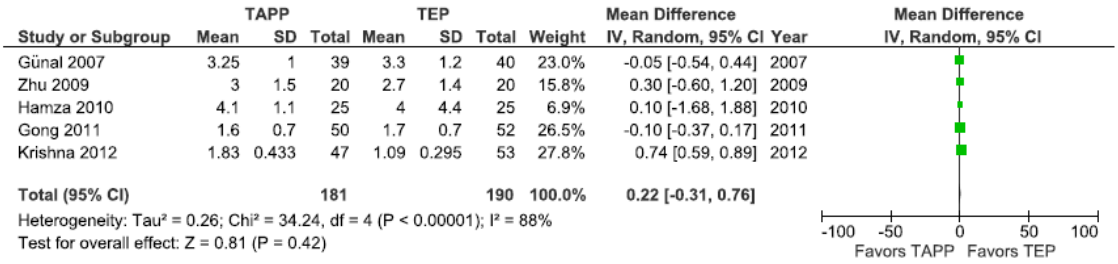


Figure 14. Forest plot shows a comparison of the odds ratios (OR) and 95% confidence intervals (95% CI) of postoperative pain.

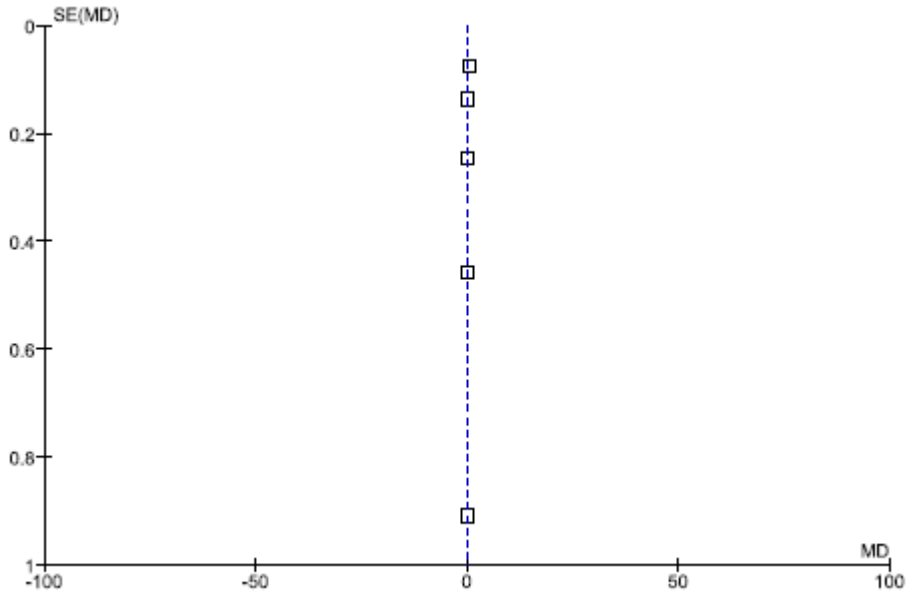


Figure 15. Funnel plot assessing the data on postoperative pain presented in Figure 13.

Hospital stay Nine studies reported on the length of hospital stay and 8 provided the respective *p*-values or confidence intervals. The mean length of hospitalization was 1.7 days for the laparoscopic group and 2.1 days for the endoscopic group (WMD 0.10, 95% CI -0.10–0.29; p = 0.33). Between-study heterogeneity was high (I^2 = 68%), whereas there was high likelihood of publication bias **(Figures 16 and 17)**.

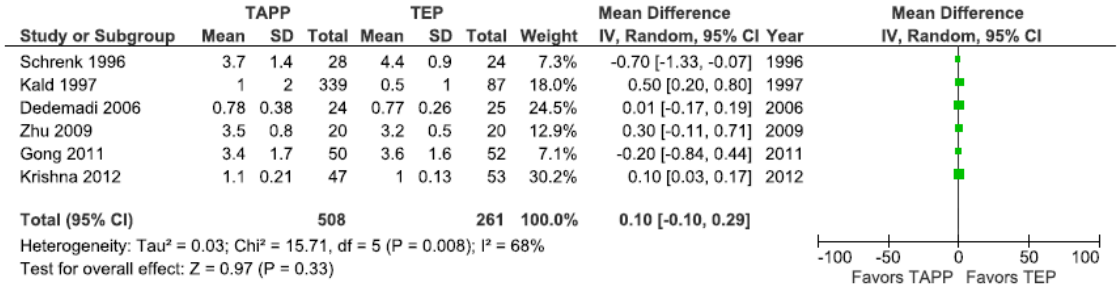


Figure 16. Forest plot shows a comparison of the odds ratios (OR) and 95% confidence intervals (95% CI) of hospital stay.

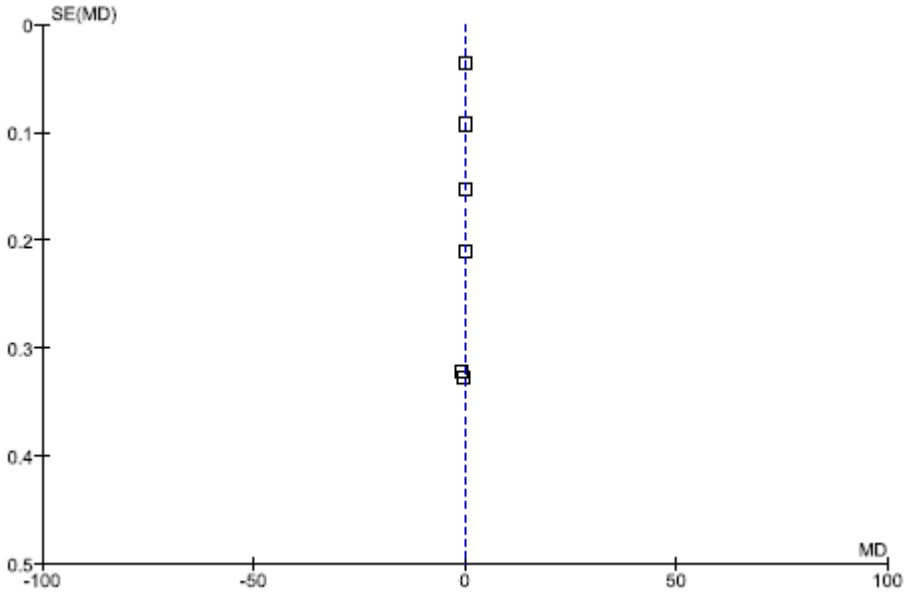


Figure 17. Funnel plot assessing the data on hospital stay presented in Figure 15.

Recovery time The mean time to resume to normal activities was 9.1 days for the laparoscopic group and 11.0 days for the endoscopic group (WMD 0.62, 95% CI -0.41–1.65; p = 0.24). Between-study heterogeneity was high (I^2 = 74%), and high evidence of publication bias **(Figures 18 and 19)**.

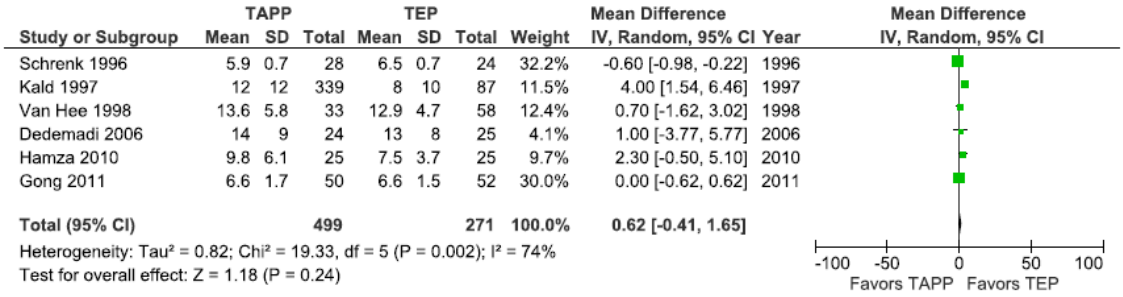


Figure 18. Forest plot shows a comparison of the odds ratios (OR) and 95% confidence intervals (95% CI) of recovery time.

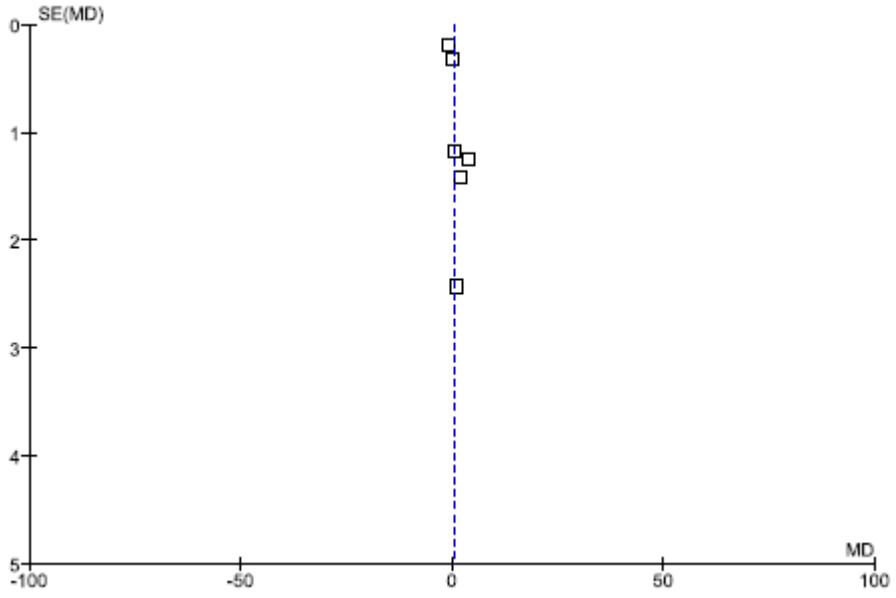


Figure 19. Funnel plot assessing the data on recovery time presented in Figure 17.

Outcome measure	Meta-analysis model	OR/WMD (95% CI)	*p*-value
Hernia recurrence	Fixed	2.00	0.08
Intraoperative complications	Fixed	1.90	0.19
In-hospital morbidity	Fixed	1.39	0.16
Long-term pain or sensory deficits	Fixed	0.54	0.10
Operative time	Random	0.35	0.43
Postoperative pain	Random	0.74	0.42
Hospital stay	Random	0.10	0.33
Recovery time	Random	0.62	0.24

OR indicates odds ratio
WMD indicates weighted mean difference
CI indicates confidence interval

Table 7. Summary of outcome measures

Sensitivity analyses

Further analyses aiming at detecting differences in outcome measures after exclusion of specific potential outcome-related biases were undertaken.

Hernia recurrence – studies with ≥ 1 year follow up[85,87,90,92,93,94]

The incidence of hernia recurrence of studies with at least 1-year follow up was 4.7% for TAPP and 4.0% for TEP (OR 1.11, 95% CI 0.33–3.73; p = 0.87). Between-study heterogeneity was not evident (I^2 = 0%) **(Figure 20)**.

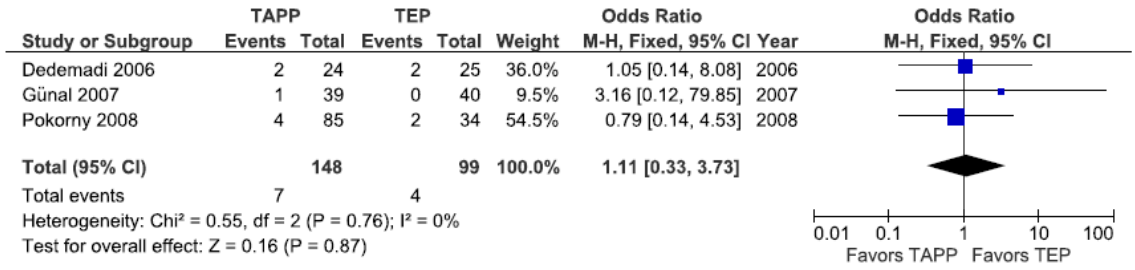


Figure 20. Forest plot shows a comparison of the odds ratios (OR) and 95% confidence intervals (95% CI) of hernia recurrence for studies with ≥ 1 year follow up.

Intraoperative complications – studies with Jadad score ≥3 or moderate EPHPP score[85,91,93,94,96]

Intraoperative complications occurred in one study only with Jadad score ≥3;[3] a meta-analytical model could thus not be applied.

Intraoperative complications – studies with patient population ≥ 100[85,87,90,96,97]

No study with at least 100 patients reporting on intraoperative complications was identified.

In-hospital morbidity – studies with Jadad score ≥3 or moderate EPHPP score[85,91,93,94,96]

The morbidity rate of studies with Jadad score ≥3 or moderate EPHPP score was 9.9% for the laparoscopic repair and 9.8% for the endoscopic repair (OR 1.20, 95% CI 0.57–2.53; p = 0.62). No significant heterogeneity among studies was identified (I^2 = 0%) **(Figure 21)**.

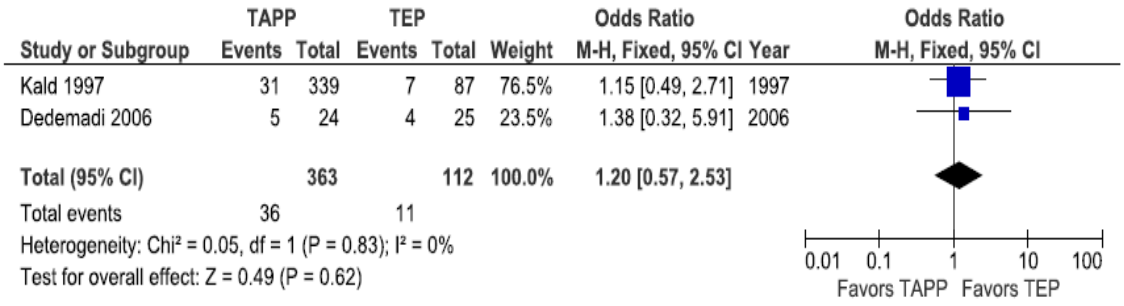


Figure 21. Forest plot shows a comparison of the odds ratios (OR) and 95% confidence intervals (95% CI) of in-hospital morbidity – studies with Jadad score ≥3 or moderate EPHPP score.

Operative time – studies with patient population ≥ 100 patients[85,87,90,96,97]

The mean length of surgical time was 78.7 minutes for the laparoscopic group and 74.8 minutes for the endoscopic group (WMD 1.82, 95% CI -5.94–9.59; p = 0.65). Significant evidence of heterogeneity among the studies existed (I^2 = 65%) **(Figure 22)**.

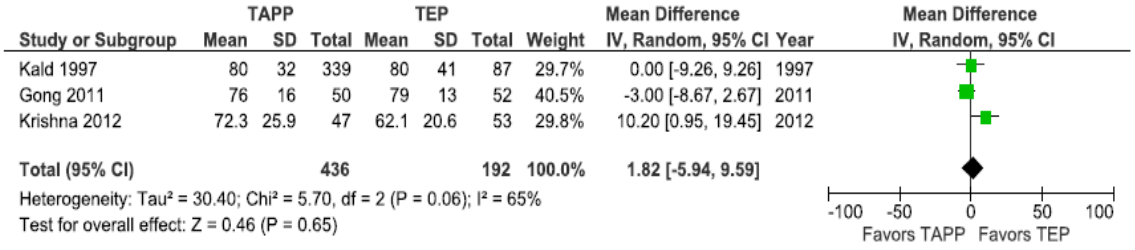


Figure 22. Forest plot shows a comparison of the odds ratios (OR) and 95% confidence intervals (95% CI) of operative time for studies with patient population ≥100 patients.

2.4 Discussion

Surgical treatment of inguinal hernia intends to restore the anatomical components of the inguinal canal and to provide long-term relief from associated symptoms. Less invasive approaches have gained wide popularity, providing lower pain scores, shorter recovery time and fewer local complications.[99-101] The surgical decisions on the optimal therapeutic approach of inguinal hernia is of paramount importance, considering the prevalence of this disease in Western societies and the subsequent economic implications on health care delivery systems.[102-104] The objective of the present review was to compare the effectiveness and the patient-oriented outcomes of the two most frequently performed minimally invasive techniques for inguinal hernia repair. Our meta-analytical model demonstrates similar recurrence rates for the preperitoneal (1.4 %) and the transabdominal approach (3.5%), with a trend in favor of the TEP repair. However, the length of follow-up time varied considerably among the studies, ranging between 3 months and 7 years. Sensitivity analysis of studies with a follow-up of at least one year did not demonstrate any difference in the incidence of recurrence (4.0% vs. 4.7%, respectively). Although low level of between-study heterogeneity existed, only three studies with a long term follow-up and a cumulative population of 247 patients reported on data on recurrence. Considering that mesh-reinforced inguinal hernia repair is associated with late rather than early recurrence,[105] at least one large randomized trial with long-term follow-up is justified.

Furthermore, the incidence of intraoperative complications was similar for the laparoscopic and the preperitoneal approach (3.6% vs. 2.0%, respectively). This outcome is more pronounced by the low level of between-study heterogeneity and the lack of evidence of publication bias. A recent meta-analysis of randomized controlled trials conducted by our team in 2012, has demonstrated higher operative morbidity for the TAPP repair (24.8% vs. 11.9%).[106] This analysis considered the cumulative peri-operative procedure-associated morbidity, because no statistically significant differences between the two approaches in terms of intraoperative complications could be demonstrated. In the present analysis, intraoperative and postoperative complications were evaluated independently. Postoperative in-hospital morbidity was, however, similar for TAPP and TEP (11.2% vs. 7.3%), with no evidence of between-study heterogeneity and no evidence of publication bias. Sensitivity analysis of best-

quality studies could not be performed, because only one such study reported on the incidence of in-hospital morbidity.

However, when interpreting these parameters, it should be taken into account that the high morbidity rates ─ 11.9% for endoscopic repair and 24.8% for laparoscopic repair ─ may be mainly attributed to the results of two single studies. Pokorny et al. considered analgesic consumption as postoperative complication in 8.4% of their patient population,[90] whereas Dedemani et al. observed a high incidence of local complications in their series of recurrent hernia repair.[93] If we exclude these studies from the calculated operative morbidity, the incidence of surgical complications for the laparoscopic and the endoscopic repair are 8.7% and 7.9%, respectively (OR 1.85, 95% CI 0.96–3.56; $p = 0.07$).[106] Sensitivity analyses of studies with methodological adequacy were not conclusive in favor of one approach. Although this statistical model confirmed the absence of statistical association between the type of endoscopic procedure and the operative morbidity, a consistent trend in favor of the preperitoneal approach in terms of procedure-associated morbidity should alert for possible differences which cannot be identified from published material.

Current evidence suggests significantly longer duration of surgery for endoscopic approaches in comparison to open repair.[91,85,87,103] The present analysis did not demonstrate significant differences between the TAPP and the TEP repair with regard to operative time (73.0 versus 70.9 minutes, respectively), whereas significant heterogeneity existed among studies. The lack of standardized techniques for minimally invasive inguinal hernia repair is a pragmatic issue, and is reflected by the wide variety of technical details presented in the contemporary literature. Modification and standardization of the operative steps, such as the method of entrance into the preperitoneal space and the creation of operative space, the extent of dissection, the size and type of mesh, and the fixation of the mesh, may result in a reduction of operative times in TEP repair. Similarly, the location of the peritoneal incision, the extent of preperitoneal dissection, the management of the hernia sac, the fixation of the mesh and the type of peritoneal closure are subjects for further evaluation with regard to their clinical effect on patient-oriented outcomes and the length of surgery in the context of laparoscopic hernia repair.

The posterior approach of minimally invasive techniques seems to result in improved pain scores, lower incidence of sensory deficits, shorter hospital stay and reduced recovery time following inguinal hernia repair in comparison to open mesh techniques.[103] Postoperative pain as expressed by the visual analogue scoring system was similar between TAPP and TEP (2.4 vs. 2.2), although heterogeneity and publication bias were evident. Furthermore, no significant differences in terms of long-term pain or sensory deficits were found between the two treatment arms. A trend in favor of the transabdominal approach could not be statistically confirmed (6.1% vs. 9.1%). The mean time to resume to normal activities was also similar between the two approaches (TAPP vs. TEP, 9.1 vs. 11.0 days, respectively), although high level of between-study heterogeneity and publication bias existed. Nevertheless, further evaluation of controversial operative trends, including the need for mesh fixation,[107-109] the use of lightweight prosthetics and the extent of dissection,[110-111] may further reduce the incidence of long-term pain and sensory complications, and the length of hospitalization.

Although similar outcomes were demonstrated for endoscopic and laparoscopic inguinal hernia repair in the present analysis, clinical interpretation of these results must be performed with caution. It is noteworthy, that several institutions routinely utilize either the endoscopic or the laparoscopic technique, which provides a greater amount of experience and probably improved outcomes with a specific procedure. Furthermore, if we consider the high learning curves of endoscopic hernia repairs,[112-114] transition to another technique is not justified for the present. However, the role of laparoscopic exploration in patients with risk factors for bilateral disease is strongly supported in the literature.[115] Furthermore, the above results have to be interpreted with caution, considering significant limitations of the cumulative analysis of the examined outcome measures. Follow-up periods varied significantly among studies, and long term follow-up was performed by telephone interview by two author teams. Although recurrent hernia was a criterion for exclusion in most studies, one article considered for analysis only patients with recurrent hernia and excluded those with primary hernia. Technical details were either not defined or inconsistently reported by different studies. Furthermore, eight of the included studies were of poor methodological quality, thus potentially introducing bias to the reported outcomes. A

further limitation to this analysis may be introduced by the potential of publication bias. Whereas the incidence of hernia recurrence and operative morbidity have been addressed by all reports, the outcome variables of long-term pain and operative time were reported by only few studies, hereby limiting the power to assess publication bias.

CONCLUSION

Considering the evolution of groin hernia, including identification of the anatomy of the inguinal canal, quantification of the mechanical features of the posterior wall, development of conservative and surgical techniques for inguinal hernia repair, and the introduction of minimally invasive surgery in inguinal hernia repair, we may assume, that surgery of the groin is rather in a dynamic and evolving state, continuously being self-ameliorated and modified, according to up-to-date clinical and experimental evidence. Current data suggest similar results for laparoscopic and endoscopic inguinal hernia repair with regard to patient-oriented outcomes. A trend toward higher recurrence rates with the TAPP repair must not be disregarded, and may suggest modification of technical details, in order to provide long-term outcomes to the patients. Discrete differences between the transabdominal and the preperitoneal repair render transition from one technique to another rather not justified according to current data. High-quality randomized trials with a longer-term follow-up are considered essential, in order to further assess the relative effectiveness of the two procedures in the prevention of hernia recurrence.

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