

Pain and Dysfunction with Sexual Activity after Inguinal Hernia Repair: Systematic Review and Meta-Analysis

Anna E Ssentongo, MPH, Eustina G Kwon, MD, MPH, Shouhao Zhou, PhD, Paddy Ssentongo, MD, MPH, David I Soybel, MD, FACS

| BACKGROUND: | The reported incidence rates of sexual dysfunction (SD) and pain with sexual activity (PSA) |
|---------------|--|
| | after inguinal hernia repair in males vary considerably. This meta-analysis explores the rates of |
| | SD and PSA after different surgical and anesthesia types to understand patient risk after |
| | inguinal hernia repair. |
| STUDY DESIGN: | We performed a systematic review and meta-analysis using Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines to search 3 databases |
| | (EMBASE, MEDLINE, and Cochrane Library). We identified retrospective, prospective, and |
| | randomized controlled trial studies, published on or before March 1, 2019, reporting on SD |
| | and PSA after inguinal hernia repair. We used random-effects models to calculate pooled |
| | estimates of incidence rates of SD and PSA after inguinal hernia repair. Subgroup meta- |
| | analyses and meta-regression were used to explore sources of variation. |
| RESULTS: | A total of 4,884 patients from 12 studies were identified. Study-level median age at the time of |
| | repair was 52.3 years old, and study-level median follow-up was 10.5 months. Definitions of SD |
| | and PSA focused on completion of intercourse for the former and pain with erection/ejaculation for the latter. The overall incidence of new-onset, postoperative SD was 5.3% (95% CI 3.6% to |
| | 7.9%) and of PSA was 9.0% (95% CI 5.8% to 13.6%). Rates of SD associated with minimally |
| | invasive surgical (MIS) and open repair were, respectively, 7.8% (95% CI 5.4% to 11.3%) and |
| | 3.7% (95% CI 2.0% to 6.8%); rates of PSA were 7.4% (95% CI 4.7% to 11.5%) and 12.5% |
| | (95% CI 6.4% to 23.3%), respectively. |
| CONCLUSIONS: | Sexual dysfunction and PSA are not rare after inguinal hernia repair. They should be included |
| | in preoperative discussions and as standard metrics in reporting outcomes of repair in large |
| | cohorts or trials. (J Am Coll Surg 2020;230:237–250. © 2019 by the American College of |
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In discussions with male patients about options for surgical management of inguinal hernia, the dominant concerns of surgeons have included short-term complications and discomfort, return to work and normal daily activities, and rates of recurrence. Added to these conversations have been the risk of chronic postoperative pain^{1,2} and

CME questions for this article available at http://jacscme.facs.org

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Support: This study was supported by the Academic Enrichment Fund and the David L Nahrwold Endowment of the Department of Surgery, Penn State Hershey College of Medicine. general considerations of quality of life (QOL).³ Recently, it has become clear that patients may experience different types of sexual dysfunction (SD) after open or minimally invasive surgical (MIS) approaches to repair.⁴⁻⁶ Types of SD include chronic genital pain, impaired ability to initiate and maintain erection, or dysejaculation.⁴⁻⁶ Sexual

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From the Departments of Surgery (A Ssentongo, Kwon, Soybel) and Public Health Sciences (A Ssentongo, Zhou, P Ssentongo), Penn State Hershey College of Medicine and Milton S. Hershey Medical Center, Hershey, PA; and the Center for Neural Engineering, Department of Engineering, Science and Mechanics, The Pennsylvania State University, University Park, PA (P Ssentongo).

Correspondence address: David I Soybel, MD, FACS, Department of Surgery, The Pennsylvania State University College of Medicine, Penn State Milton S. Hershey Medical Center, 500 University Dr, Mail Code H149, PO Box 850, Hershey, PA 17033-0850. email: dsoybel@ pennstatehealth.psu.edu

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Abbreviations and Acronyms

| HEF | = International Index of Erectile Dysfunction |
|--------|--|
| | , |
| MIS | = minimally invasive surgery |
| PRISMA | = Preferred Reporting Items for Systematic |
| | Reviews and Meta-Analysis |
| PSA | = pain with sexual activity |
| RCT | = randomized controlled trial |
| SD | = sexual dysfunction |
| TAPP | = transabdominal preperitoneal hernia repair |
| TEP | = total extraperitoneal laparoscopic hernia repair |
| | |

dysfunction and pain with sexual activity (PSA) are associated with a reduced quality of life, stress disorders, anxiety, and depression,⁷ but the place of such symptoms in decisions about indications and choices in hernia repair has not been clearly established.

Published reports of the incidence of SD, with or without PSA, after inguinal hernia repair vary considerably, from 0% to 11%.⁸⁻¹⁰ Clinical, biologic, and technical factors that contribute to the likelihood of such adverse outcomes have not been consistently identified, so the reasons for variation in their incidences remain unclear.^{8,11-14} Of interest, although this issue has been the subject of a number of reports from western and northern Europe,^{4-8,11,12,14-16} there has been little attention to SD or PSA as adverse outcomes of inguinal hernia repair from centers or cooperatives in North or South America.

Here we define SD as the inability to complete intercourse and PSA as pain with erection/ejaculation; the primary objective of this systematic review and metaanalysis was to define the pooled incidence of SD and PSA in men undergoing hernia repair. A second goal was to determine if there are substantial differences in the incidences of SD and PSA associated with different forms of repair and if there are other identifiable sources of variation. A third goal was to determine whether there is sufficient information from available studies to advise surgeons and patients about how the incidence and consequences of SD might be incorporated into discussions about indications and timing of repair. To our knowledge, this is the first report of a systematic review and meta-analysis of SD and PSA after inguinal hernia repair.

METHODS

Search strategy and selection criteria

We performed a systematic review and meta-analysis using the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (eTable 1).¹⁷ Three databases (EMBASE, MEDLINE, and Cochrane Library) were searched. We identified prospective, retrospective, and randomized control trial studies published on or before March 1, 2019 and reporting SD rates after hernia repairs. Our keyword search was based on Medical Subject Headings (MeSH) with various combinations of "Sexual Dysfunction", "Sexual Pain", "Erectile Dysfunction", "Pain", "Prospective Studies", "Ran-"Erectile domized Clinical Trial*", or "Impotence*", AND "Her-nia*" "Herniorrhaphy*" or "Inguinal Hernia*". There were no restrictions based on sex, age, ethnicity, language, country in which the study originated, use of a mesh, laparoscopic versus open repair, suture type, or anesthesia type. Initially, 2 investigators (AES and EGK) individually reviewed the titles and abstracts of identified studies in order to determine eligibility for inclusion. Studies were excluded if they were not retrospective, prospective, or RCTs, or were duplicates.

Quality assessment and data extraction

Full-text articles were downloaded and independently reviewed by AES and EGK to determine eligibility for inclusion in the analysis. If eligible, data were extracted. Disagreements between extractors were discussed with an arbiter (PS) and senior author (DIS), and a consensus was reached. The incidence of SD was extracted from each publication as well as information on mean or median age, year of publication, sex, country of origin, dates data were collected, defect size, anesthesia type, closure technique, operation type, mesh use, time between operation and SD, and SD questionnaire used.

| postopspecially organized and developed by the Institute of Sexual Medicine of the Charite University Hospital.disorders, orgasm disorders, pain or discomfort during sexual intercourse)"Aasvang2006 Danish DatabaseEuropeRetrospective18Pre- and postop1,015Developed by authors"Impairment of sexual function due to pain during sexual activity"95 (9)Aasvang2010 DenmarkEuropeProspective6Pre- and postop442Activity sexual activity""Pain that moderately or severely impairs sexual function, AAS: How much difficulty do usave performing the following activities in the last 24 hours as a result of your hernia operation? Engaging in sexual intercourse (no difficulty, a lot of difficulty, a lot of difficulty, a lot of difficulty, not able to do it, did nor do it for other reasons)." | Patient with pain during sex, n (%) |
|---|---|
| postop authors function due to pain during sexual activity" Aasvang 2010 Denmark Europe Prospective 6 Pre- and postop 442 Activity "Pain that moderately or severely impairs sexual function, the last 24 hours as a result of your hernia operation? Engaging in sexual intercourse (no difficulty, a lot of difficulty, and the order in the sexual activity and frequency of pain, pain-resons)." 12 (5) Bittner 2010 Germany Europe Prospective 6 Pre- and postop 268 Activity "Standardized questionnaire reasons)." 12 (5) Bittner 2010 Germany Europe Prospective 6 Pre- and postop 268 Activity "Standardized questionnaire reasons)." 12 (5) Bittner 2010 Germany Europe Prospective 6 Pre- and postop | Not reported |
| postop Assessment Scale (AAS) questionnaire severely impairs sexual function; AAS: How much difficulty (did you have performing the following activities in the last 24 hours as a result of your hernia operation? Engaging in sexual intercourse (no difficulty, a little difficulty, some difficulty, a little difficulty, and the ot of other reasons)." Bittner 2010 Germany Europe Prospective Pre- and postop Activity Scale (AAS) questionnaire related impairment (AAS), and sexual dysfunction" (reference given Bay- Nielsen, but sexual dysfunction isn't measured in this); "The patients were asked about the frequency and extent of impairment in their sexual activity. The patients kept a pain diary | 224 (22) |
| postop Assessment eliciting current intensity and frequency of pain, pain- related impairment (AAS), and sexual dysfunction" (reference given Bay- Nielsen, but sexual dysfunction isn't measured in this); "The patients were asked about the frequency and extent of impairment in their sexual activity. The patients kept a pain diary | 25 (6) |
| | 7 (3) |

Table 1. Attributes of Studies Included in Meta-Analysis

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(Continued)

| Author | Year | Country | Continent | Study type | Median follow-up time, mo | Timing of survey | Sample size, n | Sexual dysfunc- tion question- naire used | Definition of sexual dysfunc- tion used | Patient with sexual dysfunction, n (%) | Patient with pain during sex, n (%) |
|----------|--------|---------------------------|-----------|---------------|---------------------------------|---------------------|-------------------|---|--|---|---|
| | | | | | | | | | operation and for the first six postoperative days, documenting pain frequency and intensity (morning, afternoon, over the past 24 h) and any pain medication taken." | | |
| Bischoff | 2012 I | Danish Hernia Database | Europe | Retrospective | 6 | Pre- and postop | 805 | "A detailed questionnaire, separated into four parts" developed by authors | "Pain of any severity during sexual activity" | 88 (11) | 88 (11) |
| Schouten | 2012 M | Netherlands | Europe | Retrospective | 1.5 | Pre and postop | 386 | Similar to the questionnaire used by Aasvang 2006 | "The main endpoints of this study were the preoperative and postoperative presence of any pain during sexual activity and pain-related impairment of sexual activity. Moderate and severe pain were combined to represent substantial pain when exploring the relationship between pain and other factors; similarly, moderate and severe impact on sexual functioning were grouped as 'substantial' impairment." | | 13 (5) |
| El-Awady | 2009 E | Egypt | Africa | Prospective | 9 | Pre- and postop | 40 | Quality of Life short for 36 and IIEF | "Deteriorated total sexual score by IIEF at ninth month" | 1(2.5) | Not reported |
| Bulus | 2013 T | Гurkey | Europe | Prospective | 3 | Pre- and postop | 40 | International Index of Erectile Dysfunction (IIEF-5) questionnaire | "If total score is below 20 points, it is interpreted as a decline in sexual dysfunction." | 0 (0) | |
| Tolver | 2015 I | Denmark | Europe | Prospective | 6 | Pre- and postop | 113 | Same questionnaire | "The outcome 'pain during sexual activity' is in this study defined as | 11 (10) | 11 (10) |
| | | | | | | _ | | | | | (Continued) |

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| Author | Year | Country | Continent | Study type | Median follow-up time, mo | 0 | Sample size, n | Sexual dysfunc- tion question- naire used | Definition of sexual dysfunc- tion used | Patient with sexual dysfunction, n (%) | Patient with pain during sex, n (%) |
|-------------|---------|---------------------------|-----------|---------------|---------------------------------|----------------------------|-------------------|---|---|---|---|
| | | | | | | | | as used in Aasvang 2006 | hernia-related pain during sexual intercourse and does not include erectile dysfunction." | | |
| Andresen | 2017 I | Denmark | Europe | RCT | 6 | Pre- and postop | 259 | Same questionnaire as used in Aasvang 2006 | "Moderate or severe impairment of sexual function" | 4 (2) | 21 (15) |
| Pommergaard | 2017 1 | Danish Hernia Database | Europe | Retrospective | : 6 | Pre- and postop | 1,019 | Same questionnaire as used in Aasvang 2006 | "The term sexual dysfunction was defined as any experience of pain during sexual activity within the last month." | 115 (11) | 115 (11) |
| Rutegard | 2018 \$ | Sweden | Europe | RCT | 12 | Pre- and postop only | 273 | Global question (worse, no change, better) | "Quality of life was evaluated with the validated Euro Qol 5 dimensions (EQ-5D) instrument, while the impact on sex life was assessed with a global question (worse, no change, better)"; worsened sex life after inguinal hernia surgery. | | Not reported |



Figure 1. Flow diagram of study selection. SD, sexual dysfunction.

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Figure 2. Geographic distribution of number of included studies.

The quality of each report was assessed independently by 2 authors (AES and PS) using an approach similar to the Cochrane collaboration.¹⁸ Domains that were considered included demographic information, stratified reporting of hernia type, and SD rates. A quality score was calculated for each paper using the sum scores from the 4 domains (patient demographic information, study design, follow-up time, and sample size) ranging from 0 to 13 (low to high quality, eDocument 1).

Data analysis

Our primary outcome was the incidence of SD and our secondary outcome was PSA after hernia repair. Median follow-up time for each study is listed in Table 1. We used the metaprop function of the meta package in R to graphically display the overall rate of SD using a random-effect model.¹⁹ We used a generalized linear mixed-effects model (GLMM) with logit transformation of proportions for pooling of studies.^{20,21} Confidence intervals were calculated using the exact binomial (Clopper-Pearson) interval method. We assessed betweenstudy heterogeneity using I^2 statistic, expressed as % (low [25%], moderate [50%], and high [75%]) and Cochrane's *Q* statistic (significance level < 0.05).^{22,23} Subgroup meta-analyses²⁴ were done using the relevant clinical and epidemiologic variables such as laparoscopic vs open repair, study type, and anesthesia type. To quantify the sources of variations in SD, we conducted a metaregression analysis, using study level covariates; mean or median age in years, median follow-up time in months, study designs, sex, and publication year.²⁵ We report absolute differences (in percentage) in the overall probability

of SD. We used Egger's test, and funnel plots were used to assess small sample size bias.²⁶

RESULTS

Literature search

We identified 4,721 articles as potential candidates for inclusion in the analysis (Fig. 1). We excluded 2,907 duplicates. Also excluded were 124 studies that looked at SD from other causes, 12 studies that did not include hernia or SD, 8 published abstracts from conference proceedings, 168 studies that included only pediatric surgical patients, 135 review articles, and 49 case reports. We then assessed the full text of the remaining 1,318 studies for inclusion, and we found that 1,280 looked at other complications of hernia repair and did not report incidence rates of SD: 19 studies looked at SD not related solely to hernia repair, 3 did not include preoperative questionnaires to exclude existing cases of SD, and 4 were case studies. Twelve studies met all inclusion criteria, including 11 from Europe and 1 from Africa (Fig. 2, eFig. 3, eTable 2). Of these 12 studies reporting a total of 4,884 patients, 6 were prospective (1,127 patients), 4 were retrospective (3,225 patients), and 2 were RCTs (532 patients). Patients with new-onset, postoperative SD or PSA were included in the analysis.

Definitions of sexual dysfunction and pain with sexual activity

Summarized in Table 1 are critical attributes of the 12 studies included in the analysis. Only patients with newonset, postoperative SD or PSA were included. All studies included only males except the one by Zieren and 244



Figure 3. (A) Crude incidence rate of sexual dysfunction after inguinal hernia repair from the random-effects model. (B) Crude rate of pain associated with sexual intercourse from the random-effects model.

colleagues⁶ in 2005, which was 96.6% males. Included in this summary are the definitions used for SD and PSA in each study: one study¹¹ used the original 15-question survey developed as the International Index of Erectile Dysfunction (IIEF),²⁷ which focuses on specific events during the 4 weeks before survey. Six reports^{4,5,8,9,12,28} used the same survey tool,⁴ which addresses current perceptions of PSA and its influence on sexual life. Two studies^{29,30} used a general survey (Activity Assessment Score),³¹ which included a single question about sexual activity, with 5 Likert scale responses ranging from "no difficulty" to "not able to perform." Similar general single-item survey questions were used in 2 studies.^{6,32} In 1 study,³³ a set of detailed questions included incidence, intensity, and location of pain during sexual activity, with specific emphasis on dysejaculation, and the extent of impairment of sexual life.

Overall incidence of sexual dysfunction and pain with sexual activity

The study-level median (range) age of patients undergoing hernia repair was 52.3 (33 to 60) years, with the study level median (range) of follow-up of 10.5 (3 to 40) months. One of the 12 included studies involved female patients, although the frequency of female patients was low.⁶ Reported rates of SD varied from 0%⁸ to 11.3%.⁹ The overall crude rate for SD was 5.3 % (95% CI 3.6% to 7.9%) (Fig. 3A). With respect to PSA, reports of the incidence ranged from 3%³⁴ to Α

В

| Au | thor (Year of Publication) Incid | ence T | otal | Events per 100 observations | Ivents | 95%-CI |
|---|---|--------------------------|--|--------------------------------|--------------------------------------|---|
| Pol Aa Bis Sc Ra | trospective mmergaard 2017 svang 2006 schoff 2012 houten 2012 ndom effects model terogeneity: l^2 = 85%, τ^2 = 0.0876 | 18 | | + + + \$ | 9.36 10.93 4.66 | [9.41; 13.39] [7.64; 11.32] [8.86; 13.29] [2.79; 7.27] [6.65; 12.02] |
| Aa Bit Tol Zie El- Bu Ra | pspective svang 2010 ther 2010 ver 2015 eren 2005 -Awady 2009 lus 2013 ndom effects model terogeneity: $I^2 = 64\%$, $\tau^2 = 0.2638$ | 12 11 13 1 0 | 442 268 113 224 40 - 40 - 127 | | 4.48 9.73 5.80 2.50 0.00 | [0.94; 3.83] [2.33; 7.69] [4.96; 16.75] [3.13; 9.72] [0.06; 13.16] [0.00; 8.81] [2.30; 6.80] |
| Ru Ra | tegard 2017 tegard 2018 ndom effects model terogeneity: I^2 = 74%, τ^2 = 0.4385 | 18 | 259 - 273 532 - | + | 6.59 | [0.42; 3.91] [3.95; 10.22] [1.21; 9.27] |
| | ndom effects model terogeneity: I^2 = 91%, τ^2 = 0.4002 | 4 | 884 ┌ 0 | 5 10 15 20 25 30 35 40 45 50 | 5.30 | [3.55; 7.85] |
| А | uthor (Year of Publication) Incid | dence ⁻ | Fotal | Events per 100 observations | Events | 95%-CI |
| Po Aa Bi So R a | etrospective pommergaard 2017 asvang 2006 schoff 2012 chouten 2012 andom effects model eterogeneity: $I^2 = 96\%$, $\tau^2 = 0.3117$ | 13 | | * * * | 22.07 10.93 4.96 | [9.41; 13.39] [19.55; 24.75] [8.86; 13.29] [2.67; 8.34] [6.72; 18.37] |
| Aa Bi To R a | rospective asvang 2010 ttner 2010 olver 2015 andom effects model eterogeneity: $I^2 = 60\%$, $\tau^2 = 0.1326$ | 25 7 11 | 442 248 113 803 | * * * | 2.82 9.73 | [3.69; 8.24] [1.14; 5.73] [4.96; 16.75] [3.24; 8.82] |
| Ar Ra | CT ndresen 2017 andom effects model eterogeneity: not applicable | 21 | 144 144 | | | [9.26; 21.42] [9.71; 21.33] |
| | andom effects model eterogeneity: I^2 = 95%, τ^2 = 0.3990 | | 4048 (| 0 5 10 15 20 25 30 35 40 45 50 | | [5.84; 13.61] |

Figure 4. (A) Incidence rate of sexual dysfunction from the random effects model and (B) pain with sexual activity after inguinal hernia repair by study type.

| | Author (Year of Publication) Incid | ence | Total | Events per 100 observations | Events | 95%-CI |
|---|---|------------------------------------|--|--------------------------------|--|--|
| | Laparoscopic Pommergaard 2017 Bischoff 2012 Schouten 2012 Bittner 2010 Tolver 2015 Random effects model Heterogeneity: $I^2 = 85\%$, $\tau^2 = 0.1592$ | 115 88 18 12 11 | 1019 805 386 268 113 2591 | | 10.93 4.66 4.48 9.73 | [9.41; 13.39] [8.86; 13.29] [2.79; 7.27] [2.33; 7.69] [4.96; 16.75] [5.39; 11.27] |
| | Open Aasvang 2006 Aasvang 2010 Andresen 2017 Zieren 2005 El-Awady 2009 Bulus 2013 Rutegard 2018 Random effects model Heterogeneity: $l^2 = 84\%$, $\tau^2 = 0.4768$ | 95 9 4 13 1 0 18 | 1015 442 + 259 + 224 40 + 273 2293 < | | 2.04 1.54 5.80 2.50 0.00 6.59 | [7.64; 11.32] [0.94; 3.83] [0.42; 3.91] [3.13; 9.72] [0.06; 13.16] [0.00; 8.81] [3.95; 10.22] [1.96; 6.78] |
| A | Random effects model Heterogeneity: I^2 = 91%, τ^2 = 0.4002 | | 4884 0 | 5 10 15 20 25 30 35 40 45 | | [3.55; 7.85] |
| | Author (Year of Publication) Incid | ence | Total | Events per 100 observations | Events | 95%-CI |
| | Laparoscopic Pommergaard 2017 Bischoff 2012 Schouten 2012 Bittner 2010 Tolver 2015 Random effects model Heterogeneity: $l^2 = 89\%$, $\tau^2 = 0.2451$ | | 1019 805 262 - 248 - 113 2447 | | 10.93 4.96 2.82 9.73 | [9.41; 13.39] [8.86; 13.29] [2.67; 8.34] [1.14; 5.73] [4.96; 16.75] [4.67; 11.53] |
| | Open Aasvang 2006 Aasvang 2010 Andresen 2017 Random effects model Heterogeneity: $I^2 = 93\%$, $\tau^2 = 0.4031$ | 224 25 21 | 1015 442 144 1601 | * | 5.66 14.58 | [19.55; 24.75] [3.69; 8.24] [9.26; 21.42] [6.36; 23.26] |
| в | Random effects model Heterogeneity: $I^2 = 95\%$, $\tau^2 = 0.3990$ | | 4048 0 | 5 10 15 20 25 30 35 40 45 | | [5.84; 13.61] |



Figure 5. (A) Incidence rate of sexual dysfunction from the random effects model and (B) pain after inguinal hernia repair by surgery type.

| Table 2. | Univariate | Meta-Regress | ion for Sexu | al Dysfunc- |
|------------|--------------|-----------------|--------------|-------------|
| tion Repo | rting Absolu | ite Differences | (%) of Sexu | al Dysfunc- |
| tion Rates | ; | | | |

| Predictor of sexual dysfunction rate | Unadjusted absolute difference in rate of sexual dysfunction, % (95% Cl) | p Value |
|---|--|------------|
| Age, y | -0.09 (-0.38, 0.19) | 0.524 |
| Sex | | |
| Study only involving males | -0.05 (-7.95, 8.04) | 0.99 |
| Study with males and females | Reference | |
| Time to assessment (per monthly increment) | 0.22 (0.07-0.36) | 0.003 |
| Study type | | |
| Randomized control trial | -0.23 (-5.30, 4.84) | 0.93 |
| Retrospective | 4.77 (0.76, 8.77) | 0.02 |
| Prospective | Reference | |
| Publication year (per yearly increment) | 0.09 (-0.46, 0.63) | 0.76 |

Per 1-month increase in follow-up time, the rate of sexual dysfunction (SD) significantly increased by 0.2%, and SD rates were 5% higher in retrospective studies compared with prospective studies. No difference in SD rates between prospective studies and randomized controlled trials. Other covariates used for analysis (sex, age, and publication year) were not significantly associated with SD rates.

22%³⁵, and the calculated rate was 9.0% (95% CI 5.8% to 13.6%) (Fig. 3B). Between-study variability was large for both the endpoint of SD ($I^2 = 91\%$) and the endpoint of PSA ($I^2 = 95\%$). Because of the relatively large I^2 values, we report the results of random-effects models.

Association of study design on reported incidence of sexual dysfunction and pain with sexual activity

With respect to the type of study (Figs. 4A and 4B), we found that retrospective studies had the highest reported rates of SD. The reported occurrence of new, postoperative SD (Fig. 4A) in retrospective studies was 9.0% (95% CI 6.7% to 12.0%), in prospective studies 4.0% (95% CI 2.3% to 6.8%), and in RCTs 3.4% (95% CI 1.2% to 9.3%). Reported PSA rates (Fig. 4B) were significantly higher in RCTs (14.6%; 95% CI 9.7% to 21.3%) compared with prospective studies (5.4%; 95% CI 3.2% to 8.8%), but not when compared with retrospective studies (11.3%; 95% CI 6.7% to 18.4%).

Association of surgical procedure type on reported incidence of sexual dysfunction and painful sexual activity

Patients undergoing MIS procedures (7.8%; 95% CI 5.4% to 11.3%) had higher rates of SD than those

undergoing open procedures (3.7%; 95% CI 2.0% to 6.8%). However, this difference was not significant (Fig. 5A). In contrast, with respect to PSA (Fig. 5B), open procedures (12.5%; 95% CI 6.4% to 23.3%) had higher rates compared with laparoscopic procedures (7.4%; 95% CI 4.7% to 11.5%). Similarly, this difference was not significant.

Out of the 5 studies with laparoscopic repairs, 4 used the TAPP method^{9,28,29,33} with sample size of 2,206 patients. One study used the TEP method⁵ with a sample size of 386. Mesh was not fixated when TEP was used, and fibrin glue, tacks, or clip fixation methods were used when performing TAPP. Due to the low number of studies that would be in each group, we did not run subgroup analysis. Of the 7 studies that included open repairs, 5 studies clearly delineated the repair methods with SD and PSA.^{6,8,11,12,36} When analyzing these 5 studies, 36 of 836 patients reported SD and/or PSA, 36% of whom had plug and patch and 64% who had Lichtenstein performed. None of the participants who had the Onstep procedure¹² reported SD or PSA.

Association of anesthesia type on incidence of sexual dysfunction

Although all MIS procedures in analyzed reports used general anesthesia, different modalities were used for open procedures. General anesthesia was used in 2 included studies,^{10,23} spinal anesthesia in 2 studies,^{8,9} and local anesthesia in 2 studies.^{6,27} One study did not report the modality of anesthesia used.⁴ None of the studies reported specifically tested a hypothesis that anesthesia modality influences SD after open operation. In an analysis of only patients undergoing open procedures, general anesthesia (1.9%; 95% CI 1.1% to 3.2%) was associated with significantly lower rates of sexual dysfunction than local anesthesia (6.2%; 95% CI 4.4% to 8.7%) (eFig. 1). All studies reporting PSA used general anesthesia, and therefore we could not analyze differences in pain based on anesthesia type.

Association of gender on reported incidence of sexual dysfunction

One study⁶ included a small percentage of females (6.2%) in their analysis. There were no significant differences between the study that included females and those that did not. In sensitivity analysis, removing this study did not significantly change our results (eFig. 2). Only one study⁹ included a separate analysis of outcomes in women, indicating an incidence of PSA of about 11% and with no reference to an incidence of post-operative SD.

Association of study location on reported incidence of sexual dysfunction

Eleven of the 12 studies were conducted in Europe (Fig. 2); therefore, it was difficult to delineate differences in the rates of SD based on the continent of study origin (eFig. 3). All studies reporting PSA were completed in Europe; therefore, we could not run global spatial analysis on those data.

Exploration of heterogeneity among studies

To explore the sources of the variation in SD, we conducted a univariate meta-regression. As summarized in Table 2, follow-up time and study method were significantly associated with SD. Per 1-month increase in follow-up time, the rate of SD increased by 0.2%, and SD rates were 4% higher in retrospective studies compared with prospective studies. Other covariates used for analysis (sex, age, and publication year) were not significantly associated with SD rates.

Assessment of bias

Egger's test was performed to evaluate the possibility of bias toward positive results and outsized influence of smaller studies, and this was not significant (p = 0.94). The funnel plot displayed symmetry (eFigure. 4).

DISCUSSION

To our knowledge, this is the first systematic review and meta-analysis that assesses the incidence of SD after inguinal hernia repair. In addition to screening with specific search terms for sexual dysfunction and hernia repair in well-established citation engines (Embase, MEDLINE, and Cochrane Library), we searched and reviewed all reports of studies conducted for patients with inguinal hernia and reviewed both the abstract and the body of the report in order to determine whether any component of sexual dysfunction was included. The goal of this effort was not only to summarize what is currently known about the prevalence of new-onset sexual dysfunction after inguinal hernia repair, but also to identify gaps in knowledge that have not been addressed in previous studies.

With this strategy, we found the crude incidence of postoperative SD is 5.3%, with a high degree of variation, especially among open procedures, which is not attributable to patient preoperative characteristics, study type, or country of origin. One potential source of variation may be the type of procedure chosen, with SD possibly being somewhat higher for patients undergoing MIS than open procedures (Fig. 5). At the moment, it remains unclear whether the risks of SD and PSA are substantially different between open and laparoscopic procedures. Beyond the possible influence of the type of operation, however, our review and analysis highlight potential influences of follow-up time and study method as a possible source of variation in the appearance of SD and PSA after inguinal hernia repair. In addition, while not consistently addressed in the studies eligible for inclusion here, it seems likely that the choice of anesthesia modality may prove more consequential than might have been thought, at least with respect to open repair.³⁷⁻³⁹

With this analysis, we identified 1 clear gap in knowledge: the absence of information about SD in women. In addition, we found it striking that the problem of SD and PSA has not been well addressed in studies from centers or cooperatives in North, Central, or South America. Moreover, the influence of different subtypes of repair (transabdominal pre-peritoneal [TAPP] vs total extraperitoneal [TEP]) and the meshes used (heavy, medium, or light) could not be assessed except within individual studies.^{36,40} Many of the included studies acknowledged that it is difficult to clearly differentiate between isolated SD/PSA and inguinodynia. Lastly, we identified considerable variation in the survey tools used to assess SD and PSA and differences in follow-up intervals that may influence the accuracy of estimates of the true incidence of SD and PSA (Table 2). Despite these limitations and apparent gaps, our analysis indicates that these outcomes are common and should be part of the preoperative discussion with any patient about indications, options, and timing of inguinal hernia repair. These gaps and uncertainties should serve not only as limitations on any inferences that can be drawn, but as motivation for design of more rigorous studies in the future.

Sexual dysfunction has several different components, and is broadly addressed by the IIEF²⁷ questionnaire, which was used in 1 study included in our analysis. The IIEF has 15 questions focusing on specific activities, from the initiation of erection to ejaculation and the completion of intercourse, and includes subjective assessments of the quality of the experience. An abridged form (IIEF-5) that includes 5 items⁴¹ has been reported, which correlates well with the more comprehensive version and seems suitable for screening the presence and severity of erectile dysfunction before and after operation. In 2006, Aasvang and colleagues⁴ proposed a survey specific to hernia surgery and this was used in 6 of our 12 studies to address the topic of SD. However, this meta-analysis does not address the validity of these scales specifically for patients undergoing hernia repair. Given the relatively high prevalence of SD, however, our analysis underscores the desirability for some standardized attention to a history of sexual activity and dysfunction, before and after operation.

While some components of SD are not easily explained, it has been postulated that pain with erection, intercourse, and ejaculation may be due to the exuberant scarring reaction that forms around permanent mesh, which, in turn, leads to trapping, traction, or torsion on vulnerable nerves and the vas deferens.^{12,42} Likewise, it has been postulated that suture migration after Lichtenstein repair leads to encirclement and strangulation of the vas deferens, and the iliohypogastric and ilioinguinal nerves, resulting in dysejaculation that can be alleviated by decompressing the vas deferens and transecting the nerves.⁴³ Similar mechanisms of entrapment, pressure, or erosion have been implicated as explanations for PSA and SD in laparoscopic operations.^{33,44,45}

In this study, substantial variation between studies is an impediment to drawing definitive conclusions about SD and PSA after different forms of repair. Although the overall rate of postoperative SD was higher among patients with MIS repairs as compared with open repairs (7.8% vs 3.7%), this difference was not significant. Similarly, the overall incidence of postoperative PSA was lower for MIS repairs than for open repairs (7.4% vs 12.5%). It is not entirely clear why there might be substantial differences between the likelihood of postoperative SD and that of PSA. These considerations suggest, however, that pain is not necessarily an impediment to the completion of intercourse. In addition, they underscore the importance of surveys exploring outcomes of sexual function and satisfaction in multiple ways. With this consideration in mind, it seems reasonable to offer the IIEF survey tool or its abridged version as the most reliable instrument for following this set of outcomes after inguinal hernia repair.27,41

CONCLUSIONS

In conclusion, the incidence rate of SD after inguinal hernia repair is higher than is perhaps appreciated in regions of the world in which studies have not yet been reported that are prospective and based on formal definitions and intervals of follow-up. Our results provide some evidence that laparoscopic operations were potentially associated with a higher rate of SD compared with open procedures, despite reporting less acute pain. In addition, at least with respect to open operation, it is possible that general anesthesia might provide protection from these adverse consequences of inguinal hernia repair. Future RCTs are needed, particularly in North America, where studies are lacking.

Author Contributions

Study conception and design: Ssentongo A, Ssentongo P, Soybel

Acquisition of data: Ssentongo A, Kwon, Ssentongo P

- Analysis and interpretation of data: Ssentongo A, Ssentongo P, Zhou
- Drafting of manuscript: Ssentongo, A, Ssentongo P, Soybel
- Critical revision: Ssentongo, A, Ssentongo P, Soybel

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eDocument 1. QUALITY SCORING INFORMATION

| Detailed demographic information: max points: 3 | |
|---|--------|
| □ Average age stated: 0, 1 | |
| □ Sex mentioned: 0, 1 | |
| □ Race mentioned: 0,1 | |
| Detailed study design information: max points: 3 | |
| O Retrospective cohort: 1 | |
| O Prospective cohort: 2 | |
| O Randomized control trial | |
| Stratified reporting of follow-up time: max points: 1 | |
| ☐ Follow-up time reported: max points 1 | |
| Sample size: max points: 6 | |
| □ Overall sample size: max points 3 | |
| O Less than 50: 1 | |
| ○ 50−150: 2 | |
| O Greater than 150: 3 | |
| Percentage of patients with successful follow-up: max | points |
| 3 | |
| O Less than 50%: 1 | |
| ○ 50%−75%: 2 | |
| O Greater than 75%: 3 | |
| Total max score from 4 domains: 13 | |
| | |

| Author (Year of Publication) Incid | ence | Total | Events per 100 observations E | vents | 95%-CI |
|---|--------|------------|----------------------------------|-------|------------------------------|
| General | 9 | 440 | | 0.04 | [0.04, 0.02] |
| Aasvang 2010 Andresen 2017 | 9 4 | 442 259 | | | [0.94; 3.83] [0.42; 3.91] |
| Random effects model | 4 | 209 701 | | | [0.42, 3.91] [1.08; 3.17] |
| Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$ | | 701 | | 1.05 | [1.00, 3.17] |
| Local | | | | | |
| Zieren 2005 | 13 | 224 | | 5.80 | [3.13; 9.72] |
| Rutegard 2018 | 18 | 273 | | | [3.95; 10.22] |
| Random effects model | | 497 | \diamond | 6.24 | [4.42; 8.73] |
| Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$ | | | | | |
| Spinal | | | | | |
| El-Awady 2009 | 1 | 40 | <u> </u> | 2.50 | [0.06; 13.16] |
| Bulus 2013 | 0 | 40 | | 0.00 | [0.00; 8.81] |
| Random effects model | | 80 | | 1.25 | [0.18; 8.34] |
| Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$ | | | | | |
| Random effects model | | 1278 | | 3.03 | [1.63; 5.54] |
| Heterogeneity: $I^2 = 67\%$, $\tau^2 = 0.3198$ | | | | | |
| | | (| 0 5 10 15 20 25 30 35 40 45 50 | | |

eFigure 1. Incidence rate of sexual dysfunction after open inguinal hernia repairs by anesthesia type. Rates of sexual dysfunction were significantly lower after general anesthesia compared with local.

| Author (Year of Publication) Incid | dence | Total | Events per 100 observations E | Events | 95%-CI |
|---|-------|-------|--|---------|--------------|
| Male | | | | | |
| Pommergaard 2017 | 115 | 1019 | - | 11.29 [| 9.41; 13.39] |
| Aasvang 2006 | 95 | 1015 | - | 9.36 [| 7.64; 11.32] |
| Bischoff 2012 | 88 | 805 | | - | 8.86; 13.29] |
| Aasvang 2010 | 9 | 442 | + | 2.04 | [0.94; 3.83] |
| Schouten 2012 | 18 | 386 | ÷. | 4.66 | [2.79; 7.27] |
| Bittner 2010 | 12 | 268 | | 4.48 | [2.33; 7.69] |
| Andresen 2017 | 4 | 259 | + | 1.54 | [0.42; 3.91] |
| Tolver 2015 | 11 | 113 | | 9.73 [| 4.96; 16.75] |
| EI–Awady 2009 | 1 | 40 | | 2.50 [| 0.06; 13.16] |
| Bulus 2013 | 0 | 40 | F | 0.00 | [0.00; 8.81] |
| Rutegard 2018 | 18 | 273 | | 6.59 [| 3.95; 10.22] |
| Random effects model | | 4660 | \diamond | 5.20 | [3.32; 8.04] |
| Heterogeneity: $I^2 = 92\%$, $\tau^2 = 0.4593$ | | | | | |
| Female | | | | | |
| Zieren 2005 | 13 | 224 | | 5.80 | [3.13; 9.72] |
| Random effects model | | 224 | \diamond | 5.80 | [3.40; 9.74] |
| Heterogeneity: not applicable | | | | | |
| Random effects model | | 4884 | A state of the | 5.30 | [3.55; 7.85] |
| Heterogeneity: $I^2 = 91\%$, $\tau^2 = 0.4002$ | | | | | |
| | | | 0 5 10 15 20 25 30 35 40 45 50 | | |

eFigure 2. Incidence rate of sexual dysfunction after inguinal hernia repair by sex. There were no statistically significant differences.

| Author (Year of Publication) Incid | dence | Total | Events per 100 observations E | Events | 95%-CI |
|---|-------|-------|----------------------------------|--------|---------------|
| Europe | | | | | |
| Pommergaard 2017 | 115 | 1019 | + | 11.29 | [9.41; 13.39] |
| Aasvang 2006 | 95 | 1015 | + | 9.36 | [7.64; 11.32] |
| Bischoff 2012 | 88 | 805 | + | 10.93 | [8.86; 13.29] |
| Aasvang 2010 | 9 | 442 | + | 2.04 | [0.94; 3.83] |
| Schouten 2012 | 18 | 386 | | 4.66 | [2.79; 7.27] |
| Bittner 2010 | 12 | 268 | | 4.48 | [2.33; 7.69] |
| Andresen 2017 | 4 | 259 | +- | 1.54 | [0.42; 3.91] |
| Tolver 2015 | 11 | 113 | • • • | 9.73 | [4.96; 16.75] |
| Zieren 2005 | 13 | 224 | | 5.80 | [3.13; 9.72] |
| Bulus 2013 | 0 | 40 | • | 0.00 | [0.00; 8.81] |
| Rutegard 2018 | 18 | 273 | | 6.59 | [3.95; 10.22] |
| Random effects model | | 4844 | \diamond | 5.47 | [3.65; 8.14] |
| Heterogeneity: $I^2 = 92\%$, $\tau^2 = 0.4010$ | | | | | |
| Africa | | | | | |
| El-Awady 2009 | 1 | 40 | | 2.50 | [0.06; 13.16] |
| Random effects model | | 40 | | 2.50 | [0.35; 15.73] |
| Heterogeneity: not applicable | | | | | |
| Random effects model | | 4884 | <u> </u> | 5.30 | [3.55; 7.85] |
| Heterogeneity: $I^2 = 91\%$, $\tau^2 = 0.4002$ | | | | | |
| | | (| 0 5 10 15 20 25 30 35 40 45 50 | | |

eFigure 3. Incidence rate of sexual dysfunction after inguinal hernia repair by continent. There were no statistically significant differences.



 $\mbox{eFigure 4.}$ Funnel plot to assess bias. Eggers test revealed that $\mbox{p}=0.94,$ indicating that there was no asymmetry or publication bias.

| Section/topic | # | Checklist item | Reported on page # | |
|------------------------------------|----|---|--------------------|--|
| Title | | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | Title page | |
| Abstract | | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal, and synthesis methods; results; limitations; conclusions, and implications of key findings; systematic review registration number. | 2 | |
| Introduction | | Ť | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 4 | |
| Objective | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 4 | |
| Methods | | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (eg Web address), and, if available, provide registration information including registration number. | 5 | |
| Eligibility criteria | 6 | Specify study characteristics (eg PICOS, length of follow-up) and report characteristics (eg years considered, language, publication status) used as criteria for eligibility, giving rationale. | 5 | |
| Information source | 7 | Describe all information sources (eg databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 5 | |
| Search | 8 | Present full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated. | 5 | |
| Study selection | 9 | State the process for selecting studies (ie screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 5 | |
| Data collection process | 10 | Describe method of data extraction from reports (eg piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 6 | |
| Data items | 11 | List and define all variables for which data were sought (eg PICOS, funding sources) and any assumptions and simplifications made. | 6 | |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 6 | |
| Summary measure | 13 | State the principal summary measures (eg risk ratio, difference in means). | 6 | |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (eg I ²) for each meta- analysis. | 6 | |
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (egpublication bias, selective reporting within studies). | 6 | |
| Additional analysis | 16 | Describe methods of additional analyses (eg sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre- specified. | 6 | |
| Result | | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 7 | |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (eg study size, PICOS, follow-up period) and provide the citations. | 7 | |

eTable 1. PRISMA Checklist

(Continued)

eTable 1. Continued

| Section/topic # | | Checklist item | Reported on page # | |
|-------------------------------|----|--|--------------------|--|
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | 7 | |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 7 | |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | 7 | |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | 7 | |
| Additional analysis | 23 | Give results of additional analyses, if done (eg sensitivity or subgroup analyses, meta-regression [see Item 16]). | 7 | |
| Discussion | | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (eg healthcare providers, users, and policy makers). | 8 | |
| Limitations | 25 | Discuss limitations at study and outcome level (eg risk of bias), and at review-level (eg incomplete retrieval of identified research, reporting bias). | 8 | |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 8 | |
| Funding | | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (eg supply of data); role of funders for the systematic review. | Title page | |

Alkhaffaf

Aasvang Bittner

Linderoth

Skawran

2010

2010

2010

2011

2011

No

Yes

Yes

No

No

N/A

N/A

Author Year Included **Reason for exclusion** Notes Libman 1991 No Wrong study population Compared sexual consequences of prostatectomy and herniorrhaphy. Study endpoints did not include sexual Campos 1993 No Wrong outcome of interest dysfunction. Schrenk 1996 No Did not report incidence of sexual Did not report incidence of sexual dysfunction dysfunction. Callesen Wrong outcome of interest 1999 No Measured general chronic pain unrelated to sexual function. Mikkelsen 2004 No Did not distinguish new cases Did not perform a preoperative questionnaire to distinguish new sexual dysfunction from existing sexual dysfunction. O'Dwyer 2005 No Did not distinguish new cases Did not perform a pre-operative questionnaire to distinguish new sexual dysfunction from existing sexual dysfunction. Yes N/A N/A Zieren 2005 2006 Yes N/A N/A Aasvang 2007 No Wrong study population Compared post-hernia repair patients Aasvang who had dysejaculation vs those with chronic pain but no dysejaculation or pain-related sexual dysfunction. Ertan 2007 No Did not report incidence of sexual Did not report incidence of sexual dysfunction dysfunction. Staal 2007 Measured by PDI scale scores rather than No Did not report incidence of sexual the number of patients with and dysfunction without sexual dysfunction. Showed improvement in "sexual behavior" score in both no chronic pain and chronic pain groups when compared to preoperative. Kehlet 2008 No Review of studies Review of outcomes found by other studies using the Danish database Kehlet 2008 No Wrong outcome of interest Doesn't measure sexual dysfunction. Zieren 2008 No Wrong study population Measured sexual function after groin hernia repair with or without excision of the ilio-inguinal nerve. Eklund No Study endpoints did not include sexual 2009 Wrong outcome of interest dysfunction. 2009 No Did not perform a preoperative Agarwal Did not distinguish new cases questionnaire to distinguish new sexual dysfunction from existing sexual dysfunction. El-Awady 2009 Yes N/A N/A

Wrong study population

Wrong study population

Wrong outcome of interest

eTable 2. Reason for Inclusion/Exclusion of All Studies Describing Sexual Dysfunction after Hernia Repair

(Continued)

Only looked at the litigations resulting from various complications.

Only included patients with severe persistent pain after laparoscopic inguinal herniorrhaphy.

Study endpoints did not include sexual

N/A

N/A

dysfunction.

eTable 2. Continued

| Author | Year | Included | Reason for exclusion | Notes |
|----------------|------|----------|--|---|
| Bischoff | 2012 | Yes | N/A | N/A |
| Schouten | 2012 | Yes | N/A | N/A |
| Andresen | 2013 | No | Description of study | Protocol description with no results or analysis |
| Akpo | 2013 | No | Wrong study population | Description of inguinal hernias; not hernia repair |
| Bulus | 2013 | Yes | N/A | N/A |
| Jangjoo | 2014 | No | Did not report incidence of sexual dysfunction | Did not report overall incidence of sexual dysfunction. |
| Tolver | 2015 | Yes | N/A | N/A |
| Friis-Anderson | 2016 | No | Review of studies | Analyzed the usefulness of the Danish inguinal hernia database with no conclusions about sexual dysfunction. |
| Verhagen | 2016 | No | Wrong study population | Only included patients who had chronic groin pain after inguinal herniorrhaphy and had neurectomy of the ilioinguinal nerve and/or the genital branch of the genitofemoral nerve or funicular release if vas deferens kinked from mesh. |
| Bansal | 2017 | No | Wrong outcome of interest | Measured testicular function (volume and blood flow by Doppler, FSH, LH, testosterone levels) |
| Iakovlev | 2017 | No | Wrong study population | Study population: only included specimens of mesh and other spermatic cord structures from patients whose mesh was explained to treat chronic post-herniorrhaphy pain. |
| Mclean | 2017 | No | Wrong study population | Study population was pelvic organ prolapse, not hernia. |
| Molegraaf | 2017 | No | Wrong outcome of interest | Study endpoints did not include sexual dysfunction. |
| Nordin | 2017 | No | Wrong study population | Study population: claims from previous hernia repairs - only 2 claims were due to sexual dysfunction and doesn't report any details about the 2. |
| Andresen | 2017 | Yes | N/A | N/A |
| Pommergaard | 2017 | Yes | N/A | N/A |
| Melkemichel | 2018 | No | Wrong outcome of interest | Study endpoints did not include sexual dysfunction. |
| Rutegard | 2018 | Yes | N/A | N/A |
| Gutlic | 2018 | No | Did not distinguish new cases | Did not perform a preoperative questionnaire to distinguish new sexual dysfunction from existing sexual dysfunction. |

N/A, not applicable.