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Consensus statement for the management of chronic pelvic pain and endometriosis: proceedings of an expert-panel consensus process

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Objective: To develop recommendations for the medical and surgical care of women who present with chronic pelvic pain (CPP) and are likely to have endometriosis as the underlying cause.

Design: An expert panel comprised of practicing gynecologists from throughout the United States and experts in consensus guideline development was convened. After completion of a structured literature search and creation of draft algorithms by an executive committee, the expert panel of >50 practicing gynecologists met for a 2-day consensus conference during which the clinical recommendations and algorithms were reviewed, refined, and then ratified by unanimous or near-unanimous votes.

Patient(s): Women presenting with CPP who are likely to have endometriosis as the underlying cause.

Main Outcome Measure(s): None.

Conclusion(s): Chronic pelvic pain frequently occurs secondary to nongynecologic conditions that must be considered in the evaluation of affected women. For women in whom endometriosis is the suspected cause of the pain, laparoscopic confirmation of the diagnosis is unnecessary, and a trial of medical therapy, including second-line therapies such as danazol, GnRH agonists, and progestins, is justified provided that there are no other indications for surgery such as the presence of a suspicious adnexal mass. When surgery is necessary, laparoscopic approaches seem to offer comparable clinical outcomes to those performed via laparotomy, but with reduced morbidity. The balance of evidence supports the use of adjuvant postoperative medical therapy after conservative surgery for CPP. There is some evidence that adjuvant presacral neurectomy adds benefit for midline pain, but currently, there is inadequate evidence to support the use of uterosacral nerve ablation or uterine suspension. Hysterectomy alone has undocumented value in the surgical management of women with endometriosis-associated CPP. (Fertil Steril® 2002;78:961–72. ©2002 by American Society for Reproductive Medicine.)

Key Words: Pain, endometriosis, guidelines, consensus

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Chronic pelvic pain (CPP) and endometriosis are two of the more common symptomatic conditions in women's healthcare. Ten percent of visits to gynecologists, 20% of laparoscopic procedures performed by gynecologists, and ≤18% of hysterectomies are performed for CPP (1, 2). Chronic pelvic pain has multiple etiologies, and in many women a specific cause may remain uncertain or unknown. Endometriosis is a common cause of CPP. Currently there exist no valid epidemiological data to establish the true incidence of endometriosis in women with CPP. However, estimates of the percentage of women with CPP who also have endometriosis range as high as 70%–90% (3–5). The natural history of endometriosis remains open to speculation because no prospective observational studies have been undertaken or reported. Although endometriosis has been observed in females as young as 10.5 years, the disease usually presents during the reproductive years and is stable or regresses in 50% of women (6, 7), whereas in the remainder, progression is generally slow. The type of CPP most commonly attributed to endometriosis is dysmenorrhea, but both cyclic and noncyclic

pain as well as deep dyspareunia and dyschesia are described.

Evidence regarding the efficacy and other characteristics of available treatments, medical and surgical, for CPP and endometriosis is incomplete. As a result, management of women with CPP thought to be secondary to endometriosis varies widely and may often be suboptimal and costly. These variations and opportunities for improvement, as well as the availability of new evidence and changing opinions regarding optimal management, suggest the potential value of an evidence-based consensus statement concerning the most appropriate care for these patients based on a combination of expert opinion and a current literature review.

Herein we describe the methodology and results of an expert-panel consensus statement development process. The available evidence for clinical management guidance is also summarized. The consensus recommendations and algorithms do not address the additional diagnostic or treatment steps indicated in women for whom the presenting CPP appears to have a cause other than endometriosis, or for whom other conditions (including pelvic masses) would necessarily complicate management. Similarly, the consensus statement does not address treatment for infertility associated with endometriosis and provides only partial guidance for women with CPP that is believed to be secondary to endometriosis (whether or not infertility is demonstrated or suspected), for whom immediate fertility is a primary goal.

CONSENSUS STATEMENT DEVELOPMENT METHODS

The consensus statement (comprising clinical recommendations and algorithms) was developed by a panel of 52 practicing gynecologists and methodology experts according to accepted standards for development of clinical practice guidelines and consensus statements (8–10). Panel members were selected by a consensus statement executive committee (CSEC), based on practice credentials and geographic location. The development process included a MEDLINE literature search for articles addressing etiology and pathophysiology, epidemiology, and treatment of CPP and endometriosis. The initial search covered the period 1966 through August, 1999 and was updated through December, 2001. The article list was reviewed by four pairs of reviewers (comprising the CSEC), focusing on [1] epidemiology of CPP, [2] etiology, pathophysiology and impact of endometriosis on CPP, [3] medical therapy for endometriosis and CPP, and [4] surgical therapy for endometriosis and CPP.

The CSEC reviewed and summarized all relevant articles in a series of 5- to 10-page evidence summaries. The CSEC then developed preliminary diagnostic and treatment algorithms, and the summaries and initial clinical recommendations were distributed to the consensus panel members in advance of the conference.

The consensus panel met to review the evidence summaries and draft materials during a 2-day consensus conference. The conference began with general sessions addressing consensus statement goals and methods, followed by individual subcommittee meetings to review and revise the draft materials. Ten consensus panel members were assigned by random drawing to each of three subcommittees which addressed [1] diagnostic processes, [2] medical therapies, and [3] surgical therapies. Each subcommittee reviewed the relevant evidence summaries and draft algorithms and recommendations and revised the drafts after extensive discussion. The subcommittee presented their revisions to the entire panel in a subsequent plenary session, with ratifications by formal vote. All three subcommittees' final algorithms and recommendation statements were approved by unanimous or near-unanimous (>95%) votes.

SUMMARY OF THE EVIDENCE

Herein we present the available evidence relevant to the important areas of clinical management of CPP that occurs in association with endometriosis. Although some aspects of the diagnosis and treatment of CPP have been studied extensively, well-designed studies regarding other important aspects have not been reported or were not found during this consensus process.

Medical Therapy

Nonsteroidal Anti-Inflammatory Drugs

Nonsteroidal anti-inflammatory drugs (NSAIDs) have been studied extensively in randomized controlled trials (RCTs) for treatment of primary dysmenorrhea and are of proven efficacy (11–16). Although not specifically studied for noncyclic CPP, it is apparent that NSAIDs are used empirically as a first-line medical treatment for CPP.

Oral Contraceptives

High-dose estrogen–progestin combinations were initially employed as part of a "pseudopregnancy regimen" in the management of symptomatic endometriosis (17). Various low-dose oral contraceptives (OCs) have been studied without placebo controls as initial management of primary dysmenorrhea with a high degree of success (18–20). These studies included patients not screened by laparoscopy, suggesting the possibility that patients with CPP and endometriosis may have been included.

Only a single RCT of low-dose OCs for CPP and endometriosis has been published (21). In this 6-month trial, cyclically administered OCs were compared with a GnRH agonist (GnRH-a) in women with laparoscopically diagnosed endometriosis. Oral contraceptives were reported to be less effective for relief of dysmenorrhea and to be of similar efficacy to GnRH-a for relief of dyspareunia and nonmenstrual pain.

Danazol

Danazol is a synthetic androgen that inhibits ovarian steroid and pituitary gonadotropin release (22). A group of four 6-month RCTs (with possible patient overlap) compared danazol with placebo after laparoscopic diagnosis of endometriosis in which danazol was more effective than placebo (23–26). One of these studies also reported a significant improvement in painful symptoms after treatment with danazol compared with placebo in patients who had not undergone surgery (24). No other studies were found that reported the use of danazol in the management of CPP or dysmenorrhea or in patients with clinically suspected endometriosis.

Gonadotropin-releasing Hormone Agonist

Gonadotropin-releasing hormone agonist effectively induces a "functional oophorectomy" in treated patients, thereby dramatically reducing estradiol production. Only one published RCT compared a GnRH-a (leuprolide acetate) to placebo (27). Because most (27 of 31) placebo patients dropped out by 3 months because of symptoms, valid scientific comparisons could not be made between the groups. Nevertheless, a substantial degree of pain relief was demonstrated in the GnRH-a group.

The majority of studies compared GnRH-a with danazol (400–800 mg/d) administered to women with laparoscopically confirmed symptomatic endometriosis. A large group of studies demonstrated the danazol and GnRH-a treatment regimens to be equally efficacious (28–42).

Empiric use of GnRH-a was tested by RCT in 100 women with noncyclic pelvic pain who had not undergone assessment by laparoscopy but nevertheless had clinically suspected endometriosis (5). After 12 weeks of therapy with depot leuprolide acetate (3.75 mg/mo), decreases in dysmenorrhea, pelvic pain, and tenderness were noted in the treatment group. Endometriosis was visualized at subsequent laparoscopy in 78% of the leuprolide-treated and 87% of the placebo-treated groups. Women who did not present visual evidence of endometriosis, however, also responded to treatment with GnRH-a in this study.

Steroidal and nonsteroidal agents have been employed in the context of add-back regimens to allow maintenance of the function and efficacy of the GnRH-a while suppressing side effects such as osteopenia and vasomotor symptoms. A number of RCTs have demonstrated the efficacy of add-back regimens with various GnRH-a for treatment of endometriosis during 6-month courses (43–48).

Two RCTs have assessed the role of add-back with depot leuprolide acetate (depot GnRH-a) during therapy for >6 months (49, 50). In an open-label trial of 19 patients who received GnRH-a with either norethindrone (10 mg/d p.o.) or norethindrone (2.5 mg/d) + cyclic etidronate (400 mg/d) during a 48-week trial (49), pain symptoms, extent of disease, and vasomotor symptoms were all suppressed without significant change in bone density in either group. Hornstein et al. (50) reported 201 patients treated with depot leuprolide acetate for 52 weeks and randomized into one of four add-back groups. Groups received placebo, norethindrone acetate (5 mg/d) alone, or norethindrone acetate (5 mg/d) in conjunction with conjugated equine estrogens (0.625 or 1.25 mg/d). Pain symptoms were alleviated in each treatment arm, although the highest number of dropouts due to persistent or recurrent pain was noted in those receiving the higher estrogen doses. Vasomotor symptoms were suppressed in all three add-back groups. Lumbar spine bone mineral density decreased 3.2% in 6 months and 6.3% in 12 months without add-back, but no significant decrease was observed in any of the add-back groups. Adverse lipid changes shown with danazol and GnRH-a consist of decreased high-density lipoprotein (HDL) cholesterol and increased total and low-density lipoprotein (LDL) cholesterol, with greater adverse effects of danazol than those of GnRH-a on lipids (32, 51). Add-back with norethindrone acetate with or without low-dose or high-dose equine estrogen resulted in increased HDL and decreased LDL cholesterol (50). The mechanism of action is unclear but may be related, in part, to hepatic conversion of small but clinically significant amounts of norethindrone acetate to ethinyl estradiol.

Progestins

Medroxyprogesterone acetate (MPA) may be beneficial for patients with CPP secondary to known or suspected endometriosis. Progestins induce decidualization and acyclicity of endometrium and endometriotic tissue. One review article by Vercellini et al. (52) analyzed 27 trials of various progestins for treatment of symptomatic endometriosis, four of which were RCTs (21, 53–55). Variously, progestins were compared with danazol (23), with danazol and an OC (24), with a depot preparation of a GnRH-a (21), and with placebo (25). Dydrogesterone (2 different doses) was found to be no more effective than placebo. In one 12-month trial, MPA depot (150 mg every 90 days) used alone had effects equivalent to those of GnRH-a. In two 6-month trials, the progestins desogestrel (56) or cyproterone acetate (57) were combined with ethinyl estradiol. Overall, odds ratios (OR) for these two non–placebo-controlled randomized trials varied from 0.3 to 2.5, with a common nonsignificant OR of 1.1 (confidence interval [95% CI] = 0.4–3.1). Oral MPA in a 50-mg daily dose was effective in reducing pain scores at the end of therapy, but the benefit was not sustained (58).

Medical Adjunctive Therapy

Many of the agents reviewed above can be used before, after, or both before and after either conservative or radical surgery. Adamson and Nelson (59) suggested that preoperative medical therapy may result in less risk of injury to ureters, blood vessels, and the bowel, although none of these potential benefits have been proved.

Danazol has been evaluated as postoperative adjuvant therapy in three randomized trials (60–62). A dose of 600 mg/d for 6 months after surgery was found to be equivalent to 100 mg/d of MPA and to be superior to placebo although side effects occurred, including bleeding, weight gain, and acne (60). A randomized trial to compare a similar dose of danazol with no therapy (no placebo) for 3 postoperative months demonstrated no advantage with respect to pain recurrence (61). Morgante et al. (62) evaluated low-dose danazol (100 mg/d) in a cohort of women who underwent conservative laparoscopic surgery and 6 months of GnRH-a therapy (62). The danazol group had lower pain scores than did those patients who did not use danazol after the postoperative GnRH-a treatment.

Despite the existence of RCTs evaluating the issue, there is controversy regarding the value of GnRH-a after conservative surgical therapy. An Italian group compared 3 months of postoperative nafarelin (400 μg/day) with placebo nasal spray and found no difference in pain scores at 12 months (63). A larger Italian multicenter RCT of 269 patients, however, has shown that adjuvant GnRH-a therapy was efficacious at 6 months after conservative surgery but failed at 1 to 2 years postoperatively (64).

In a third RCT that was done in the United States, investigators found that women treated with a GnRH-a had better outcomes than women treated with surgery alone (65). Winkel and Bray (66) recently reported the results of a 24-month follow-up of 240 women with endometriosis and CPP who underwent excision alone, laser ablation alone, or laser ablation followed by treatment with leuprolide acetate for 3 to 6 months. In this nonrandomized trial, only 23% of the ablation group was pain free at 24 months, whereas 70% of the ablation plus GnRH-a–treated group remained pain free after the same time interval.

Surgical Therapy

Evaluation of the treatment effect of surgery on endometriosis-associated pain is difficult because few RCTs have been performed and none have compared surgical management to medical treatment.

Surgery Directed at Endometriosis: Overview

Sutton (67) reported that 70% of women treated for endometriosis with laparoscopically directed techniques were improved at 1 year. Redwine (68) reported a cumulative rate of recurrence and persistence (defined as visualizing endometriosis at repeat laparoscopy without regard to symptoms) of 19% by 5 years. Both uncontrolled studies employed retrospective data collection, inconsistent approaches to the measurement of symptoms, and heterogeneity of surgical technique.

In a double-blind RCT, Sutton et al. (69) reported the results of laparoscopically directed conservative surgery (laser vaporization, adhesiolysis, uterosacral nerve ablation) vs. diagnostic laparoscopy alone for stage I–III endometriosis-associated CPP. Ninety percent of those with improvement at 6 months continued to demonstrate improvement at 1 year. Unfortunately, the addition of uterosacral nerve ablation to the surgical procedure confounded interpretation of the efficacy of endometriosis destruction alone in producing pain relief. However, investigators from the same center performed a subsequent double-blind RCT in which all women underwent laparoscopic laser vaporization of endometriosis; half of the women were randomized to receive uterosacral nerve ablation as well (69). At 6 months of follow-up, all patients in the trial were significantly improved compared with baseline, but those with vaporization alone had pain scores that were similar to or better than those of women who underwent vaporization and uterosacral nerve ablation. These findings suggest that local destruction of endometriotic lesions is associated with improvements in pelvic pain, at least at 6 to 12 months after surgery.

Surgery Directed at Endometriosis: Type of Treatment

There are a number of techniques by which endometriosis can be removed or destroyed, and each has potential advantages, disadvantages, and differences in efficacy. However, no RCTs were found that compare surgical excision with energy-based ablation techniques that include vaporization, fulguration, or coagulation. Winkel and Bray (67) reported a 24-month follow-up of women who underwent surgical treatment by excision alone, laser vaporization alone, or laser vaporization plus GnRH-a. Twelve months after surgery, 96% of excision patients were pain free, whereas 69% of those undergoing coagulation were without pain. At 2 years, the corresponding figures were 69% and 23%, respectively. Although these results suggest that excision may be superior to ablation, the retrospective design of the study leaves such a conclusion open to criticism.

Management of Endometriosis-associated Cystic Ovarian Masses

There exist a number of approaches to the surgical management of ovarian cysts encountered in the treatment of endometriosis, including cystectomy, simple drainage, drainage and coagulation, and drainage followed by stripping of the cyst lining. Not all ovarian cysts associated with endometriosis are endometriomas (in one study, none of the excised cysts or cyst linings contained histologically demonstrated endometriosis) (70). In another retrospective study, however, the authors compared outcomes in 231 women managed laparoscopically either with fenestration and ablation (n = 70) or by cystectomy (n = 161) (71). Reoperation rates at 42 months were 23.5% after excision and 57.8% after fenestration and ablation. Somewhat similar results were reported by Beretta et al. (72), who performed an RCT comparing cystectomy with drainage and bipolar electrosurgical coagulation of the lining in 64 women operated on via laparoscopy. Although complication rates were similar, there

were significantly different outcomes in favor of cystectomy for each of the three types of pain evaluated, including dysmenorrhea (15.8% vs. 52.9%), deep dyspareunia (20% vs. 75%), and nonmenstrual pain (10% vs. 52.9%).

Laparoscopy vs. Laparotomy

The literature is replete only with comparisons of laparoscopic and laparotomic surgery that include AFS stage IV endometriosis. Crosignani et al. (73) evaluated women with CPP and stage IV endometriosis after laparoscopic surgery (n = 47) or at the time of laparotomy (n = 108) surgery selected by the surgeon. Many of the women also received medical therapy after surgery. At 24 months, the laparoscopic and laparotomy approaches were about equally effective (approximately two thirds of patients were pain free). Recurrence rates for dysmenorrhea were 16.4% to 20.3% for laparoscopic surgery vs. 20.3% to 27.7% for those performed via laparotomy; 28.6% to 33.3% for deep dyspareunia for laparoscopy vs. 10.4% to 15.4% for dyspareunia; and 17.5% to 25% vs. 15.9% to 20.1% for nonmenstrual CPP.

Conservative surgery at laparotomy was compared with the laparoscopic approach in 81 patients who required repeat surgery for endometriosis (AFS stages I–IV) (74). They were similar with respect to recurrence rates for dysmenorrhea (28.6% vs. 25%), dyspareunia (25% vs. 30%), and noncyclic CPP (23% vs. 34%). Similar results were reported in 132 women with stage III and IV endometriosis who also were found to have ovarian cysts (75).

The incidence of pain recurrence was 19% after laparotomic surgery and 13.4% after laparoscopy in a retrospective study with 12-month follow-up done by Bateman et al. (76). Laparoscopic technique was associated with equivalent operating time, reduced hospital stay, and a more rapid return to work.

Surgery Directed at Pain Transmission

Uterosacral Nerve Ablation. Laparoscopic uterosacral nerve ablation (LUNA) is designed to disrupt the efferent nerve fibers in the uterosacral ligament to diminish uterine pain. However, there seems to be little evidence to support the performance of this procedure. In a cohort study, Lichten and Bombard (77) reported >80% relief from menstrual pain after LUNA that declined to 50% after 12 months. The double-blind RCT reported by Sutton et al. (69), discussed previously, showed that adding LUNA to laser vaporization of endometriosis did not improve pain scores. In fact, in this well-designed double-blinded trial, patients who had LUNA added to the procedure had less successful 6-month outcomes with respect to both dysmenorrhea and chronic nonmenstrual pain.

Presacral Neurectomy. Presacral neurectomy (PSN) is a procedure designed to interrupt sympathetic pathways from the uterus. There have been three reported RCTs, one evaluating PSN as performed via laparoscopy and two that assess results at laparotomy. Although Candiani et al. (78) found that adding PSN to conservative surgery markedly reduced the midline component of menstrual pain, in long-term follow-up, there were no differences between the two groups in the frequency and severity of dysmenorrhea, pelvic pain, and dyspareunia. Tjaden et al. (79) also found that the addition of PSN to standard surgical therapy by laparotomy enhanced pain relief for midline pain. Although this was reported as an RCT, only 8 of 26 patients were randomized, and the study was terminated before completion because of significant reduction in midline pain experienced by the patients undergoing PSN. Chen et al. (80) reported the only RCT evaluating laparoscopic PSN in 68 patients assigned to either PSN or LUNA. These patients had primary dysmenorrhea and were not known to have endometriosis. At 3-month follow-up, both groups were equal in terms of symptom relief (87.9% vs. 82.9%), but the efficacy of PSN was significantly better than that of LUNA (81.8% vs. 51.4%) at 12 months.

Role of Gonadectomy and Hysterectomy

Removal of the ovaries (bilateral oophorectomy), with or without hysterectomy, is generally regarded as the most effective procedure for women who have recurrent symptomatic endometriosis and who have no desire to retain reproductive function. A number of investigators have evaluated the incidence of symptom recurrence after hysterectomy with ovarian retention. One group demonstrated that 18 of 29 women experienced recurrent pain and 9 (31%) underwent reoperation after hysterectomy with ovarian retention (81). Retained ovarian function had an 8.1 OR (CI = 2.1–31.3) of requiring reoperation for CPP. The incidence of persistent or recurrent CPP after hysterectomy and bilateral salpingo-oophorectomy was 10% (11 of 109).

Uterine Suspension Procedures

The consensus group could find no data supporting or refuting the place for uterine suspension as an adjunct in the treatment of endometriosis-associated pelvic pain. Individual practitioner experience can guide the use of this procedure.

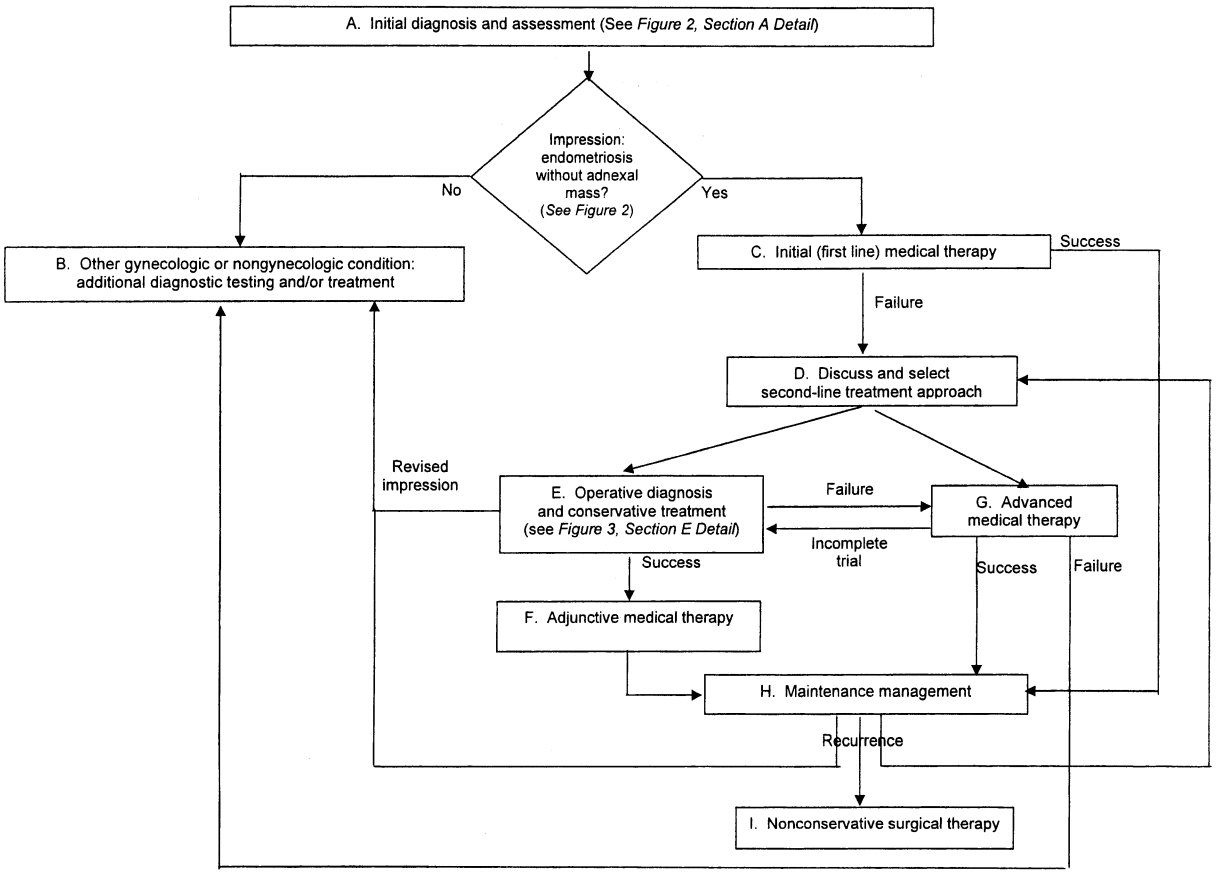
CLINICAL RECOMMENDATIONS AND ALGORITHMS

The overall algorithm produced and approved by the consensus panel (Fig. 1) provides a general guide for the assessment and management of women presenting with CPP. Subalgorithms were created for sections A and E of the overall algorithm, as discussed below.

Section A (seen in detail in Fig. 2) addresses the diagnostic approach to women with CPP, including an assessment of patient preferences and values, leading to an initial diagnostic impression. Significantly, this algorithm identifies women who may have CPP secondary to diagnoses other than endometriosis (section B). Management of these clinical entities, although extremely important, was not consid-

FIGURE 1

Algorithm that delineates the steps for the assessment, diagnosis, and treatment options of patients with chronic pelvic pain and presumed endometriosis: overall approach.



Gambone. Chronic pelvic pain and endometriosis. Fertil Steril 2002.

ered to be within the purview of this expert panel and therefore was not developed further. Sections C through I address management of the target group for the consensus statement. A detailed algorithm is provided for section E in Figure 3.

Section A: Initial Diagnosis and Assessment

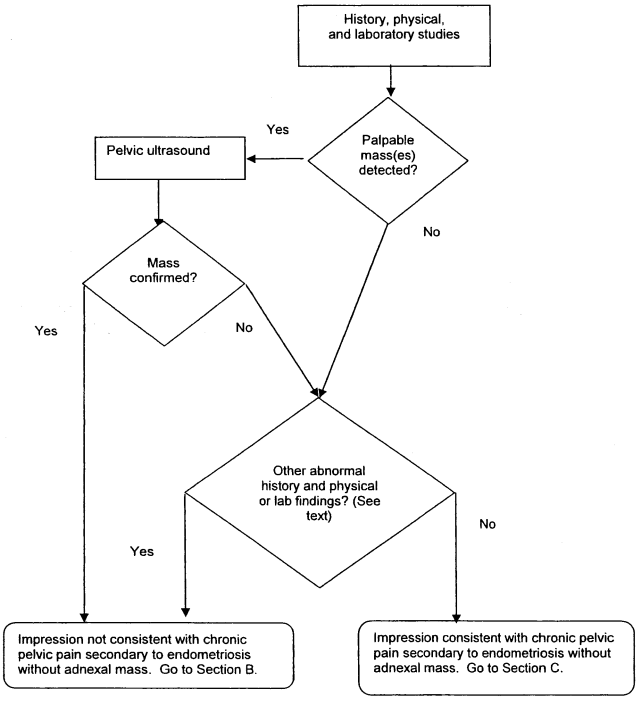
Clinical History

A thorough history of the woman's symptoms, and previous diagnoses and treatments should include, but should not be limited to, the following:

- The presenting pain, including its location, magnitude, timing, relationship to physical exertion, sexual activity, menses, pregnancy, abdominal distention, gastrointestinal (GI) and genitourinary (GU) function, as well as other significant events
- Prior and current diagnoses and treatments for endometriosis, GI or GU problems, infections, musculoskeletal problems, and psychiatric conditions, including information on response to any previous treatments for endometriosis or other conditions related to the presenting pain
- Previous symptoms suspicious for endometriosis, GI or GU problems, infections, musculoskeletal problems, psychological or psychiatric conditions, sexual abuse, or physical abuse
- Menstrual, contraceptive, and sexual histories, including previous menstrual disorders; use of intrauterine devices, OCs, and other contraceptive methods; age of onset of menses; a history of all pregnancy outcomes; and other reproductive tract–related signs or symptoms
- Family history of relevant clinical conditions, including malignancies and pain disorders such as endometriosis

FIGURE 2

Closer view of section A of overall algorithm shown in Figure 1: initial assessment of patients with chronic pelvic pain and presumed endometriosis.



Gambone. Chronic pelvic pain and endometriosis. Fertil Steril 2002.

Physical Examination

A complete gynecologic and targeted physical examination should be conducted considering both potential gynecologic and nongynecologic causes of the pain as well as the concepts of referred pain and the existence of trigger points. Specifically, it should include the following:

- Pelvic exam, focusing on tenderness and its location, the presence or absence of nodularity, particularly in the cul-de-sac, and the detection of palpable masses also in the cul-de-sac or the adnexal regions
- Abdominal exam, focusing on the presence or absence of abdominal distention and the location of the symptoms and tenderness, if present
- Straight leg–raising test, focusing on its ability to induce lower right or left quadrant tenderness

Laboratory and Imaging Studies

Appropriate laboratory tests and imaging studies can be conducted to evaluate for nongynecological causes of CPP and, if endometriosis is present, to assess the extent of the disease. These tests and studies are as follows:

- Pregnancy test
- Urinalysis
- Blood tests, including complete blood count with differential and erythrocyte sedimentation rate
- CA-125 (in selected cases, e.g., evidence of ascites)
- Pelvic ultrasound (if a mass is palpated)
- Magnetic resonance imaging (in selected cases, e.g., if it is necessary to identify deep infiltrative disease preoperatively, although the accuracy of magnetic resonance imaging for this diagnosis is controversial)

Patient Preferences and Values

A thorough discussion and assessment of the patient's preferences and values should be conducted, addressing her near-term and long-term plans and desires regarding fertility, her attitudes and preferences regarding medical and surgical treatments, and other relevant issues.

Development of the Initial Impression

On the basis of the history, physical examination, laboratory, and any indicated imaging studies, an initial impression should be developed. If one or more findings are consistent with a condition other than endometriosis without adnexal mass, then further diagnostic testing and/or treatment should be conducted, as appropriate (see section B of the algorithm). If no findings are consistent with another gynecologic or nongynecologic diagnosis, then endometriosis should be strongly suspected, and first-line medical therapy should be considered.

Section B: Nongynecologic Causes

When a patient's CPP is thought to be due to nongynecological conditions such as irritable bowel syndrome or urologic problems such as chronic cystitis or is associated with psychological problems secondary to physical or sexual abuse, an appropriate workup for these nongynecologic conditions is recommended. Details about specific interventions for nongynecologic conditions or management of women who have adnexal masses were beyond the scope of this consensus group.

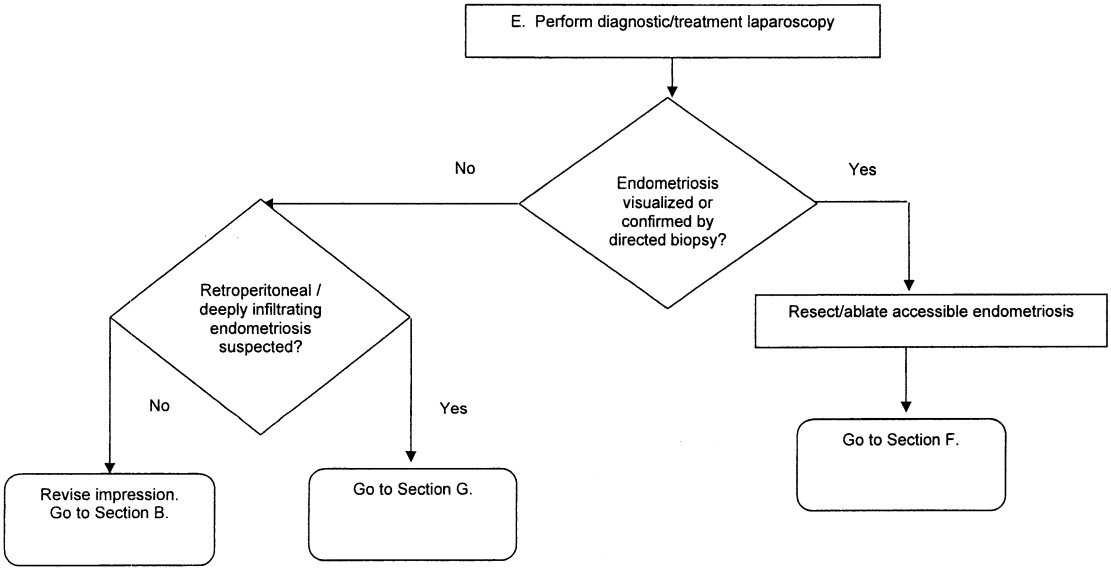
Section C: First-Line Medical Treatment

Medical treatment of women with CPP suspected to be related to endometriosis should begin with a trial of NSAIDs or OCs or a combination of both. Selection of a first-line medical therapeutic agent should be based on the nature of the pain (cyclic or noncyclic), contraindications to NSAIDs or OCs (including a history of GI problems), desire for contraception, and other factors. Nonsteroidal anti-inflammatory drugs should be used around the time of menses in women with cyclic pain, intermittently for those with intermittent cyclic pain, or continuously, based on the patient's symptoms or response to initial therapy. If adequate pain relief is obtained from NSAIDs or OCs (individually or in combination), then a maintenance management regimen should be considered (see section H of the algorithm).

If the initial medical therapy fails to relieve the pain

FIGURE 3

Closer view of section E of overall algorithm shown in Figure 1: laparoscopic diagnosis and conservative treatment of endometriosis.



Gambone. Chronic pelvic pain and endometriosis. Fertil Steril 2002.

symptoms, then a trial of a second-line treatment should be considered (see section D of the algorithm).

Section D: Options for Second-Line Treatment

If first-line medical therapy fails, there are two therapeutic options to consider. First, a trial of advanced medical therapy should be considered (see section G of the algorithm). Alternately, an operative procedure such as laparoscopy or laparotomy may be considered (see section E of the algorithm). Considerations relevant to the selection of one of these treatment options include the following:

- Several available second-line medical treatments are effective and are relatively free of serious complications.
- Laparoscopy and other surgical procedures may be less effective than medical therapies and are reported to entail greater cost and surgical complication rates (reported to be $\geq$1%).
- Patient preferences, cost, effect on future fertility, and the possibility and consequences of a false presumptive diagnosis should always be taken into account.

Section E: Operative Diagnosis and Conservative Surgical Treatment

If patients with CPP undergo diagnostic laparoscopy and endometriosis is identified and thought to cause or contribute to the pain, conservative treatment with laparoscopically directed excision, ablation, or both should be strongly considered provided that the operator is adequately experienced. The location and/or extent of disease in combination with the patient's desires regarding future fertility are important considerations. Patients with dysmenorrhea who have not responded to medical therapy may be offered PSN at laparotomy or, if the operator is adequately experienced, via laparoscopy. Available evidence suggests that LUNA does not benefit women with CPP associated with endometriosis.

Section F: Adjunctive Medical Treatment

Adjunctive medical therapy should be provided to women after conservative surgical treatment for endometriosis and may consist of danazol, GnRH-a, or progestins, based on individual response to previous trials of medical therapy, patient preference, and other factors. There is no published evidence supporting OCs as an adjunctive medical treatment, although a trial and continuation when effective seems reasonable.

Section G: Advanced Medical Therapy

Advanced medical treatment instead of surgery is recommended for women with CPP that has not responded to NSAIDs or OCs or for whom these agents are contraindicated.

Unless contraindicated, advanced medical therapy should begin with a 2-month trial of full-dose danazol, GnRH-a, or a progestin such as MPA and continued for 6 months or

longer if relief is obtained. If a GnRH-a is selected, an appropriate add-back regimen should be considered (unless contraindicated) to minimize treatment side effects.

When side effects or other considerations preclude a complete trial of danazol, GnRH-a or MPA, or if all such agents are contraindicated, then surgical evaluation should be considered.

If adequate pain relief is not obtained from a complete trial of an advanced medical therapy, then alternative diagnoses should be considered (section B above).

If adequate pain relief is obtained from the selected agent, then an appropriate maintenance management regimen should be initiated (section H below), keeping in mind that pain often has multiple causes and may recur, requiring reevaluation and treatment revisions.

Section H: Surveillance and Medical Maintenance

Maintenance, after acute treatment, should include periodic monitoring for return of symptoms, continuing treatment with NSAIDs or OCs, or continuing treatment with second-line medical therapies such as danazol, GnRH-a, or progestins.

Selection of appropriate maintenance management should be based on the history of symptoms, treatment effectiveness, and patient preference, as follows:

- Women who obtain adequate relief from NSAIDs or OCs but for whom symptoms return upon completion or cessation of medical treatment should be maintained on the therapeutic regimen that previously produced relief.
- Women who obtain relief from advanced medical therapies but for whom symptoms return upon reversion to NSAIDs or OCs should be considered for long-term treatment with advanced medical therapies.
- Women who obtain relief from laparoscopic resection and/or ablation should be considered for continuation treatment with NSAIDs or OCs or with advanced medical therapy if symptoms return.

Section I: Nonconservative Surgical Therapy

Bilateral salpingo-oophorectomy, with or without hysterectomy, should be reserved for women who have completed their child bearing and who realize the potential impact of castration on other health parameters such as risk of osteoporosis, sexual dysfunction, and other menopausal issues. Hysterectomy alone has little or no place in the management of women who have CPP secondary to endometriosis alone.

DISCUSSION

A substantial portion of current medical and surgical practice is primarily opinion based. Opinions underlying clinical decision-making are not always based on the best currently available evidence (82, 83). Nevertheless, there remain significant gaps in the body of evidence available for many important clinical problems, a situation that continues to make the opinions of panels of experts a necessary and essential part of clinical decision making (84). This methodology combines a search for the best evidence in conjunction with a formal opinion-based process to gain consensus when available evidence does not provide specific guidance.

Chronic pelvic pain is a common clinical complaint that is responsible for 40% of laparoscopies and 6%–18% of hysterectomies, either alone or in combination with other indications. There is evidence that a substantial proportion of women with CPP have nongynecologic causes for their symptoms (85) and that $\leq$50% have a history of current or previous physical or sexual abuse (86–88). Endometriosis is a histologic diagnosis frequently associated with pain, including CPP. The literature is not consistent regarding the link between visualized endometriosis (the basis of AFS staging) and CPP. Clearly, endometriosis can be asymptomatic, and women with CPP may harbor asymptomatic endometriosis together with other causes for their symptoms. This may be one explanation for therapeutic failure or recurrence, including the persistence of CPP in $\leq$10% of women who have had a hysterectomy and bilateral salpingo-oopherectomy (89, 90). Consequently, it is incumbent on the clinician to consider the potential for entities other than endometriosis when evaluating women with CPP.

Many women with CPP have normal pelvic exams, and many have findings consistent with endometriosis. There have been no published clinical trials that have compared directly surgical and medical therapy for CPP and endometriosis. On the basis of the results of the current review, they could be considered equally effective, however. Consequently, the consensus panel supported the notion of primary medical therapy for women with CPP that is suspected to be related to endometriosis. Should this therapy fail, a trial of advanced medical therapy with danazol, GnRH-a, or continuous progestins is considered an appropriate option without prior laparoscopy. However, when a pelvic or adnexal mass is detected, operative evaluation or surgical exploration is recommended because of the possibility of neoplasia.

For women in whom surgery is performed, the nature of the procedure should be individualized and tailored to the desires of the patient regarding future fertility, the location and extent of disease, and the experience and expertise of the surgeon. It is clear that successful surgical results may be temporary and that the use of postoperative adjuvant medical therapy appears to reduce or delay the return of CPP. Although there is some evidence that presacral neurectomy provides relief of midline pain in women with endometriosis, available evidence suggests that uterosacral ablation is not effective. We were unable to find evidence that adjuvant uterine suspension has undergone critical evaluation.

For women who have no desire for future fertility and who are willing to deal with the risks of surgical menopause,

bilateral oophorectomy, with or without hysterectomy, has been shown to relieve symptoms, provided that endometriosis is the cause of the CPP or at least is a significant contributor to it.

Finally, we demonstrated the use of a formal consensus development process in facilitating the critical review and interpretation of a body of evidence by a panel of practicing gynecologists.

This process and the participation of a large panel of practicing gynecologists differed from other consensus development processes, which often rely on a much smaller group of academic experts, with far less geographic and practice-setting diversity and representation. Although the advanced preparation and initial formulation of consensus statements were performed by a smaller executive committee (CSEC), thereby limiting the breadth of opinion, substantial changes were made by the larger panel during a 3-day conference. The consensus statement resulting from this process may be more acceptable to physicians in diverse community-based practice settings, given the central role that such physicians played in the statement's final development.

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