RECOMMENDATION

Should we perform subtotal hysterectomy associated with sacral colpopexy for genital prolapse to prevent the risk of endometrial cancer?

Faut-il réaliser systématiquement une hystérectomie subtotale lors d’une promontofixation pour prolapsus génital en prévention du risque de cancer de l’endomètre ?


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Received 5 March 2021; accepted 20 March 2021
Available online 16 April 2021

KEYWORDS
Subtotal hysterectomy; Pelvic organ prolapse; Endometrial carcinoma; Sacral colpopexy

Summary
Objective. — In a menopausal woman scheduled for curative surgery for pelvic organ prolapse (POP) by sacral colpopexy (SC), the question of concomitant hysterectomy is frequently considered by the surgeon. The risk of endometrial cancer (EC) exists in this population, and increases with age and body mass index. The French college of gynecologists and obstetricians (CNGOF) decided to issue good practice guidelines on subtotal hysterectomy (SH) for postmenopausal women scheduled for SC for POP.
Methods. — The CNGOF has decided to adopt the AGREE II and GRADE systems for grading scientific evidence. Each recommendation for practice was allocated a grade, which depends on the quality of evidence (QE) (clinical practice guidelines).

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https://doi.org/10.1016/j.purol.2021.03.006
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Introduction

In a menopausal woman scheduled for curative surgery for pelvic organ prolapse (POP), the question of concomitant hysterectomy is frequently considered by the surgeon. Several potential benefits have been underlined. An enlarged uterus is sometimes surgically problematic, since the suspension may place the uterine fundus above the promontory. Concerning the risk of POP recurrence, sacral hysteropexy is as effective as sacral colpopexy (SC) and hysterectomy in anatomical outcomes. However, SC and hysterectomy are associated with an increase in operating time and blood loss. Total hysterectomy should be avoided since it is associated with an increased risk of vaginal mesh exposure [1]. Conservation of the uterus is not associated with improved sexual function. Therefore, when hysterectomy is necessary during SC, subtotal hysterectomy (SH) should be performed. The decision to perform SH should take into account the choice of the patient and the risk—benefit balance based on the patient’s age, history, and symptoms and on surgical risks. A preoperative assessment including imaging and an endometrial sample reduces the rate of occult endometrial carcinoma (EC), without, however, eliminating it. The prevalence of occult EC found on pathological analysis after SH in this context (concomitant SH associated with SC) is low. The risk of EC increases with age and body mass index.

Results. — The prevalence of occult endometrial cancer (EC) found on pathological analysis after SH in this context (concomitant SH associated with SC) is low (<1%) (QE: high). Few studies have assessed the value of preoperative uterine exploration. Performing SH during SC is associated with its own risks, which may diminish the potential “carcinological prevention benefit”. Uterine morcellation, performed by laparoscopy or a robot-assisted procedure, is associated with a low risk (<0.6%) of dissemination of an unknown sarcoma/EC (QE: moderate). A risk of dissemination of parasitic myomas (<0.5%) is also possible (QE: moderate).

Conclusion. — It is not recommended to perform a subtotal hysterectomy associated with sacral colpopexy for the sole purpose of reducing the occurrence of endometrial cancer (Recommendation: STRONG [GRADE 1—]; the level of evidence was considered to be low and the risk—benefit balance was considered not to be favorable).

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Résumé

Objectif. — Chez une femme ménopausée qui doit avoir une promontofixation pour un prolapsus génital, la question de l’hystérectomie concomitante est fréquemment envisagée par le chirurgien. Le risque de cancer de l’endomètre (CE) existe dans cette population et augmente avec l’âge et l’indice de masse corporelle. On peut se poser la question de l’éventuel effet préventif de cette hystérectomie subtotale sur le risque de CE dans cette population. Le Collège français des gynécologues et obstétriciens (CNGOF) a décidé de publier des recommandations de bonne pratique sur l’hystérectomie subtotale (SH) des femmes ménopausées programmées en promontofixation pour prolapsus génital.

Méthodes. — Le CNGOF a décidé d’adopter les systèmes AGREE II et GRADE pour le classement des preuves scientifiques. Chaque recommandation de pratique s’est vu attribuer une note, qui dépend de la qualité des preuves (QP).

Résultats. — La prévalence du cancer de l’endomètre occulte trouvé sur l’analyse pathologique après hystérectomie subtotale dans ce contexte (lors d’une promontofixation) est faible (<1%) (QP : élevée). Peu d’études ont évalué la valeur de l’exploration utérine préopératoire (biopsie d’endomètre et échographie pelvienne). La réalisation d’une hystérectomie subtotale en cours de promontofixation est associée à des risques propres, qui peuvent diminuer le bénéfice éventuel de prévention carcinologique. Le morcellement utérin, réalisé par coelioscopie ou avec ou sans assistance robotisée, est associé à un faible risque (<0,6%) de dissémination d’un sarcome ou cancer de l’endomètre méconnu (QP : modérée) Un risque de dissémination de myomes parasitaires (<0,5%) est également possible (QP : modérée).

Conclusion. — Il n’est pas recommandé de pratiquer une hystérectomie subtotale associée à une promontofixation dans le seul but de réduire la survenue d’un cancer de l’endomètre (Recommandation : FORTE [GRADE 1—] ; le niveau de preuve a été jugé faible et le rapport bénéfice/risque était considéré comme non favorable).

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Since the prevalence of EC is less than 1% for these women, the number of patients to be treated (by SH) would be too high to avoid EC. Moreover, this risk is probably decreased in asymptomatic women (no vaginal bleeding) in whom preoperative pelvic ultrasound revealed no increased endometrial thickness. A preoperative endometrial biopsy may also be discussed before surgery.

The French college of gynecologists and obstetricians (CNGOF) decided to issue good practice guidelines on SH for postmenopausal women scheduled for SC for POP. The aim of this study was an exhaustive literature review to enable the drawing up of guidelines.

**Methods**

These guidelines were developed by a committee of experts from the CNGOF [2]. The committee included specialists in gynecologic surgery with expertise in the management of patients with benign disease, uterine/cervical cancer, as well as specialists in pelviperineology/urogynecology and methodologists with experience in evidence synthesis and guideline development. Following formulation of PICO (Patient intervention comparison outcome) clinical questions, the guideline process continued with a series of telephone conferences and electronic-based discussions between committee members. A final face-to-face meeting was held in October 2020 to decide on the guideline recommendations. In collaboration with the methodologists, a search strategy was designed using key terms and keywords for each clinical question. The search was limited to human studies written in English or in French. The PubMed platform was used to search MEDLINE. The Cochrane Central Register of Controlled Trials (CENTRAL), the Cochrane Database of Systematic Reviews, EMBASE, and the UK National Health Service’s Economic Evaluation Database were also used. MeSH terms and non-MeSH terms were used. Search equations used “AND” and “OR” on MEDLINE/PubMed. Key words used were: “subtotal hysterectomy”; “hysterectomy”; “pelvic organ prolapse”; “endometrial carcinoma”; “sacral colpopexy”; “endometrial cancer”; “sacral hysteropexy”.

The working method used to draw up the guidelines was GRADE®, which, after quantitative analysis of the literature, can be used to determine separately the quality of evidence, i.e., to estimate the confidence one can have in the analysis of the effect of the quantitative intervention and in the level of recommendation. The quality of evidence was divided into four categories ranging from high (future searches will very probably not change the confidence in the estimation of the effect) to very low (the estimation of the effect is very uncertain). The quality of evidence is analyzed for each study, and then an overall level of evidence is defined for a given question and criterion. The final formulation of the guidelines is binary, either positive or negative, either strong (should be done or should not be done [GRADE 1+ or 1−]) or weak (should probably be done or should probably not be done [GRADE 2+ or 2−]).

The strength of the guideline is determined as a function of key factors validated by the experts after a vote, using the Delphi method and the GRADE grid, according to the different parameters: estimation of the effect; overall level of evidence (the higher it is, the more likely the guideline will be strong), balance between wanted and unwanted effects (the more favorable the balance, the more likely the guideline will be strong), the values and preferences ideally obtained directly from the people concerned (patient, doctor, decision maker), and cost (the greater the cost or the use of resources, the more likely the guideline will be weak). To formulate a guideline, at least 50% of the participants must have an opinion and less than 20% prefer the opposite proposal. To formulate a strong guideline, at least 70% of the participants must be in agreement. The following situations were excluded and have not been addressed in these clinical practice guidelines: recurrence of POP, hysterectomy in a patient on anticoagulant treatment or with a coagulation disorder. The PICO question was as follows: ‘‘In a postmenopausal woman undergoing sacral colpopexy for pelvic organ prolapse (P), is subtotal hysterectomy (I) more effective (O) than conservation of the uterus (C) in reducing the incidence/prevalence of cancer of the uterus?’’ An external expert panel from university hospitals, general hospitals, and private practice reviewed the guidelines and the final version included their suggestions/criticisms when appropriate.

**Results**

**Prevalence of occult uterine cancer in women undergoing POP surgery**

Von Bargen et al. studied the prevalence of diagnosis of occult EC among 1214 patients, including 1044 SH and 410 SC procedures in 3 centers [3]. Among the population with POP, 3 cases of hyperplasia with or without atypia (0.7%) and 2 cases of EC (0.5%) were found. No uterine sarcoma was described. The average age of the population was 48 years old. Hyperplasia and EC were found in patients of mean age 53 years and 48.5 years, respectively. Among the 6 cases of hyperplasia and the 8 cancers in the entire study population, preoperative endometrial biopsies revealed no abnormality in 67% and 50% of cases, respectively [3]. Ackenbom et al. were interested in the discovery of occult cancers among 1196 cases of POP surgery with hysterectomies (mean age 62.3 years), including 42.8% (n = 512) of robotic-assisted procedures or laparoscopies with uterine morcellation in 494. Among this subgroup, no case of endometrial cancer or sarcoma was found. Only 2 cases of hyperplasia were described. The incidence of occult cancers in the cohort of 1196 women presenting with POP was 0.8% [4]. Hill et al. described 2 cases of EC in 63 (3.17%) SH procedures during robotic-assisted SC. No preoperative endometrial biopsy was performed. The 2 cases corresponded to 2 postmenopausal patients without preoperative symptoms [5]. Osmundsen et al. described the presence of 2 cases of EC after morcellation among 45 robotic-assisted SH procedures associated with SC in predominantly postmenopausal patients (78%), i.e., a rate of 4.4% [6]. Saliba et al. did not find neoplastic lesions in 64 SH procedures among 94 laparoscopic SC procedures in patients of average age 60 years [7]. A preoperative endometrial biopsy was performed only if preoperative pelvic ultrasound revealed increased endometrial thickness. Desai et al. studied the prevalence of occult EC in
a retrospective multicenter cohort (registered in New York state) of 229,536 benign hysterectomies including 13.8% of POP surgical procedures (n = 31,567) and 28.6% (n = 65,000) SH procedures. The median age of patients was 47 years old. There was no information concerning the number of SC. Occult cancer was described in 2207 (0.96%) cases in the entire population, including 1716 EC (0.75%) and 495 uterine sarcomas (0.22%). The risk of cancer diagnosis was dependent on the surgical indication and the patient’s age. The risk of occult EC was increased in patients between 60 and 64 years of age compared to patients between 45 and 49 years of age (RR = 7.08; 95% CI: 5.34–9.39). Compared to patients with hysterectomy performed for fibroids, those with hysterectomy performed for POP had a reduced risk of diagnosis of occult cancer (RR = 0.29; 95% CI: 0.22–0.39). Obesity, diabetes, and high blood pressure were associated with an increased risk of EC [8]. In addition, the prevalence of occult lesions in the event of a hysterectomy performed for presumed benign diseases, whatever the indication, is low. In a multicenter cohort study, 36,470 fragmentation hysterectomies were extracted from a registry of 232,882 minimally invasive hysterectomies performed in 500 US hospitals [9]. Among these 36,470 cases, uterine cancer was identified in 99 cases (prevalence of 0.27%), endometrial hyperplasia in 368 (1.01%), and other gynecological cancers in 26 (0.07%). Age was the main risk factor for cancer and uterine hyperplasia. Compared with women < 40 years, the prevalence of uterine cancer was multiplied by 5 (95% CI, 1.91–12.93) between 50 and 54 years, by 19 (95% CI, 7.66–48.95) between 55 and 59 years, by 21 between 60 and 64 (95% CI, 7.22–63.21), and by 36 over 65 years (95% CI, 14.14–91.53) [9].

Preoperative assessment

Few studies have assessed the value of preoperative uterine exploration. Vallabh-Patel et al. studied the prevalence of neoplastic lesions found after fragmentation in cases of SH performed during 786 SC in patients of average age 59 years. Four EC (3 adenocarcinomas and 1 serous papillary) were diagnosed [10]. Based on clinical history, 124 patients out of 679 had a preoperative endometrial biopsy before 2013; during this period, 4 cases of abnormality were diagnosed (3.2%). After 2013, 107 patients had a systematic endometrial biopsy; during this second period, no case of neoplasmia was found in 227 women [10]. One study assessed the effectiveness of a systematic preoperative endometrial biopsy in asymptomatic patients before hysterectomy for POP [11]. Out of 708 hysterectomies (mean age = 56 years) including 18% of laparoscopic or robot-assisted procedures, 125 patients (18%) had an endometrial biopsy, 43 patients (6%) had only preoperative pelvic ultrasound, and 21 patients (3%) had both exams. Of the 5 cases (0.6%) of uterine cancers diagnosed, preoperative examination (endometrial biopsy and/or pelvic ultrasound) was “negative” in 4: in three women, the preoperative endometrial biopsy revealed no abnormality [11]. In a single-center series of hysterectomies for POP in 644 patients, the prevalence of uterine lesions diagnosed postoperatively was 2.6% (5 endometrial hyperplasia, 3 complex endometrial hyperplasia, 7 atypical complex hyperplasia and 2 EC). In premenopausal patients (n = 178), no abnormality was diagnosed. Among 466 postmenopausal patients, 98 with preoperative bleeding but no abnormality on preoperative evaluation (biopsy and/or ultrasound) had a 13.3% risk of uterine abnormality at final pathological analysis (5 hyperplasia and one EC). In asymptomatic postmenopausal women, the prevalence was significantly decreased (2.6% vs. 13.3%; P = 0.003) [12]. In their retrospective study of 640 women who underwent a surgical procedure for POP by the vaginal route, Wan et al. [13] found a 0.47% prevalence of diagnosis of an occult cancerous lesion or precancerous lesions (complex hyperplasia with or without atypia). Among the 184 symptomatic patients who had a preoperative evaluation by pelvic ultrasound and endometrial biopsy, 2 cancers (1.09%) and one precancerous lesion (0.54%) were discovered on specimen analysis [13]. In a study of 6981 hysterectomies for POP, Parsons et al. found occult EC in 13 cases (0.19%), in 10 of which preoperative biopsy because of bleeding was “negative”. Among these 13 cases, 54% of the patients were postmenopausal, 62% had hormonal therapy, and 50% had a family history of cancer [14].

Risk associated with subtotal hysterectomy

Performing SH during SC is associated with its own risks, which may diminish the potential “carcinological prevention benefit”. Uterine morcellation, performed by laparoscopy or a robot-assisted procedure, is associated with a low risk (< 0.6%) of dissemination of an unknown sarcoma/EC [15–18]. A risk of dissemination of parasitic myomias (< 0.5%) is also possible [15]. We cannot ignore the other surgical risks inherent in the SH procedure (intraoperative bleeding or ureteral/bladder/bowel injury, transfusion, re-hospitalization) [19–21]. On the other hand, uterine preservation is associated with a decrease in operative duration and blood loss, without evidence of an increased rate of recurrence of POP [22].

Conclusion

Routine SH associated with SC is not recommended for the sole purpose of reducing the occurrence of endometrial cancer (low quality of evidence, strong agreement).

Disclosure of interest

TG gets receipt of honoraria or consultation fees from: AstraZeneca, GSK. XD has receipt of honoraria or consultation fees from: Allergan, UrgoTech, Coloplast, Laborie, Leopharma, Mylan, B-Braun, Astellas; and is stock shareholder at Sanofi, and Nanobiotix. The other authors declare that they have no competing interest.

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