

## EDITORIAL

# How does Endometriosis affect Women's Life, focusing on Endometriomas?

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## BACKGROUND

Endometriosis is one of the frequent female diseases that can be better diagnosed today by the help of laparoscopy and hysteroscopy than ever before.

Karl Freiherr von Rokitanski, a Viennese pathologist and philosopher, was the first who described this disease in 1860. The pathologist referred to the condition in his writings as "adenomyoma." It is unfortunate that our understanding of the disease has not progressed very far since that time.

We have novel insights into the pathogenesis of endometriosis and are addressing the state-of-the-art in clinical markers of endometriosis, describe genetic imprints, and look for immunological or anatomical correlations. We know how the adverse health impacts of endometriosis often compromise our patients in diverse ways for years to decades of their lives.

The cumulative impact of endometriosis on the health of women across the lifespan can be divided into three sets of issues, namely those of assessment of the pelvic/intraperitoneal and extraperitoneal compartment, treatment by surgical, mainly endoscopic, and endocrine modalities, which in spite of ongoing research are the only real tools of treatment we seem to have and potentially systemic more remote risks, in terms of location (other tissues/organs), malignancy, and disease in the lifespan of a woman.

Endometriosis is indeed a disease with a unique pathophysiology. We know that it is subchronic to chronic,

predominantly intraperitoneal, but in about 10% disease also invades into bowels, urinary tract organs, and distant locations, often progressive and destructive inflammatory disease that has a massive impact on the health of many postpubertal women. Given the known role of chronic inflammation as a prominent factor in the occurrence of numerous other diseases, we must determine the extent to which this process in the intraperitoneal compartment does or does not continue into systemic inflammation that creates other health risks. Only with a real understanding of this disease can we develop and implement a helping strategy for care of those who suffer from endometriosis as a chronic disease.

## ENDOMETRIOMAS

Let us focus in this Editorial on "endometriomas," which occur frequently, require surgery or estrogen suppressive treatment which in spite of our best intentions with surgical or medical/endocrine treatment is still in a good percentage unsuccessful and leaves morbidity.

We, as doctors, may consider endometrioma surgery or an estrogen suppressive hormonal treatment as easy procedures, but, please, let us be aware of how this disease, particularly on the ovaries, can interfere with life, love, and happiness of our patients.

At the Department of Obstetrics and Gynecology, University Hospitals Schleswig Holstein, Kiel, Germany, we analyzed 3,057 patients' medical records and surgical reports retrospectively from 1995 to 2004. In those we histologically verified 550 patients with ovarian endometriotic cysts undergoing either laparoscopic conservative excision (95%) or laparotomy.

## MATERIALS AND METHODS

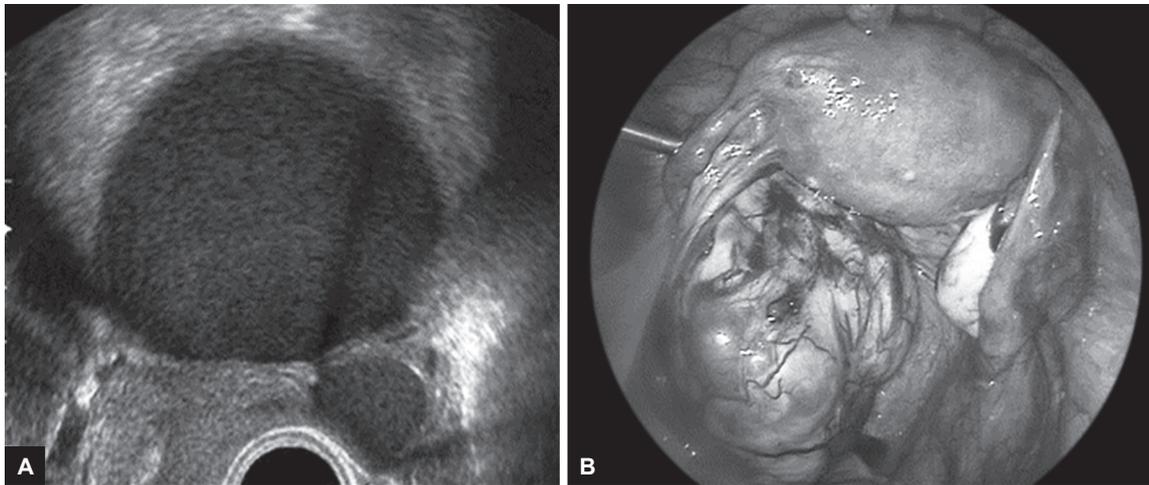
Looking at this endometrioma (Fig. 1) we find that it is easy to enucleate, measures 6 cm in diameter, and should be surgically resected. This patient had slight lower abdominal pain attacks and desired to get pregnant. We performed a laparoscopic endometrioma enucleation, but internationally there is no clear and common understanding about the primary necessity to enucleate such an endometrioma, although I am very much for it.

The evaluations of questionnaires in our study with a final return rate of 52.5% left a total of 289 patients in

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**Figs 1A and B:** Transvaginal ultrasonogram of a 6-cm diameter, left ovarian endometrioma and its corresponding laparoscopic view

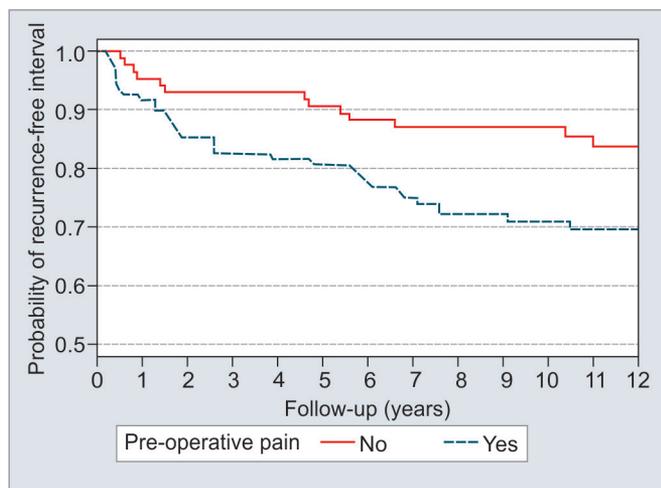
the follow-up study.<sup>1</sup> Factors associated with recurrence of dysmenorrhea were younger age ( $p < 0.01$ ), nulliparity ( $p < 0.05$ ), and large cyst size ( $p < 0.05$ ). Previous laparoscopic surgery for ovarian endometrioma ( $p < 0.05$ ) was found as the only significant risk factor for recurrence of pain.

One hundred ninety-seven patients were initially diagnosed with endometriomas at the time of surgery, and, of those, 47 patients showed recurrent ovarian endometrioma (23.9%) in the follow-up period. Of those 47 patients, 68.1% (32 of 47) underwent a reoperation in the follow-up period. Of those 32 patients, 17 patients (53.1%) needed one reoperation; 9 patients (28.1%) required two reoperations; and 6 patients (18.8%) required  $\geq$ three reoperations due to new endometriosis cysts. The probability of a recurrent-free interval was 76.1% for all primarily diagnosed endometriomas in our study period.

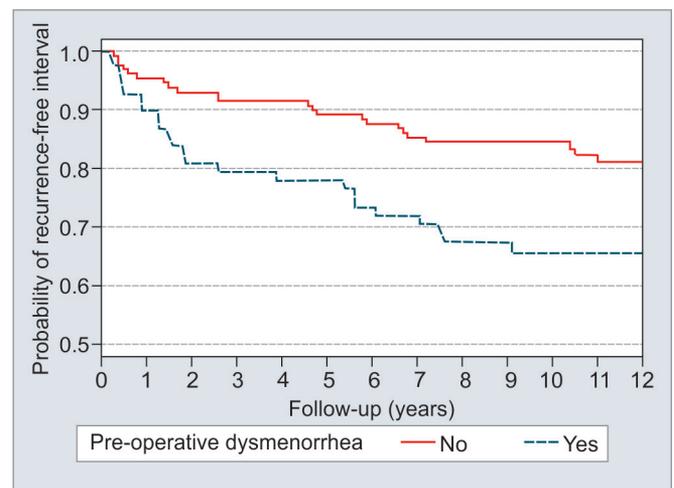
Patients with preoperative pain showed a significantly higher recurrence rate (log-rank test;  $p = 0.013$ ).

The Kaplan–Meier graph demonstrates that patients without preoperative pain had a significantly higher recurrence-free interval of 84.7% when compared with patients with a history of preoperative pain who were recurrence-free only 69.4% by the end of the follow-up period (Graph 1). Another statistically significant risk factor for endometrioma recurrence was preoperative dysmenorrhea (log-rank test;  $p = 0.013$ ). The Kaplan–Meier curve (Graph 2) illustrates that women without preoperative dysmenorrhea have a recurrence-free interval of 81.4% compared with a recurrence-free interval of only 66.2% in women with preoperative dysmenorrhea.

Other risk factors that were not significant but showed an association with higher recurrence were larger cyst size [ $>8$  cm; rate of recurrence was 33.3% (5 of 15) *vs* 16.3% (15 of 92) in cyst size 5–8 cm and 16.8% (24 of 143) in cyst size  $<5$  cm], younger age at surgery [ $<25$  years: 6.4% (3 of 47) in the recurrence cohort *vs* 2.8% (8 of 289) in the follow-up cohort], and preoperative cyst rupture [rate of recurrence



**Graph 1:** Probability of recurrence-free interval within the follow-up period in patients with and without preoperative pain



**Graph 2:** Probability of recurrence-free interval within the follow-up period in patients with and without preoperative dysmenorrhea

was 28.6% (2 of 7) vs 20.5% laparotomy], symptomatic. By transition from laparoscopy to laparotomy, only 43.7% were asymptomatic.

In 111 of 289 patients (38.4%) the wish for postoperative pregnancy was found. Combined surgical and hormonal treatment was given to 61 of 111 patients (55.0%), whereas surgery alone was performed in 50 of 111 patients (45.0%). Among these patients, the postoperative spontaneous pregnancy rate was 54.1% (60 of 111). Of these 60 patients, 46 of 111 (41.4%) had surgical treatment combined with medical treatment and 14 of 111 (12.6%) had surgery alone. A statistically significant difference ( $p < 0.001$ ) between combined surgical and hormonal therapy and exclusive surgery was observed. A limitation of this study is its study model, a retrospective cohort study, which has lower evidence and validity compared, for example, with a randomized controlled study. The definition of recurrence varies in the literature. Some studies define recurrence as a typical morphological change represented in a vaginal ultrasonogram, whereas others define it as a recurrence or worsening view of subjectively perceived pain. Although the general definition of a recurrent endometriosis remains to be determined, our definition represents a limitation because it is based on a questionnaire. We considered a positive response to the presence of a cyst or tumor in the questionnaire as a recurrence of endometriosis.

## CONCLUSION

In conclusion, let me state that biases in this study include the alternating surgeon's experience, the low return rate of questionnaires, and the development in hormonal treatment within the period of data collection and observation [e.g., danazol, in spite of its interesting immunosuppressive effects, is now not any more very commonly applied, as drugs with less side effects like gonadotropin-releasing hormone (GnRH) analogues and pure "gestagen" preparations, like Visanne, are on the market in most every country of the world]. Among the strengths of the study

are the long follow-up period, large sample size, and the fact that all patients were operated on in the same hospital. Patients with ovarian endometriomas and a desire for pregnancy seem to profit from additional postoperative medical treatment. For patients with completed family planning, the indication of additional postoperative medical treatment needs to be well evaluated according to patients' preferences and the amount of their pain. As this article focuses only on endometriomas, I want to stress again that the disease has, unfortunately, many other forms of expression that are not discussed in this article and are much more difficult to address.

Across the lifespan of a female there are definitely ample opportunities to pursue research regarding the impact of endometriosis in all its appearances as superficial, ovarian, deep infiltrating, or distant endometriotic lesions. It is necessary to follow the development of a number of therapeutic strategies that could plausibly be expected to be both safe and beneficial for women suffering with this systemic disease. This is not an argument for taking our eye off the fact to find endometriosis as the primary disease, but rather we owe it to each of our patients to consider all of the impacts at all times in life that this disease may incur.<sup>2</sup>

Neither the treatment of endometriomas nor the diagnosis and treatment of this chronic systemic disease has as yet found its specific diagnosis and treatment.<sup>3</sup>

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