

Minimally invasive surgery when treating endometriosis has a positive effect on health and on quality of work life of affected women

M.F. Wullschleger^{1,*}, S. Imboden², J. Wanner², and M.D. Mueller²

¹Department of Physiology, University of Bern, 3012 Bern, Switzerland ²Department of Obstetrics and Gynecology, University of Bern, 3010 Bern, Switzerland

*Correspondence address. E-mail: marcel.wullschleger@alumni.unisg.ch

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STUDY QUESTION: What is the effect of the minimally invasive surgical treatment of endometriosis on health and on quality of work life (e.g. working performance) of affected women?

SUMMARY ANSWER: Absence from work, performance loss and the general negative impact of endometriosis on the job are reduced significantly by the laparoscopic surgery.

WHAT IS KNOWN ALREADY: The benefits of surgery overall and of the laparoscopic method in particular for treating endometriosis have been described before. However, previous studies focus on medical benchmarks without including the patient's perspective in a quantitative manner.

STUDY DESIGN, SIZE, DURATION: A retrospective questionnaire-based survey covering 211 women with endometriosis and a history of specific laparoscopic surgery in a Swiss university hospital, tertiary care center. Data were returned anonymously and were collected from the beginning of 2012 until March 2013.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Women diagnosed with endometriosis and with at least one specific laparoscopic surgery in the past were enrolled in the study. The study investigated the effect of the minimally invasive surgery on health and on quality of work life of affected women. Questions used were obtained from the World Endometriosis Research Foundation (WERF) Global Study on Women's Health (GSWH) instrument. The questionnaire was shortened and adapted for the purpose of the present study.

MAIN RESULTS AND THE ROLE OF CHANCE: Of the 587 women invited to participate in the study, 232 (232/587 = 40%) returned the questionnaires. Twenty-one questionnaires were excluded due to incomplete data and 211 sets (211/587 = 36%) were included in the study. Our data show that 62% ($n = 130$) of the study population declared endometriosis as influencing the job during the period prior to surgery, compared with 28% after surgery ($P < 0.001$). The mean (maximal) absence from work due to endometriosis was reduced from 2.0 (4.9) to 0.5 (1.4) hours per week ($P < 0.001$). The mean (maximal) loss in working performance after the surgery averaged out at 5.7% (12.6%) compared with 17.5% (30.5%) before this treatment ($P < 0.001$).

LIMITATIONS, REASONS FOR CAUTION: The mediocre response rate of the study weakens the representativeness of the investigated population. Considering the anonymous setting a non-responder investigation was not performed. A bias due to selection, information and negativity effects within a retrospective survey cannot be excluded, although study-sensitive questions were provided in multiple ways. The absence of a control group (sham group; e.g. patients undergoing specific diagnostic laparoscopy without treatment) is a further limitation of the study.

WIDER IMPLICATIONS OF THE FINDINGS: Our study shows that indicated minimally invasive surgery has a clear positive effect on the wellbeing and working performance of women suffering from moderate to severe endometriosis. Furthermore, national net savings in indirect costs with the present number of surgeries is estimated to be €10.7 million per year. In an idealized setting (i.e. without any diagnosis delay) this figure could be more than doubled.

STUDY FUNDING/COMPETING INTEREST(S): The study was performed on behalf of the University Hospital of Bern (Inselspital) as one of the leading Swiss tertiary care centers. The authors do not declare any competing interests.

Key words: endometriosis / quality of life / national retrospective study / health economics

Introduction

Women from all ethnic and social groups, predominantly of reproductive age, may be affected by endometriosis. This common gynecological disease is defined as the presence of endometrial-like tissue outside the uterus that induces a chronic, inflammatory reaction (Kennedy et al., 2005). Well-recognized symptoms of endometriosis are cramping menstrual pain, lower abdominal and pelvic pain, deep dyspareunia and infertility (Garry et al., 2000). Estimates of the prevalence of endometriosis among women of reproductive age vary between 2 and 10% (Eskenazi and Warner, 1997). Endometriosis is a chronic disease and the treatment of affected patients is demanding and includes analgesics and hormonal therapies, conservative (e.g. laparotomy) and minimally invasive surgery (e.g. laparoscopy), assisted reproduction or a combination of these (Kennedy et al., 2005). As for many chronic pain patients, a patient-centered approach toward endometriosis care with mind-body medicine, counseling and other psychological interventions is recommended for the long-term management of the symptoms.

The negative effect of endometriosis on wellbeing of affected women and on costs has been well recognized and confirmed in recent prospective studies (Simoens et al., 2011, 2012; De Graaff et al., 2013). In this retrospective study, we focus on the effect of an up-to-date laparoscopic approach when treating endometriosis. Former studies investigating laparoscopic excision of endometrial-like tissue found a significant improvement of the measured criteria, including pain scores and quality of life indices (Garry et al., 2000; Abbott et al., 2003). However, in the present study we concentrate on the patient's perspective (without laboratory values or surgical findings; the study was run anonymously) and in particular we inquire economic characteristics, e.g. the effect on working performance and on absence in a direct 'before versus after surgery' comparison. The effect of endometriosis on work has recently been reported to be a highly relevant issue (De Graaff et al., 2013). Indirect costs due to productivity loss were calculated as a dominant portion (66%) of the total cost of endometriosis (Simoens et al., 2012).

Materials and Methods

Study population

For this retrospective cohort study a total of 587 women were contacted in 2012 with a questionnaire in order to determine the various characteristics and scores, as shown in the Results. Appropriate values were requested for the situations before the first surgery and after the last surgery. Women were selected based on a history of at least one therapeutic laparoscopic surgery (see 'Surgical technique') due to endometriosis. The contacted cohort represented the following stages (%) of the disease (according the revised American Fertility Society classification of endometriosis): rAFS I (7.4%), rAFS II (15.8%), rAFS III (21.6%), rAFS IV (55.2%). All surgery had been conducted in the University Hospital of Bern, Switzerland. Basically, all respective women with a known address received the questionnaire. The questionnaires were to be submitted anonymously no later than 31 March 2013. Hence, no callbacks (e.g. due to incomplete data) were possible. From the 587 women contacted, 157 (157/587 = 26.7%) were surgically unburdened from superficial endometriomas. A total of 227 patients (227/587 = 38.7%) underwent additional surgical treatment of the ovaries and tubes. For 203 women who received the questionnaire (203/587 = 34.6%) the intervention included the treatment of deep infiltrating endometriosis (DIE). Ninety-one women (91/587 = 15.5%) also had bowel

resection. Ten patients (10/587 = 1.7%) of these 91 women received 3-month protective ileostomy.

Surgical technique

In all patients, a radical laparoscopic endometriosis resection was performed. In our endometriosis center, high value is given to the minimally invasive approach. Standardized techniques have been developed: four laparoscopic ports are usually used, 10 mm umbilical ports and three 5 mm ports in the lower abdominal wall. Excision is performed with monopolar scissors or, when close to the bowel, with an ultracision device (HARMONIC® Ultrasonic Devices).

All peritoneal lesions are excised completely and no coagulation is performed. The patients consent to the complete removal of all endometriotic lesions, including intestinal resection, if needed, and in this context consent also to mini-laparotomy and colostomy. If bowel involvement is presumed, pre-operative bowel preparation is given.

If DIE is present in the rectovaginal septum, first a lateral preparation along the rectum is performed bilaterally, sparing the splanchnic nerves, until the node is medialised from the sacrouterine ligaments. Then, if the vagina is also infiltrated, the vagina is opened under digital control cranial to the lesion. In this way, the node is mobilized until it is adherent only with the rectum. At this point, the depth of the invasion can be evaluated and a decision can be taken whether the node can be totally removed without bowel resection, or if a partial resection is necessary. The goal is to have a total removal of all endometriotic tissue. If a bowel resection is needed, a segment resection is performed laparoscopically, or in selected cases a disc resection of the anterior wall is performed.

In the treatment of endometriomas, the idea of a total resection is also dominant. If the endometrioma has a diameter of over 4 cm, often a second-look operation after primary fenestration and followed by 3 months of GnRH analogue, or more recently Visanne (Dienogest, Bayer [Schweiz] AG), is indicated. In a second step, either an enucleation of the endometrioma can be performed or the base of the endometrioma can be evaporated with a CO₂ laser.

In the following sections, the term 'surgery' implies the laparoscopic intervention as described above.

Data collection

Missing values were not imputed for data analysis. Questionnaires with a fraction of >0.2 of unanswered questions were excluded from analysis. A total of 211 returned questionnaires were integrated in descriptive statistics.

Statistical analysis

Categorical data are reported as relative frequency data, continuous data are indicated as mean with SD. For comparisons between groups, a two-sided, paired student *t*-test was applied. Analysis was performed in R (version 3.0.1, R Foundation for Statistical Computing, Vienna, Austria. URL <http://www.R-project.org/>).

Ethical approval

The retrospective setting of the study did not require an ethical approval.

Results

Out of 587 women requested to participate in the study and sent a questionnaire, 232 women returned the questionnaire. Twenty-one questionnaires were excluded due to incomplete data and 211 sets (211/587 = 36%) were included in the study.

Table 1 Characteristics of diagnosis and surgery for the women with endometriosis who returned the study questionnaire on health and on quality of work life.

Characteristic	Mean (SD)	Minimum-maximum	n
Year of diagnosis 'endometriosis'	2006 (5.9)	1972–2012	211
Number of surgeries per patient	2.0 (1.3)	1–8	211
Time from diagnosis to 1st surgery ¹	0.8 (3.3)	0–31	211
Time from diagnosis to 2nd surgery ¹	2.7 (4.5)	0–35	129
Time from diagnosis to 3rd and higher surgery (average) ¹	6.0 (6.5)	1–37	44

¹[years].

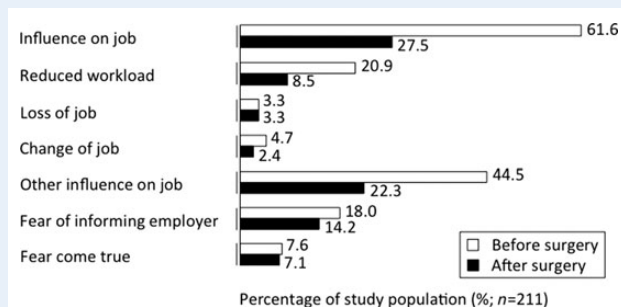


Figure 1 Influence of endometriosis on the job. The negative influence on the job was eliminated by >30% of the study population as a result of surgical treatment. The reduction in workload (e.g. with a lower employment factor) due to endometriosis affected <9% of the study population as opposed to >20% before surgery. The 'other influence on job' was halved to 22% of the study population (this included mostly 'working under pain' and/or 'under the intake of analgesics' as well as 'loss in performance'). Each patient could mark several categories (percentages do not add up to 100%).

The baseline characteristics of the participating women did not disclose any peculiarities resulting from a bias in selection (Supplementary Table S1). The represented characteristics such as age, height, weight, hair color and ethnic origin did not deviate from the average population living in Switzerland. The mean employment factor of the women (percentage of full-time work) was 71% and the mean year of diagnosis was 2006. More than two-third of the women represented in the study ($n = 211$) underwent either one or two surgeries due to endometriosis (Supplementary Fig. S1). On average, a patient underwent two surgeries due to endometriosis and the mean time from diagnosis to surgery was 10 months. However, for some women longer time spans extending over several decades were found (Table 1).

One major aim of the study was to identify quantitatively the effect of the surgical treatment on the wellbeing (i.e. on the job), which was previously reduced by endometriosis. According to Fig. 1, nearly 62% of the study population initially viewed endometriosis as influencing the job (in any way). This value was halved to 28% by the surgery. Often endometriosis forced affected women to reduce their workload; the surgery helped to lessen this effect from 21 to 9%. Summarized as 'other

influence on job' (in Fig. 1), the loss in performance (without reducing the workload), the necessity to work under pain and/or the intake of analgesics could be reduced from 45 to 22% of the women involved in the study. Less distinct is the improving effect on the already relatively low-influence categories such as the loss or change of the job and the (fear of) negative consequences when informing the employer (Fig. 1).

Figure 2 shows the impact of endometriosis on working time and performance. The mean working time after surgery was slightly less (33 versus 31 h per week) mainly due to one outlier in the maximum. Specific surgical treatment reduced mean absence from work from 2 h per week (4.4 SD) to 0.5 h per week (2.0 SD; significant, $P < 0.001$). On a scale from 0 to 10, the mean impact of endometriosis during work could be reduced from 3.6 (3.0 SD) to 1.6 (2.2 SD; significant, $P < 0.001$). The loss in working performance due to endometriosis averaged out as 17.5% (22.7 SD) before surgery. Thereafter, this value was 5.7% (12.9 SD; significant, $P < 0.001$). Similar results were found for the maxima of each category (Fig. 2 and Supplementary Table SII).

Discussion

Improved quality of life and economic relevance

The positive effect of surgery when treating endometriosis can be formulated quantitatively in terms of subjective wellbeing and performance of affected individuals. The figures found in this study (e.g. absence and loss in working performance due to endometriosis and the shift due to surgery) allow us to model the outcome in terms of economic costs. Our theoretical model extrapolates to costs at the national level using the following data: average income (Federal Statistical Office [FSO], 2010); of the national number of women of reproductive age (e.g. 16–46 years of age; FSO, 2011), 7% are affected by 'moderate to severe endometriosis' (Simoens *et al.*, 2012), and of these ~2.7% undergo specific surgery at least once during their reproductive years (i.e. a national prevalence of ~3100 patients being cost-effective every year, e.g. 200 surgeries per year). Accordingly, the current net saving (due to specific surgical intervention) in indirect costs per year may be estimated for Switzerland to be around 13 million Swiss francs (i.e. €10.6 million). Thereby, costs due to absence and loss in working performance are considered as additive data. This number is vastly above the yearly direct costs for the surgical treatments (estimated to be 1.3 million Swiss francs per year).

Potential national economic savings

An idealized setting with only minimal pre-operative restriction (e.g. minimal time of high loss in performance, i.e. with no diagnosis delay) would allow for an additional economic savings ranging up to 16.9 million Swiss francs (or 29.9 million Swiss francs net in total, e.g. €24.5 million). These dimensions are in line with other national cost estimates shown elsewhere (Simoens *et al.*, 2012), as we restrict our analysis to endometriosis patients undergoing specific surgery. Also, we use a narrow definition of indirect costs (e.g. costs primarily carried by the employer). Other costs that might be incurred by the family (e.g. for other treatments, informal care, transportation, support of household activities) would increase total costs but also net savings as those increase in proportion to the included costs. Such other costs average out to about 6.4% of the indirect costs of productivity loss (Simoens *et al.*,

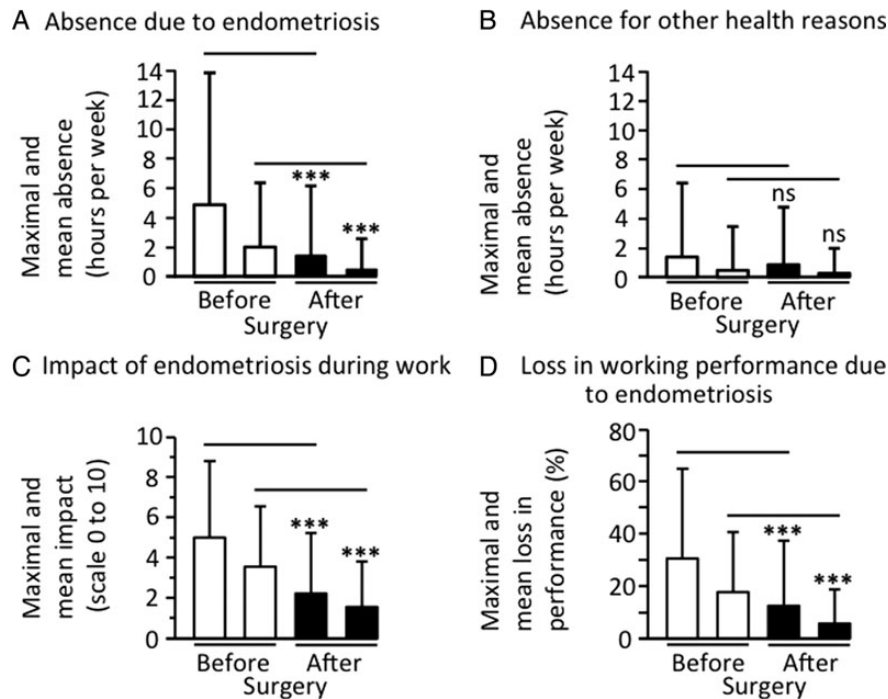


Figure 2 Absence and performance loss due to endometriosis. Surgical treatment of endometriosis leads to a significant reduction in maximal and mean absence from work (**A**). Absence for other health reasons is not affected by the specific intervention (**B**). The negative impact of endometriosis during work (**C**) as well as the accompanied loss in performance (**D**) both can be significantly reduced although not completely eliminated. Each bar graph gives mean value and SD ($n = 211$, $***P < 0.001$, ns: not significant). The white bar graphs represent mean values for the situation before surgery, while the black bar graphs represent mean values for the situation after surgical treatment. Each panel represents the following (from left to right): average maximal value before surgery, average mean value before surgery, average maximal value after surgery, average mean value after surgery (patients reported individual maximal and mean values). For comparison (before versus after surgery) within maximal and within mean values, a two-sided paired student *t*-test was applied.

2012). When considering these other costs, current net savings increase by 0.8 million Swiss francs (e.g. €0.7 million) to 13.8 million Swiss francs. Additionally, the potential additional economic saving increases from 16.9 to 17.9 million Swiss francs per year.

Minimal need of surgery as an aim

Considering the chronic aspect of the disease, we appraise the surgical therapy as being one element out of a set of treatment approaches each allowing for partial cure. Accordingly, the superior therapeutic objective is to stabilize the patient in a non-invasive manner (e.g. medication) as soon as possible. If surgical treatment is advisable, the minimally invasive method should be prioritized. Moreover, we seek to minimize the recurrent surgery rate, which is non-trivial as the recurrent surgery rate depends on several factors (e.g. surgical technique, drug therapy, healing process, etc.). Timely diagnosis and intervention may contribute to, but does not guarantee, minimal recurrent surgery rates. Most likely to benefit from surgery is the group with the most invasive intervention (e.g. including DIE). Assuming the study population ($n = 211$) features the same proportionality as the contacted cohort ($n = 587$), the most invasive group (the group including DIE, e.g. top 34.6% of study population; with highest limitation in working performance before surgery) exhibits an improvement effect from 43 to 11% in loss of working performance (mean values). For the other two (less invasive) groups this effect would be less distinct

(e.g. from 7 to 4% for the second group; 38.7% of study population, with surgical treatment of ovaries and tubes) or even be below threshold for this specific parameter of interest (e.g. 0% before and after surgery; 26.7% of study population, superficial endometriomas). The latter does not exclude an improvement effect elsewhere.

Limitations and strengths of the study

We consider that this evaluation based on 211 completed questionnaires provides a sufficiently robust outcome. Within a retrospective study, selection bias and information bias limit the validity of this type of investigation. Furthermore, the relatively low response rate of 36% allows for some uncertainty regarding the representativeness of the included patients. As the survey data were returned anonymously, one can only speculate about non-responsiveness. However, a selection bias toward severity was not obvious, as a wide range of possible impact scores of endometriosis (scale 0 to 10; e.g. Fig. 2C) was covered within the responses. A potential bias in the population of patients responding cannot therefore be excluded. The anonymity favored honest responsiveness, which was reflected by the comments in the questionnaires. On the level of the individual feedback, there may be a negativity bias with a possible overstatement of a negative experience in the past. Overall and referring to the baseline characteristics an ordinary selection of women was represented in the study. As all

surgery covered in the study was performed in a leading Swiss tertiary care hospital, there is some limitation in the validity of the study for smaller health institutions. The absence of a control (sham) group is important to note, as the placebo effect of any treatment, especially those associated with technical interventions, can be significant. For minimal to moderate endometriosis, a clear placebo effect of laparoscopic surgery for pain at 3 months after intervention has been described (Sutton *et al.*, 1994). At 6-month follow-up, this temporary effect seems to disappear (Sutton *et al.*, 1994). A potential placebo effect could have influenced the data from the patients who underwent surgery in 2012. We evaluated this subset ($n = 35$, 16.6% = 35/211) separately, in which no conspicuous difference to the complete dataset could be found regarding the absence from work and the impact of endometriosis during work. However, the drop in performance loss (improvement effect) due to the surgery in 2012 was 22% greater than the drop in the complete dataset; this indicates a possible placebo effect. For example, the mean absence from work was reduced from 2.4 h per week (4.4 SD) to 1.2 h per week (4.2 SD; significant, $P < 0.01$) due to the surgery. The mean impact of endometriosis during work changed from 4.5 (3.1 SD) to 2.4 (2.8 SD; significant, $P < 0.001$), and the loss in working performance showed a reduction from 23.1% (23.4 SD) to 8.7% (19.3 SD; significant, $P < 0.001$).

Conclusion

Evaluated from a patient's perspective, the negative effects of endometriosis are clearly reduced in women undergoing indicated surgery. The improvements in health and performance are distinct. However, on average, surgically treated patients are still facing respective (but much smaller) limitation. Related absence from work is reduced to one fourth of the corresponding value before surgery. The negative impact on work and the loss in working performance are reduced to between one half and one third of the respective values for the time before surgical intervention. The use of an up-to-date laparoscopic technique is an important element of an effective treatment strategy for accurately selected women with endometriosis. Timely diagnosis and subsequent treatment of the few indicated patients with suitable surgery followed by non-invasive therapy may further help to minimize suffering and to reduce economic costs at once.

Supplementary data

Supplementary data are available at <http://humrep.oxfordjournals.org/>.

Authors' roles

M.F.W., S.I., J.W. and M.D.M. designed the study, analyzed and interpreted the data. M.F.W. and S.I. wrote the first draft of the manuscript. All authors were involved in the data collection and critical revision of the manuscript.

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Conflict of interest

None declared.

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