

# Predictors of postoperative hemoglobin drop after laparoscopic myomectomy

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## Abstract

**Introduction:** Laparoscopic myomectomy (LM) can be associated with significant bleeding.

**Aim:** To identify factors influencing the postoperative hemoglobin (Hb) drop after LM.

**Material and methods:** This is a retrospective, single-center study. We evaluated data of 150 consecutive patients undergoing LM due to intramural myomas between 2010 and 2015.

**Results:** The median age of the patients was 37 (23–53) years. The mean diameter of the largest myoma was  $5.7 \pm 2.3$  (1.5–12) cm. The mean surgical time was  $83 \pm 38$  (35–299) min. The median number of sutures was 3 (1–11). The mean postoperative Hb drop was  $1.6 \pm 1.2$  (0–6) g/dl, and the mean estimated blood loss was  $261 \pm 159$  (50–1700) ml. In the univariate analysis, the postoperative Hb drop correlated with the duration of surgery ( $p < 0.001$ ), diameter of the largest myoma ( $p < 0.001$ ), cumulative myoma weight ( $p < 0.001$ ), and number of sutures ( $p < 0.001$ ), but not with patients' age or number of intramural myomas. In the multivariable analysis, the surgical time ( $\beta = 0.395$ ,  $p < 0.001$ ), diameter of the largest myoma ( $\beta = 0.292$ ,  $p = 0.03$ ) and preoperative Hb concentration ( $\beta = 0.299$ ,  $p < 0.001$ ) predicted the postoperative Hb change.

**Conclusions:** Surgical time and dominant myoma diameter are independent predictors of the postoperative Hb drop after LM.

**Key words:** bleeding, gynecological laparoscopy, myomectomy, hemoglobin change, surgical time.

## Introduction

The cumulative incidence of uterine leiomyomas until menopause is almost 70% in white women and over 80% in black women [1]. About 25% of uterine myomas are symptomatic and require treatment, e.g. because of heavy menstrual bleeding, pelvic pain or concerns about fertility impairment [2]. Laparoscopic myomectomy (LM) is the gold standard in surgical treatment of uterine myomas [3–8]. The rate of perioperative complications is generally low, and LM can be offered to the most patients, regardless of the size, number, or location of the myomas [5,

9, 10]. Agdi and Tulandi [11] recommend the laparoscopic approach for fibroids up to 15 cm in diameter. The LM is generally associated with less morbidity (e.g. less postoperative pain, rapid recovery, shorter hospital stay, smaller incisions) as compared with laparotomy [8, 11, 12], but the intraoperative blood loss remains a critical challenge in LM [6, 13–16].

Despite efforts and improvements in perioperative management (e.g. application of vasoconstrictive agents, hemostatics, barbed sutures or mechanical maneuvers [16–21]), the average intraoperative blood loss during LM is between 100 and 450 ml (ranging from 20 to 2000 ml) [7, 10, 14, 16, 21, 22]

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and can be higher as in laparoscopic hysterectomy for similar indications [15].

The postoperative hemoglobin (Hb) change is an objective parameter of intraoperative blood loss after LM [4, 5, 8, 18, 21, 23] and correlates better with the actual blood loss than a subjective estimation [24]. Studies on predictors of intraoperative blood loss in LM are rare. Yoo and Lee [25] identified patient's age, more than 5 intramural fibroids, myoma diameter > 8.2 cm, posterior wall localization, concomitant adenomyosis and previous pelvic-abdominal surgery as risk factors for discontinuation of a laparoscopic procedure and conversion to laparotomy. According to Saccardi *et al.* [22], diameter and type (intramural vs. subserosal) of the myomas were the best predictors of blood loss and surgical time in LM. Walid and Heaton [9] identified solely the myoma diameter as the main predictor of blood loss in LM. Identification of factors influencing perioperative blood loss in LM is crucial for reducing the risk of transfusions, complications and conversions to hysterectomy [16].

## Aim

In the present study, we evaluated factors influencing the postoperative Hb change – as the most quantifiable parameter for perioperative blood loss – after laparoscopic removal of intramural myomas.

## Material and methods

### Patients

In 2010, LM was established at our institution as a standardized procedure including myometrium suturing. In this retrospective, single institution study, we analyzed records of 207 consecutive laparoscopic myomectomies conducted between February 2010 and December 2015 at the Department of Gynecology and Obstetrics, St. Josefskrankenhaus, Freiburg, Germany. Data were collected by chart review and documented in a database by the principal investigator (RW). Forty-nine patients were excluded because of subserosal (with no need for myometrial sutures) or pedunculated myoma localization. We included in the study only intramural myomectomies, in all cases requiring myometrium suturing. From the total of 158 intramural myomectomies, 8 (5.1%) cases were excluded because of conversion to laparotomy. One hundred and fifty laparoscopic intramural myomectomies entered the final analysis.

The study was approved by the Institutional Review Board of the University of Freiburg, Germany (Reference No. 554/15).

### Surgical procedure

All surgeons performing LM were board-certified. Additionally, in all procedures there participated (as first or assisting surgeon) one or both surgeons with the highest surgical volume (RW, CJ), certified by the German Society for Gynaecological Endoscopy (RW, CJ) and the European Society for Gynaecological Endoscopy (RW). No patient was pre-treated with GnRH analogs. The surgery was performed in a standardized way, similar to the description of Alkatout [26]. The patient was positioned on the operating table in the supine position and received general anaesthesia by endotracheal intubation. The abdominal cavity was approached by four ports, one umbilical 10 mm port for the laparoscope and three ancillary ports in the lower abdomen: one suprapubic 10 mm port and two lateral 5 mm ports, placed 2 cm medially to each iliac crest. In order to avoid cardiovascular complications, we never injected vasoconstrictors into the myometrium. A bipolar coagulation trace was made on the serosa overlying the leiomyoma prior to incision. The serosa and myometrium were incised vertically by monopolar scissors until the cleavage plane (myoma pseudocapsule) was visible. The edges of the retracting myometrium were held with grasping forceps, and the protruding myoma was grasped with a 10 mm laparoscopic single toothed tenaculum. The myoma was enucleated using traction and countertraction, supported by blunt dissection from the capsule (by use of forceps or an irrigator). Small capsular vessels were punctually coagulated with bipolar forceps. The vascular supply of the myoma was coagulated and cut. After removal of the myoma, the myometrium was sutured in all cases. The uterine defect was closed in one (129/150; 86%) or two (21/150; 14%) layers, depending on the surgeon's choice. The principle in all cases was that the whole myometrial thickness should be restored. The uterine defect was closed using separate, introflexing U-inverted stitches with intramyometrial knots tied by an extracorporeal knot-pusher. In all cases, delayed absorbable sutures (polydioxanone monofil, Endo-Naht Serasynt, Se-rag-Wiessner, Naila, Germany) were used. In cases of two-layer closure, the first layer was performed

using (running or separate) polyglactin 910 sutures (Vicryl, Ethicon, Norderstedt, Germany) knotted intracorporeally, and the second layer was applied to the outer myometrium and serosa with separate, polydioxanone sutures in the same manner as described above. Extraction of the myomas followed under direct vision via the suprapubic route, using an electric morcellator (Rotocut G1, Karl Storz, Tuttlingen, Germany). A visual check and meticulous cleansing of the abdominal cavity completed the procedure. The removed myomas were sent for pathologic examination in each case.

### Laboratory measures

Peripheral blood samples were collected from all patients preoperatively (24 h prior to surgery) and postoperatively (24–48 h after surgery) by peripheral vein puncture. The hemoglobin concentration was estimated in whole EDTA blood by the cyanide-free, sodium laurel sulfate method (XT-2000i Hematology Analyzer, Sysmex, Kobe, Japan), according to the manufacturer's instructions.

### Statistical analysis

Values are given as means with standard deviation (SD) or medians with range or rates (percent), where appropriate. Since this was a purely explorative study, a formal sample size and power calculation were not applicable. Correlations of baseline characteristics with postoperative Hb change were expressed by Spearman's correlation coefficient  $\rho$ . Two-group comparisons were performed using the independent samples *t*-test. A multivariable linear regression model using postoperative Hb drop as the outcome variable and all baseline characteristics as independent variables was estimated to determine the influence of these variables on the postoperative Hb drop. The importance of each variable for predicting the postoperative Hb drop was expressed by partial  $R^2$  values, resulting from the drop in  $R^2$  caused by omitting each variable in turn. The statistical analyses were performed with the software package Statistica 13 Test Version (Dell Inc., Tulsa, USA). Two-sided *p*-values < 0.05 were considered statistically significant.

### Results

Information about patients' age, surgeon, duration of surgery, estimated blood loss, and number of

removed myomas was available in all cases. Myoma weight was reported in the pathological reports in 148 (98.7%) cases. Information about myoma diameter and number of sutures was available in 147 (98%) and 143 (95.3%) cases, respectively. Sufficient data for calculation of the postoperative hemoglobin change (preoperative Hb concentration missing in 13 cases, postoperative Hb concentration missing in 19 cases) were available in 122 (81.3%) cases.

The median age of the patients was 37 (range: 23–53) years (Table I). The indications for surgery were: combination of bleeding disorders and pain in 78 (52%), infertility believed to be associated with myoma in 32 (21.3%), asymptomatic myoma growth in 23 (15.3%), and isolated bleeding disorders in 17 (11.3%) patients. The mean weight of removed myomas was 97 g (SD = 5.8, median: 56 g, range: 4–656 g), the mean number of removed myomas was 1.5 (SD = 1.1, range: 1–7), and the mean diameter of the largest myoma was 5.7 cm (SD = 2.3, range: 1.5–12 cm). The mean operation time was 83.4 min (SD = 37.8, range: 35–299 min). The median number of sutures was 3 (1–11). The mean postoperative Hb drop was 1.6 g/dl (SD = 1.2, range: 0–6 g/dl), and the mean estimated blood loss was 261 ml (SD = 159, range: 50–1700 ml). The mean hospital stay was 3.1 days (SD = 1.1, range: 1–8 days).

The univariate analysis is presented in Table II. Briefly, the postoperative Hb drop was positively associated with the duration of surgery ( $r = 0.42$ ,  $p < 0.001$ ), diameter of the largest myoma ( $r = 0.33$ ,  $p < 0.001$ ), cumulative weight of all removed myomas ( $r = 0.36$ ,  $p < 0.001$ ), number of sutures ( $r = 0.41$ ,  $p < 0.001$ ) and preoperative Hb concentration ( $r = 0.23$ ,  $p = 0.01$ ), but not with patients' age or number of intramural myomas. In an additional analysis, the duration of surgery was most strongly associated with the number of sutures ( $r = 0.59$ ,  $p < 0.001$ ), followed by weight ( $r = 0.43$ ,  $p < 0.001$ ) and number ( $r = 0.33$ ,  $p < 0.001$ ) of removed myomas, and diameter of the dominant myoma ( $r = 0.23$ ,  $p < 0.001$ ). As demonstrated in Table III, only the duration of surgery ( $\beta = 0.395$ ,  $p < 0.001$ ), diameter of the largest myoma ( $\beta = 0.292$ ,  $p = 0.03$ ) and preoperative Hb concentration ( $\beta = 0.299$ ,  $p < 0.001$ ) predicted the postoperative Hb drop in the multivariable analysis.

Additionally, the intraoperative blood loss – as estimated by the surgeon – correlated with postoperative Hb drop at  $r = 0.48$  ( $p < 0.001$ ). The postoperative Hb drop did not differ between the two

**Table I.** Patient characteristics

Variable	Valid N	% of valid observations	Median (25 <sup>th</sup> –75 <sup>th</sup> percentiles)	Mean (standard deviation)
Patient age [years]	150	100	37 (33–42)	37.5 (5.8)
Duration of surgery [min]	150	100	75.5 (58–95)	83.4 (37.8)
Hospitalization [days]	150	100	3 (2–3)	3.1 (1.1)
Intramural myomas, <i>n</i>	150	100	1 (1–2)	1.5 (1.1)
Diameter of the largest myoma [cm]	147	98	5 (4–7)	5.7 (2.3)
Cumulative weight of removed myoma(s) [g]	148	98.7	56 (25–127)	97 (5.8)
Sutures, <i>n</i>	143	95.3	3 (2–4)	3.5 (1.7)
Estimated intraoperative blood loss [ml]	150	100	200 (200–300)	261 (159)
Preoperative hemoglobin concentration [g/dl]	137	91.3	13.2 (12.1–13.9)	12.8 (1.6)
Postoperative hemoglobin nadir [g/dl]	131	87.3	11.5 (10.4–12.3)	11.3 (1.6)
Difference between the pre- und postoperative Hb concentration (“Hb change”) [g/dl]	122	81.3	1.4 (0.8–2.1)	1.6 (1.2)

**Table II.** Univariate analysis of correlations (Spearman’s rho) between investigated variables\*

Variable	Preoperative Hb concentration [g/dl]	Postoperative Hb change [g/dl]
Patient age [years]	$r = -0.1$ ( $p = 0.24$ )	$r = -0.14$ ( $p = 0.13$ )
Duration of surgery [min]	$r = -0.1$ ( $p = 0.2$ )	<b><math>r = 0.42</math> (<math>p &lt; 0.001</math>)</b>
Cumulative myoma weight [g]	$r = 0.04$ ( $p = 0.62$ )	<b><math>r = 0.36</math> (<math>p &lt; 0.001</math>)</b>
Intramural myomas ( <i>n</i> )	$r = -0.03$ ( $p = 0.74$ )	$r = 0.07$ ( $p = 0.48$ )
Dominant myoma diameter [cm]	$r = 0.15$ ( $p = 0.08$ )	<b><math>r = 0.33</math> (<math>p &lt; 0.001</math>)</b>
Sutures ( <i>n</i> )	$r = 0.06$ ( $p = 0.5$ )	<b><math>r = 0.41</math> (<math>p &lt; 0.001</math>)</b>

\*Significant results are printed in bold.

**Table III.** Predictors of postoperative Hb change analyzed by multiple linear regression<sup>a,b</sup>

Variable	Regression coefficient ( $\beta$ )	95% confidence interval	<i>P</i> -value	Partial $R^{2c}$
Duration of surgery [min]	<b>0.395</b>	<b>0.16–0.63</b>	<b>&lt; 0.001</b>	<b>0.32</b>
Weight of all myomas [g]	–0.1	(–0.35)–0.15	0.43	–0.08
Intramural myomas ( <i>n</i> )	–0.088	(–0.28)–0.10	0.36	–0.09
Diameter of the largest myoma [cm]	<b>0.292</b>	<b>0.03–0.56</b>	<b>0.03</b>	<b>0.21</b>
Sutures ( <i>n</i> )	0.068	(–0.18)–0.32	0.59	0.05
Preoperative Hb concentration [g/dl]	<b>0.299</b>	<b>0.14–0.46</b>	<b>&lt; 0.001</b>	<b>0.34</b>

<sup>a</sup>Significant results are printed in bold; <sup>b</sup>total  $R^2$  of the regression equation 0.335; <sup>c</sup>partial correlation between the current variable and the dependent variable after controlling for other independent variables.

surgeons with the highest surgical volume (1.5 vs. 1.8 g/dl,  $p = 0.4$ ). One patient – with current vaginal bleeding and preoperative Hb 7.1 g/dl – required

perioperative transfusion of one unit of packed red blood cells. We noted no post-operative complications requiring readmission or reoperation.

## Discussion

Although the minimally invasive approach is generally associated with less morbidity in comparison to open surgery, LM, “even though feasible, is considered to be a bloody procedure” [27]. In the present study, the duration of surgery was the strongest independent predictor of postoperative drop after LM. The second significant predictor was the diameter of the dominant myoma.

The duration of surgery depends on various biological factors (e.g. diameter, consistency, localization and number of removed myomas, hematological status or general comorbidities of the patient) as well as surgery-related factors (e.g. equipment, experience of the surgical team, anaesthesiological management).

It is evident that each of these factors taken separately – as shown by the univariate analysis of our data – contributes to the perioperative blood loss in LM. In our study, the Hb drop strongly correlated with the surgical time, number of sutures, diameter of the largest myoma, and cumulative myoma weight, but the independent significance of some factors disappeared in the multivariate analysis, leaving the preoperative Hb concentration, total duration of surgery (regardless of what influenced this time) and the diameter of the dominant myoma as the only significant predictors of the postoperative Hb drop. One possible explanation is that while several small fibroids can be removed via one small myometrial incision, it is not possible to remove a large myoma without creating a proportionally large myometrial incision, which in turn enlarges the bleeding area. The finding that the diameter of the dominant myoma is the most useful predictor of perioperative blood loss in LM – as compared to other pre-operative myoma characteristics, e.g. their number or localization – can help the surgeon in planning the operative strategy and the pre-operative counseling of the patients.

Walid and Heaton [9] also identified the myoma diameter as the main predictor of blood loss after LM. Interestingly, in our setting the diameter of the dominant myoma was comparable, but the surgical times and complication rates were lower than those reported from other German institutions [3]. Conversely, Yoon *et al.* removed larger myomas within similar operating times, but otherwise with higher postoperative Hb drops [6]. These variations show

that – although it is obvious that both biological and surgical factors contribute to postoperative Hb drop – some factors can weight differently in different settings.

Focusing on the main predictor of the postoperative Hb change, the *duration of surgery*, we identified its strongest association with the restoration of the uterine wall (as expressed by the number of sutures), followed by the weight and number of removed myomas, as well as the diameter of the dominant myoma. Similarly, in the study of Sizzi *et al.* [5], operative time was most significantly correlated with the dominant myoma diameter, followed by the number of removed myomas, but not with the myoma localization. Hsu *et al.* [28] observed a strong correlation between sonographically estimated myoma weight and operation time. Torng *et al.* [29] suggested that operative experience is a major factor influencing operative time, regardless of the weight or number of removed myomas. Additionally, numerous studies evaluating modifications of the traditional myomectomy techniques (e.g. use of vasoconstrictors, modifications of suturing technique, temporary uterine artery occlusion) have consistently indicated that shorter operating times were associated with decreased perioperative blood loss [16–21]. A recent study demonstrated impressively that the total operating time depends not only on the organ pathology but is a result of steps and delays including – not always predictable or avoidable – “microcomplications” (e.g. missing instruments, instrument changes, anaesthesia-related delays) [30].

Notably, the preoperative Hb concentration correlated neither with patients’ age nor any myoma features, although bleeding disorders (isolated or in combination with pain) were the most common indication for surgery. Thus, the finding that preoperative Hb concentration predicted the postoperative Hb change is surprising and requires further investigation.

The surgical time seems to strongly correlate with Hb drop regardless of surgical approach. In their recent study Książakowska-Łakoma *et al.* analyzed 76 minilaparotomies for uterine fibroids. The age of the patients (37 years), mean surgical time (68 min), the range of myoma diameter (1.5 and 15 cm), as well as the mean Hb drop (1.5 g/dl) were very similar to those of our cohort. The obvious advantage of mini-laparotomy was that the majority of procedures (76%) could be performed in spinal anesthesia. Despite this, patients treated via minilaparotomy recov-

ered longer from the surgery (longer hospitalization times), which finally confirmed the superiority of the laparoscopic approach to myomectomy [31].

The limitation of our study is its retrospective and explorative character. However, since all consecutive cases were included, the surgical technique was standardized and the availability of data was high, the results seem to be robust and valid.

## Conclusions

Our study demonstrated that both the myoma diameter (as the most important *myoma-related* factor) and the duration of surgery (as the most relevant *surgery-related* factor) influenced the postoperative Hb drop. Our results could be useful in pre-operative counseling of the patients and could stimulate gynecologic surgeons to reflect more on the potentially modifiable factors influencing the surgical time, e.g. operative technique, type of sutures, and reduction of “microcomplications”.

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## Conflict of interest

The authors declare no conflict of interest.

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